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*Published in:*  
Heart Rhythm

*DOI:*  
[10.1016/j.hrthm.2024.11.040](https://doi.org/10.1016/j.hrthm.2024.11.040)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

#### *Document Version*

Version created as part of publication process; publisher's layout; not normally made publicly available

*Publication date:*  
2024

[Link to publication in University of Groningen/UMCG research database](#)

#### *Citation for published version (APA):*

Verheul, L. M., Guglielmo, M., Hirsch, A., Figliozzi, S., van der Harst, P., Bourfiss, M., Prakken, N. H. J., Velthuis, B. K., Yap, S. C., & Hassink, R. J. (2024). Cardiac magnetic resonance feature tracking reveals abnormalities in patients with idiopathic ventricular fibrillation. *Heart Rhythm*. Advance online publication. <https://doi.org/10.1016/j.hrthm.2024.11.040>

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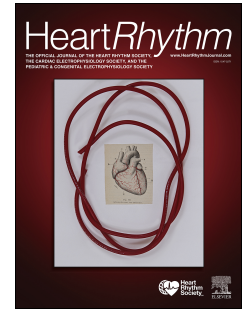
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# Journal Pre-proof

Cardiac magnetic resonance feature tracking reveals abnormalities in patients with idiopathic ventricular fibrillation

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PII: S1547-5271(24)03624-5

DOI: <https://doi.org/10.1016/j.hrthm.2024.11.040>

Reference: HRTM 10923

To appear in: *Heart Rhythm*

Received Date: 4 November 2024

Revised Date: 18 November 2024

Accepted Date: 22 November 2024

Please cite this article as: Verheul LM, Guglielmo M, Hirsch A, Figliozzi S, van der Harst P, Bourfiss M, Prakken NHJ, Velthuis BK, Yap SC, Hassink RJ, Cardiac magnetic resonance feature tracking reveals abnormalities in patients with idiopathic ventricular fibrillation, *Heart Rhythm* (2024), doi: <https://doi.org/10.1016/j.hrthm.2024.11.040>.

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1 **Cardiac magnetic resonance feature tracking reveals abnormalities in**  
2 **patients with idiopathic ventricular fibrillation**

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19 \* Member of the European Reference Network of rare, low prevalence, and complex diseases  
20 of the heart; ERN GUARD-Heart (<http://guardheart.ern-net.eu>)

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22 **Running title:** Feature tracking analysis and idiopathic VF

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24 **Conflict of interest:** A. Hirsch received a research grant and consultancy fees from GE  
25 Healthcare and speaker fees from GE Healthcare and Bayer. He is also a member of the  
26 medical advisory board of Medis Medical Imaging Systems and was MRI corelab supervisor  
27 of Cardialysis BV until 2022. S.C. Yap is a consultant for Boston Scientific and has received  
28 lecture fees and research grants from Medtronic, Biotronik and Boston Scientific. The other  
29 authors have no conflicts of interest to disclose.

30

31 **Funding:** This work is funded by the Dutch Heart Foundation (CVON2017-13VIGILANCE).

32

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38 **Word count:** 796

39 **Keywords:** idiopathic ventricular fibrillation, cardiac magnetic resonance, feature tracking

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49 *Research letter*

50 The cause of sudden cardiac arrest remains undefined in approximately 5% of patients, the  
51 latter receiving the diagnosis of 'idiopathic ventricular fibrillation' (IVF). Unraveling the  
52 mechanisms underlying the arrest is a clinical need for these often young patients who may be  
53 negatively impacted by uncertainties about their prognosis, including the risk for recurrences.<sup>1</sup>  
54 By definition, IVF patients lack specific structural abnormalities. However, advanced imaging  
55 techniques, such as deformation imaging, can reveal early preclinical abnormalities preceding  
56 the alterations of conventional parameters like left ventricular ejection fraction (LVEF).<sup>2</sup>  
57 Therefore, abnormal deformation imaging may serve as an indicator of a subclinical  
58 cardiomyopathy in IVF patients. Groeneveld et al demonstrated that strain values determined  
59 with echocardiography differed between IVF patients and controls.<sup>3</sup> This study further  
60 investigated the use of deformation imaging through cardiac magnetic resonance (CMR)  
61 feature tracking (FT) analysis. FT can be performed by using standard balanced steady-state  
62 free-precession sequences, which are part of routine CMR protocols included in the diagnostic  
63 work-up after an arrest.

64 We retrospectively evaluated IVF patients from two Dutch academic centers (UMC Utrecht  
65 and Erasmus MC) and one Italian center (IRCCS Humanitas Research Hospital) who had a  
66 CMR of sufficient quality for FT (e.g., no left bundle branch block, regular cardiac rhythm  
67 without premature ventricular complexes) and LVEF $\geq$ 50%. Patients were compared with an  
68 age- and sex-matched control group. CMR images were acquired on various 1.5T or 3T  
69 scanners according to local protocols at each CMR performing center. Standard short-axis and  
70 long-axis (2-, 3-, and 4-chamber views) cine images were acquired using breath-hold  
71 balanced steady-state free-precession sequences. FT analysis was performed with Circle  
72 Cardiovascular Imaging (CVI<sup>42</sup>® 6.1.1, Calgary, Canada). Endocardial and epicardial borders  
73 were contoured for the LV in short-axis and at least two long-axis images, depending on

74 availability. Global peak circumferential strain (GCS), global peak longitudinal strain (GLS)  
75 and global peak radial strain (GRS) were derived. Chi-square was performed to compare  
76 categorical variables. Student's *t*-test or Mann-Whitney U test was used to compare  
77 continuous variables, as appropriate. Univariate and multivariate linear regression analyses  
78 were performed to further explore the influence of LVEF and IVF status on GLS. The study  
79 was conducted in accordance with the 2013 Declaration of Helsinki.

