Abstract

Background: The study was designed to investigate the effect of heart rate and pacing mode on QRS fragmentation (f-QRS). Moreover, the usefulness of f-QRS in distinguishing patients with impaired left ventricular ejection function (EF) and ventricular tachycardia (VT) from patients with normal EF was assessed.

Methods: Three hundred and six recipients, with dual-chamber device, with intrinsic narrow or wide QRS complex and preserved atrioventricular conduction were grouped into normal-EF or impaired-EF VT. We analyzed intrinsic narrow f-QRS and wide f-QRS as well as ventricular-paced f-QRS following different heart rates (baseline, 100 bpm) and pacing modes.

Results: In the baseline state, overall, patients with impaired-EF VT (35 ± 9%), compared to those with normal-EF, had more f-QRS (56% vs 27%, *P* < .001) and ventricular-paced f-QRS (62% vs 16%, *P* < .0001). Ventricular pacing conferred both at baseline and at higher heart rate more ventricular-paced f-QRS in patients with impaired-EF VT than in normal-EF (*P* < .001). Detection of ventricular-paced f-QRS markedly improved overall specificity (84%) and positive predictive value (91%) in identifying patients with impaired-EF VT.

Conclusions: Increased heart rate or/and ventricular pacing uncover QRS fragmentations. Detection of ventricular-paced f-QRS adds value toward noninvasive identification of patients with impaired-EF VT.

KEYWORDS

heart rate, left ventricular function, pacing, QRS fragmentation, ventricular tachycardia

1 | INTRODUCTION

Early noninvasive risk stratification of sudden cardiac death (SCD) to determine the appropriate candidate who would benefit from implantable cardioverter defibrillator (ICD) therapy remains indispensable. Although the left ventricular systolic ejection fraction (EF) is currently the cornerstone risk factor utilized for prophylactic ICD in clinical practice, only a small subgroup of patients with low EF will suffer SCD, whereas EF has not been proved sufficiently sensitive in predicting the substantial risk of SCD in the large pool of patients who do not have low EF. This applies to patients with coronary artery disease as well as to dilated cardiomyopathy.

Fragmentation of the QRS complex (f-QRS) on the 12-lead electrocardiogram (ECG), defined as the presence of additional notches buried within the QRS, reflects derangement of ventricular conduction due to myocardial scar or fibrosis. f-QRS may be associated with prior myocardial infarction, left ventricular dysfunction, and adverse arrhythmic events in various cardiac diseases; however, their utility to risk stratification strategies remains unclear. Addressing as yet unresolved issues in the evaluation of whether and to what extent f-QRS is associated with increased SCD risk is required.

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extent heart rate change or/and mode of pacing affects the detection of f-QRS might help to improve SCD risk prediction with the simple, inexpensive and easily available ECG.

The aim of this study was (i) to investigate the effect of heart rate and mode of pacing on the presence of f-QRS in implanted dual-chamber device recipients with normal or impaired EF, and in relation to the baseline intrinsic narrow or wide QRS complex; and (ii) to examine whether the detection of f-QRS might be useful in the identification of high-risk patients with impaired EF who are prone to ventricular tachycardia (VT).

2 | METHODS

2.1 | Study population

We studied 306 outpatients who were implanted with a dual-chamber pacemaker or an ICD system due to symptomatic bradycardia or documented sustained monomorphic VT for secondary prevention, respectively. Eligible patients were on sinus rhythm and had long-term preserved atrioventricular conduction with narrow QRS (< 120 ms) or wide QRS (≥ 120 ms). Patients were divided according to their history and echocardiographic EF into two main groups: those with normal-EF, and those with impaired-EF VT. Normal-EF patients did not have apparent structural heart disease or history of VT, and had a normal EF of ≥ 55%. Impaired-EF VT patients had ischemic or dilated cardiomyopathy based on the history or objective assessment of coronary artery disease from coronary angiography and in addition had documented sustained VT that required ICD therapy. An intrinsic wide QRS pattern of intraventricular conduction delay was classified as a left bundle branch block (LBBB), right bundle branch block (RBBB), or nonspecific intraventricular conduction delay (IVCD).18 For subgroups analysis, patients were categorized into subgroups according to EF and QRS pattern as follows: normal-EF with narrow QRS; normal-EF with wide QRS; impaired-EF VT with narrow QRS; impaired-EF VT with IVCD; impaired-EF VT with LBBB; impaired-EF VT with RBBB.

Patients should have their medications unchanged for at least 1 week before the study and were excluded if they had symptoms or signs of heart failure on the basis of physical examination and chest X-ray. During the examination, most patients underwent hand-held echocardiography by VScan (GE Healthcare) to gross confirm the findings of transthoracic echocardiography. Standard two-dimensional echocardiographic measurements were routinely performed to obtain cardiac dimensions, EF, and wall contraction abnormalities. In all patients, active fixation leads were placed on the right atrial appendage and the right ventricle mid-septum. The true septal position was verified in both right and left anterior oblique view by determining lead orientation toward the spine and in the middle of cardiac silhouette, respectively.

2.2 | ECG definitions

Standard 12-lead ECGs were obtained after device implantation during routine follow-up visits in the context of assessing proper device function. The widest QRS complex duration was taken defined as the interval between the initial QRS depolarization and the J point in any of the 12 ECG leads. The earliest QRS onset and the latest QRS offset were considered from the six simultaneously limb or precordial leads. The J point was taken at the beginning of the isoelectric ST segment, or if this landmark was not distinguishable, the tangent to the descending part of the R wave or the ascending part of the S wave and the isoelectric line drawn through the ST segment. The right ventricular-paced QRS complex was defined as a widest QRS complex in any lead measured from pacing spike to the end of QRS. The right ventricular-paced QRS complex was defined as a widest QRS complex in any lead measured from pacing spike to the end of QRS.

The f-QRS was identified visually in the presence of intrinsic narrow or wide QRS complex. In narrow QRS complexes, the intrinsic fragmented QRS complex (narrow f-QRS) was defined as various RSR patterns with ≥ 2 R or S wave notches, or the presence of fragmentation in ≥ 2 contiguous leads corresponding to a major coronary artery.3 In wide QRS complexes, the intrinsic fragmented QRS complex (wide f-QRS), as well as the fragmented ventricular-paced QRS (ventricular-paced f-QRS), was defined as the presence of > 2 notches in the R wave or the nadir of the S wave in ≥ 2 contiguous leads.7

The ECGs were recorded using a Nihon Kohden electrocardiograph (Nihon Kohden Inc, Cardiofax S, Tokyo, Japan; 25 mm/s; 10 mm/mV; filter range 0.15-100 Hz) and were analyzed by two independent cardiologists blinded to the clinical, echocardiography, and cardiac catheterization results. Measurements of QRS duration were performed manually using an electronic digitizer. Interobserver concordance for measurements was generally > 95%. In case of disagreement, the final decision was achieved with mutual consent.

2.3 | Study protocol

The patients were studied in supine position under standardized conditions and continuous ECG monitoring. Four activation stages of the QRS complex were analyzed. Following the baseline ECG recording with the intrinsic narrow or wide QRS during spontaneous sinus rhythm or during atrial-based pacing at the lowest programmed rate of 50 bpm, the pacing modes of the devices were used for heart rate increase. A first, the intrinsic QRS complex was recorded with atrial pacing at 100 beats/min. For the assessment of the ventricular-paced QRS, devices were programmed in DDD mode with the atrioventricular delay set short at 100 ms to ensure as much as possible complete ventricular capture, firstly at the low heart rate and then at 100 bpm. Cases with very short PR interval and predominant fused QRS complexes during ventricular pacing were disregarded.