80 We included 52 IVF patients (33 (64%) males, median age 35 [25-47] years) who were  
81 compared with 52 matched controls (median age 38 [25-47],  $p=0.637$ ). IVF patients  
82 underwent CMR at a median of 9 [5-13] days after the arrest. LVEF, LV end-diastolic and  
83 end-systolic volumes were comparable between IVF patients and controls (57 [53-61]% vs.  
84 58 [55-63]%,  $p=0.123$ , Figure 1A). GLS was slightly reduced for IVF patients compared with  
85 controls ( $-17.1\% \pm 2.1$  vs.  $-18.9\% \pm 1.8$ ,  $p < 0.001$ , Figure 1B). No statistical differences were  
86 found for GCS ( $-18.2\% \pm 2.0$  vs.  $-18.7\% \pm 1.7$ ,  $p=0.118$ , Figure 1C) and GRS ( $30.4\% \pm 5.4$  vs.  
87  $31.4\% \pm 4.8$ ,  $p=0.330$ , Figure 1D). After multivariate linear regression analysis, both LVEF  
88 and IVF status influenced GLS values. In the follow-up echocardiography conducted after a  
89 median duration of 5 [4-10] years, the mean LVEF remained at  $56 \pm 4\%$  among the 28 (54%)  
90 patients assessed. When stratifying by initial GLS values, no significant LVEF progression  
91 differences were noted between different baseline GLS values.

92 To our knowledge, this is the first study to explore the value of FT deformation imaging in  
93 IVF patients. Our results indicate that GLS was the only deformation imaging variable  
94 significantly impaired in this study group. GLS mainly reflects the function of the endocardial  
95 layer of the heart<sup>4</sup>, and compared to LVEF, GLS appears superior for the detection of early  
96 cardiomyopathies, but also as a predictor for cardiovascular events.<sup>2</sup> Thus, our findings may  
97 suggest a presence of an underlying cardiomyopathy in a subgroup of IVF patients. A reduced  
98 GLS value at baseline might warrant a more thorough follow-up to detect early structural

99 abnormalities in IVF patients. As a clear recommendation for IVF patients regarding imaging  
100 follow-up is currently lacking, this finding might provide more guidance. However, it cannot  
101 entirely be excluded that differences between IVF patients and controls might be related to  
102 transitory ischemia during the arrest itself which resulted in a temporarily reduced GLS. On  
103 the contrary, Purkinje fibers, one of the known origin sites of short-coupled premature  
104 ventricular complexes inducing VF in IVF are located in the endocardium.<sup>5</sup> It can be  
105 hypothesized that minor (undetected) structural abnormalities inducing these premature  
106 ventricular complexes influence GLS values.

107 The definitive clinical value remains to be determined, as these are preliminary exploratory  
108 results. Especially in combination with a comparable GCS and GRS between IVF patients and  
109 controls and a normal LVEF at follow-up, the clinical value remains unclear. However,  
110 because FT analysis does not require additional CMR sequences, it may be clinically  
111 beneficial to investigate strain with FT at baseline. Future studies should investigate larger  
112 cohorts, including IVF subtypes with structural abnormalities like inferolateral mitral annular  
113 disjunction, and incorporating right ventricle and regional strain assessment.

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155 **Figure legend**

156 **Figure 1.** Table of conventional CMR measurements (A). Boxplot of GLS (B), GCS (C) and  
157 GRS (D) values stratified by IVF patients and controls. GLS significantly differed between  
158 IVF patients and controls, other global strain variables were comparable. Abbreviations: GCS;  
159 global circumferential strain, GLS; global longitudinal strain, GRS; global radial strain;  
160 LVEF; left ventricular ejection fraction, LVEDV: left ventricular end-diastolic volume,  
161 LVESV; left ventricular end-systolic volume IVF; idiopathic ventricular fibrillation.

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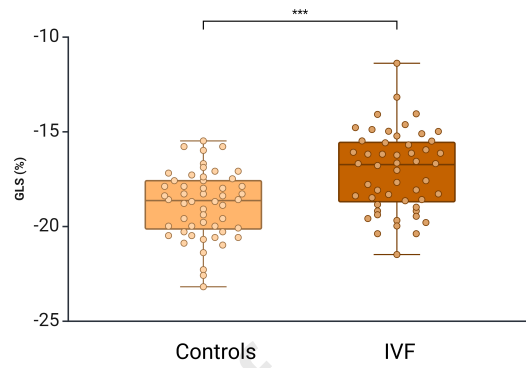
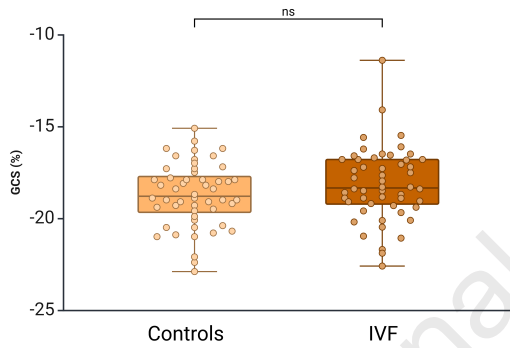
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**A Conventional measurements**

	IVF (n=52)	Controls (n=52)	P-value
LVEF (%)	57 [53 - 61]	58 [55 - 63]	0.123
LVEDV (ml)	175±40	185±34	0.196
LVESV (ml)	79±18	76±21	0.561

**B Global longitudinal strain (%)****C Global circumferential strain (%)****D Global radial strain (%)**