Figure 1 demonstrates the four steps of our methodology for assessing within-patient different QRS complexes. The QRS complexes were evaluated during constant 1:1 atrioventricular conduction and were discarded if there was atrioventricular conduction block or ventricular fusion, or appearance of BBB during atrial pacing.
2.4 | Statistical analysis

Results are expressed as mean values ± SD or as a percentages for categorical variables and analyzed with the unpaired t test and chi-square test for variables of patient characteristics. The Wilcoxon signed-rank test for paired data was used to assess the effect of heart rate (baseline, 100 bpm) on the intrinsic QRS and the paced QRS duration, and the McNemar’s test was used to assess the significance of changes in patients with or without f-QRS. A P-value of less than .05 was considered statistically significant. Sensitivity was the percentage of impaired-EF VT patients with the detection of QRS fragmentation. Specificity was the percentage of normal-EF patients with no detectable QRS fragmentation. Positive predictive value (PPV) and negative predictive value (NPV) were calculated as the proportion of patients with true positive or true negative detection of QRS fragmentation. For all statistical evaluations, the IBM SPSS Statistical package was used.

3 | RESULTS

3.1 | Clinical and electrocardiographic characteristics

A total of 306 patients aged 69 ± 10 years (range 36-95 years) were enrolled. Baseline characteristics are summarized in the Tables 1 and 2. Patients with impaired-EF VT compared to those with normal EF were more likely to be men (88% vs 51%, P < .001), had wider QRS complex (139.5 ± 34 ms vs 106 ± 25 ms, P < .0001), longer QTc interval (461 ± 43 ms vs 421 ± 29 ms, P = .0001), and greater LV end-diastolic dimension (62 ± 7 mm vs 48 ± 3 mm, P < .0001). All normal-EF patients with wide QRS had a RBBB pattern. All impaired-EF VT patients were on long-term amiodarone treatment, whereas in the normal-EF group, six patients (7%) were receiving propafenone.

Table 2 shows the behavior of QRS duration under the influence of heart rate as well as following change in pacing mode. The intrinsic QRS duration of patients with normal EF and narrow or wide QRS, as whole groups, was shorter compared to patients with impaired-EF VT (P < .01) and did not change significantly following heart rate increase within either the subgroup of patients with normal-EF or impaired-EF VT (P = NS). The paced QRS duration of patients with impaired-EF VT and either narrow or wide QRS compared to their normal-EF counterparts as whole groups was longer at baseline (P = .11 and P < .003, respectively), and it was more marked increased following heart rate increase (P < .0001).

3.2 | Influence of heart rate on f-QRS

At baseline, overall, an f-QRS was present in 27% (24 of 89) of patients with normal-EF and was more frequently seen in 56% of patients (122 of 217) with impaired-EF VT (P < .001) (Table 2). Impaired-EF VT patients compared to their normal-EF counterparts had both more narrow f-QRS (61.5% vs 30%, P < .0005) as well as wide f-QRS (53% vs 18%, P < .0005). In the patient group with impaired-EF VT, wide f-QRS was less frequently present in IVCD patients than in those with RBBB and LBBB (both P < .005) even though the QRS widths were almost similar among these groups (P = NS). The increased heart rate with atrial pacing showed a similar incidence of narrow f-QRS or wide f-QRS to that during baseline heart rate within any subgroup of patients with normal-EF or impaired-EF VT (P = NS). Overall, there were no significant differences in the occurrence of f-QRS in patients with ischemic as compared with nonischemic cardiomyopathy (P = NS).
Influence of ventricular pacing on ventricular-paced f-QRS

At baseline, an ventricular-paced f-QRS was identified more frequently in 62% (135 of 217) of patients with impaired-EF VT compared to 16% (14 of 89) of patients with normal-EF (P < .0001), irrespective of the presence of intrinsic narrow or wide QRS (61.5% vs 16% and 63% vs 14%, respectively, both P < .0001) (Table 2, Figure 1). Compared to the corresponding intrinsic f-QRS, there was similar ventricular-paced f-QRS obtained in patient with either normal-EF or impaired-EF VT, except for a statistical significant increase in ventricular-paced f-QRS in the patients with impaired-EF VT-wide QRS/IVCD (P < .001). At increased heart rate, ventricular pacing in patients with normal-EF did not significantly change the detection of

### TABLE 1 Patient characteristics

|                  | Normal EF (n = 89) | Impaired-EF VT (n = 217) |
|------------------|--------------------|--------------------------|
|                  | Narrow QRS (n = 67) | Wide QRS (n = 22) | P-value | Narrow QRS (n = 78) | Wide QRS/IVCD (n = 69) | Wide QRS/RBBB (n = 28) | Wide QRS/LBBB (n = 42) | P-value |
| **Age, years**   | 69 ± 11            | 72 ± 9                  | .219     | 68 ± 8               | 70 ± 9                  | 70 ± 11                | 67 ± 12               | .793    |
| **Male, N (%)**  | 28 (42)            | 17 (77)                 | .004     | 73 (94)              | 59 (86)                 | 27 (96)                | 33 (79)               | .077    |
| **CM, N (%)**    |                    |                        |          |                      |                        |                        |                      |         |
| Ischemic         | -                  | -                      | NA       | 62 (79)              | 51 (74)                 | 25 (89)                | 14 (33)               | .023    |
| Nonischemic      | -                  | -                      | NA       | 16 (21)              | 18 (26)                 | 3 (11)                 | 28 (67)               | .023    |
| **EF, %**        | 61 ± 3             | 61 ± 2                 | .554     | 39 ± 8               | 31 ± 7                  | 37 ± 8                 | 33 ± 9                | <.001   |
| **LVEDD, mm**    | 48 ± 3             | 49 ± 3                 | .03      | 59 ± 6               | 64 ± 6                  | 61 ± 7                 | 65 ± 8                | <.001   |
| **ECG**          |                    |                        |          |                      |                        |                        |                      |         |
| HR, beats/min    | 63 ± 10            | 61 ± 9                 | .509     | 64 ± 9               | 65 ± 8                  | 62 ± 8                 | 68 ± 9                | .567    |
| PR, ms           | 193 ± 32           | 202 ± 37               | .367     | 204 ± 41             | 215 ± 46                | 208 ± 49               | 220 ± 38              | .070    |
| QTc, ms          | 413 ± 26           | 441 ± 25               | <.001    | 429 ± 27             | 465 ± 38                | 468 ± 28               | 498 ± 42              | <.001   |

CM, Cardiomyopathy; EF, left ventricular ejection fraction; IVCD, intraventricular conduction delay; LBBB, left bundle branch block; RBBB, right bundle branch block; N, number (Percentage, %); values are mean ± SD.

### TABLE 2 QRS duration and QRS fragmentation

| Patient groups                  | QRS—BL | QRS—100 bpm | P-value | pQRS—BL | pQRS—100 bpm | P-value |
|---------------------------------|--------|-------------|---------|---------|--------------|---------|
| Normal EF—narrow QRS            |        |             |         |         |              |         |
| QRS, ms                         | 93 ± 12| 92 ± 11     | .077    | 148 ± 16| 156 ± 14     | <.001   |
| Fragmented QRS (%)              | 29.9   | 36.7*       |         | .375    | 16.4         | 29.9    |
| Normal EF—wide QRS              |        |             |         |         |              |         |
| QRS, ms                         | 145 ± 9| 143 ± 15    | .329    | 151 ± 15| 162 ± 16     | .013    |
| Fragmented QRS (%)              | 18.2   | 31.8        |         | .250    | 13.6         | 40.9    |
| Impaired-EF VT—narrow QRS       |        |             |         |         |              |         |
| QRS, ms                         | 103 ± 11| 103 ± 14     | .639    | 153 ± 20| 172 ± 24     | <.001   |
| Fragmented QRS (%)              | 61.5   | 62.9*       |         | 1.000   | 61.5         | 76.9    |
| Impaired-EF VT—wide QRS/IVCD    |        |             |         |         |              |         |
| QRS, ms                         | 152 ± 25| 150 ± 29    | .933    | 186 ± 53| 196 ± 29     | <.001   |
| Fragmented QRS (%)              | 36.2   | 43.9*       |         | .125    | 69.6         | 92.8    |
| Impaired-EF VT—wide QRS/RBBB    |        |             |         |         |              |         |
| QRS, ms                         | 162 ± 17| 158 ± 18     | .247    | 167 ± 30| 183 ± 27     | <.001   |
| Fragmented QRS (%)              | 75.0   | 80.0*       |         | 1.000   | 57.1         | 78.6    |
| Impaired-EF VT—wide QRS/LBBB    |        |             |         |         |              |         |
| QRS, ms                         | 171 ± 26| 169 ± 25     | .284    | 194 ± 56| 190 ± 27     | .138    |
| Fragmented QRS (%)              | 66.7   | 66.7*       |         | .500    | 54.8         | 59.5    |

BL, baseline heart rate; pQRS, paced QRS; QRS-BL and QRS-100 bpm = intrinsic QRS at baseline and during atrial pacing 100 bpm; *n=60, *n=62, *n=57, *n=20, *n=30; values are mean ± SD.

3.3 Influence of ventricular pacing on ventricular-paced f-QRS

At baseline, an ventricular-paced f-QRS was identified more frequently in 62% (135 of 217) of patients with impaired-EF VT compared to 16% (14 of 89) of patients with normal-EF (P < .0001), irrespective of the presence of intrinsic narrow or wide QRS (61.5% vs 16% and 63% vs 14%, respectively, both P < .0001) (Table 2, Figure 1). Compared to the corresponding intrinsic f-QRS, there was similar ventricular-paced f-QRS obtained in patient with either normal-EF or impaired-EF VT, except for a statistical significant increase in ventricular-paced f-QRS in the patients with impaired-EF VT-wide QRS/IVCD (P < .001). At increased heart rate, ventricular pacing in patients with normal-EF did not significantly change the detection of
ventricular-paced f-QRS compared to the corresponding intrinsic f-QRS at baseline ($P = NS$). However, impaired-EF VT patients with intrinsic either narrow QRS ($P < .05$) or IVCD ($P < .001$) had significantly more ventricular-paced f-QRS compared to their corresponding f-QRS at baseline (overall $P < .001$; Table 2, Figure 2).

### 3.4 | QRS fragmentation to identify impaired-EF VT

Table 3 presents results on the diagnostic performance of QRS fragmentation to identify patients with impaired-EF VT. At baseline, the presence of f-QRS yielded overall low sensitivity of 56% and specificity of 73%, with the separate assessment of wide f-QRS to perform better with respect to the highest specificity of 82% and PPV of 95% (corresponding values for narrow f-QRS 70% and 71%, respectively). Detection of f-QRS at the higher rate offered similar sensitivity but lower specificity with those observed at baseline, with again the wide f-QRS to show higher specificity and PPV compared with the narrow f-QRS (68% vs 63% and 90% vs 64%, respectively). The ventricular-paced f-QRS performed overall best at baseline with respect to specificity (84%) and PPV (91%), whereby patients with baseline wide QRS showed maximal values compared to those with baseline narrow QRS (86% vs 84% and 97% vs 81%, respectively). At higher rate, the ventricular-paced f-QRS maximized overall sensitivity at 79% and NPV at 57%, with a peak NPV for the narrow QRS patients of 72% (corresponding value for wide QRS 32%). Overall, compared to the corresponding f-QRS, ventricular pacing contributed at baseline to the fewest false-positive (16% vs 27%) and at higher rate to fewest false-negative (21% vs 44%) results.

### 4 | DISCUSSION

#### 4.1 | Main findings

This study showed that heart rate increase or/and pacing facilitates the detection of QRS fragmentation, particularly in patients with impaired-EF VT. Fragmented QRS unmasked by ventricular pacing performed better compared to the corresponding intrinsic f-QRS with respect to the discrimination of patients with impaired-EF VT from patients with normal EF, regardless of the baseline QRS duration.

#### 4.2 | Effect of heart rate and pacing on QRS fragmentation

Detection of narrow f-QRS has been reported in 19.7% of apparently healthy subjects, whereas a narrow or wide f-QRS was more commonly found in 22-75% of patients with ischemic or nonischemic etiology.\textsuperscript{5,7,15,16} Das et al\textsuperscript{7} observed ventricular-paced f-QRS in 44.8% of patients and suggested sensitivity and specificity for myocardial scar of 89.8% and 95.7%, respectively. In our study, intrinsic f-QRS was more frequently observed in patients with impaired EF as compared to those with normal EF which agrees with data supporting its higher prevalence in patients with left ventricular dysfunction.\textsuperscript{8,9} Our results extend previous research on the evaluation of paced QRS by

![FIGURE 2 Example of fragmented QRS complexes revealed by ventricular pacing (low right panel C, arrows) in a patient with intrinsic wide QRS complex of 140 ms. Intrinsic QRS complexes do not show fragmentation at baseline (upper panel A) and during increased heart rate with atrial pacing (low left panel B)](image-url)

**TABLE 3** Diagnostic performance of QRS fragmentation to discriminate patients with impaired-EF VT from patients with normal EF

| Patient groups | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|----------------|----------------|----------------|---------|---------|
| f-QRS—BL       | 56.2           | 73             | 83.6    | 40.6    |
| f-QRS—100 bpm  | 59.2           | 64.6           | 77.5    | 43.4    |
| f-pQRS—BL      | 62.2           | 84.3           | 90.6    | 47.8    |
| f-pQRS—100 bpm | 78.8           | 67.4           | 85.5    | 56.6    |

BL, baseline heart rate; f-pQRS, fragmented paced QRS; f-QRS, fragmented intrinsic QRS; NPV, negative predictive value; PPV, positive predictive value.
the identification of an even higher prevalence of ventricular-paced f-QRS in patients with impaired EF compared to those with normal EF, regardless of the morphology of their intrinsic wide QRS complex.

There are no data available regarding the influence of heart rate or pacing on the QRS fragmentation. We considered the hypothesis that the increase in rate might enhance conduction abnormality thereby invoking changes in QRS fragmentation analogous to those described on the QRS duration. On the other hand, in particular with ventricular pacing, the changed conduction velocity and orientation of ventricular activation front might render QRS fragmentation to become “unmasked,” more prominent and visible. We addressed this issue with a method of measuring and directly comparing each patient’s intrinsic and paced QRS fragmentation by the ability of the devices for incremental atrial as well as synchronized ventricular pacing, thereby limiting extraneous confounding influences.

Our study showed that heart rate increase exerts a substantial effect on the detection of both the intrinsic and the paced QRS fragmentation. The more frequent detection of QRS fragmentation in particular when ventricular pacing was instituted in the same patients compared to their intrinsic f-QRS paralleled prolongation of QRS duration, which indicates increased intraventricular delay in response to the increased heart rate and pacing mode. This was most impressive in patients with wide QRS/IVCD, where ventricular pacing even at the baseline rate exerted a significant prolonging effect on QRS duration which followed by more apparent QRS fragmentation compared to the intrinsic QRS (152 ± 25 ms vs 186 ± 53 ms and 36.2% vs 69.6%, respectively, both P < .0001). These consistent findings in patients with impaired-EF VT, irrespective of their baseline narrow or wide QRS complex, would suggest that our concept of mode of pacing may be used as a diagnostic test to refine and uncover f-QRS identification. Furthermore, the direct evidence of increased conduction delay during both low and higher ventricular pacing rate, as expressed by the prolongation of QRS duration and the simultaneous higher incidence of ventricular-paced f-QRS, adds to the clinical view of the detrimental consequences of pacing on impending heart failure and ventricular tachyarrhythmia occurrence in patients with left ventricular dysfunction.

Limited and discordant data link QRS fragmentation to ventricular tachyarrhythmias. Das et al showed that wide f-QRS was a predictor of mortality, and related ventricular-paced f-QRS to significantly reduced time to death compared with nonfragmented wide QRS. Sha et al found both narrow f-QRS and wide f-QRS predictors of arrhythmic events in patients with idiopathic cardiomyopathy and depressed EF. In patients with ICDs, narrow f-QRS in a study of Das et al and wide f-QRS in MADIT II patients were associated with appropriate ICD discharge, but this was not proven by others.

### 4.3 QRS fragmentation to identify patients with impaired-EF VT

Most SCD cases have associated coronary artery disease or nonischemic cardiomyopathy, whereby ventricular tachycardia and fibrillation have been reported as the most frequent culprits. Ventricular tachycardia has been early identified as adverse outcome independent predictor of arrhythmic death and total mortality. Furthermore, recognizing the unpredictable nature of VT occurrence and that not rarely its appearance is first disease manifestation, there is still quest for an risk stratification tool which identify most of the patients who will experience VT and exclude those who will not. QRS fragmentation is an attractive parameter for further investigation as it reflects the anatomical myocardial scar substrate that is critical to VT.

The present study attempted to retrospectively the ability of QRS fragmentation to separate high-risk patients with impaired-EF VT from low-risk patients with normal EF. Although the overall detection of f-QRS at basal heart rate appeared to be a weak tool, the presence of wide f-QRS could be useful for the identification of patients with impaired-EF VT given its acceptable specificity of 82% and high PPV of 95%. Our concept of assessing intrinsic f-QRS under the influence of higher heart rate did not offer better results, but the use of ventricular pacing contributed largely in the discrimination of patients with impaired-EF VT. Thus, detection of ventricular-paced f-QRS increased overall specificity at baseline from 73% to 84%, and sensitivity at higher heart rate from 56% to 79%. As a consequence, we suggest that ventricular-paced f-QRS performs better than intrinsic f-QRS in distinguishing patients with impaired-EF VT from patients with normal EF by providing fewer false-positive and false-negative results. Nevertheless, overall, the absence of QRS fragmentation does not appear to predict low-risk patients with normal EF and lack of VT, even with the best performance of ventricular-paced f-QRS at higher rate (moderately good sensitivity of 79% and low NPV of 57%). On the other hand, the overall acceptable specificity and high PPV of both ventricular-paced f-QRS and wide f-QRS (82%-86% and 91%-97%, respectively) suggest individualized benefit with specific therapies and possible guiding selection for primary prevention ICD therapy among patients with impaired EF.

### 4.4 Limitations

Our method of ventricular pacing to expose QRS fragmentation can be used only in pacemaker or ICD recipients. Nevertheless, our intrinsic f-QRS data at baseline rate or following atrial-based heart rate increase may be representative of the general population. Second, our study of using QRS fragmentation to stratify patients was retrospectively designed and thus our results will require prospective evaluation. Another limitation relates to the assessment of QRS fragmentation in response to heart rate increase. The rate-dependent manifestation of QRS fragmentation could have been more clearly studied if more pacing cycle lengths were used. Nevertheless, the arbitrary high heart rate choice of 100 bpm represents usual heart rate response to exercise in the vast majority of patients. Last, the more frequent appearance of f-QRS in impaired-EF patients compared to the normal-EF patients may be to some degree attributable to amiodarone which prolongs intraventricular conduction. However, this was an intrapatient comparison study completed during the same session which allowed us to examine the net effect of the increased heart rate and pacing on QRS fragmentation.
5 | CONCLUSIONS

Fragmented QRS complexes are more commonly observed in patients with impaired-EF VT with ischemic or nonischemic cardiomyopathy than in patients with normal EF, regardless of the baseline narrow or wide QRS. Increased heart rate and ventricular pacing increase QRS fragmentation and add value to arrhythmic risk stratification. The higher prevalence of ventricular-paced f-QRS following improves the discriminatory ability to identify high-risk patients with impaired-EF VT, particularly in patients with baseline wide QRS. Nevertheless, given the overall negative predictive value, the absence of QRS fragmentation does not identify satisfactory patients at low-risk with normal-EF.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

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