Clinical valuation of ST changes in a group of patients with ventricular arrhythmias: The inSighT Study

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Abstract

Background: The inSighT study was designed to determine the prevalence of ischemic changes as recorded by implantable cardioverter-defibrillator (ICD) ST deviations in intracardiac electrocardiograms (EGM) over the 24 h preceding malignant ventricular arrhythmias (VT/VF).

Methods: The study enrolled patients with known coronary artery disease (CAD) or high risk of future development of CAD implanted with an ICD equipped with an ST monitoring feature (Ellipse™/Fortify Assura™, St. Jude Medical). Device session records were collected at each in-clinic follow-up. EGM ST levels of the beats over the 15 minutes prior to VT/VF events were compared using a t test with those from a baseline period of 23–24 h prior to the VT/VF event. All events with p < .05 were visually inspected to confirm they were evaluable; additional criteria for exclusion from further analysis included inappropriate therapy, aberrant conduction, and occurrence of VT/VF within 24h prior to the current event.

Results: The study enrolled 481 ICD patients (64 ± 11 years, 83% male) in 14 countries and followed them for 15±5 months. A total of 165 confirmed VT/VF episodes were observed, of which 71 events (in 56 patients, 34% of all patients with VT/VF) were preceded by significant (p < .05) ST-segment changes unrelated to known non-ischemic causes. None of the analyzed demographic and clinical factors proved to be associated with greater odds of presenting with ST-segment changes prior to VT/VF episode.

Conclusion: In this exploratory study, characteristic ST-segment changes, likely representative of ischemic events, were observed in 34% of all patients with VT/VF episodes.

KEYWORDS
implantable cardioverter-defibrillator, intracardiac electrocardiograms, ST-segment changes, ventricular fibrillation, ventricular tachycardia
INTRODUCTION

The role of implantable cardioverter-defibrillators (ICDs) in the prevention of sudden cardiac death (SCD) is well documented in a number of randomized trials and supported by guideline documents of various cardiac societies (Al-Khatib et al., 2017; Ponikowski et al., 2016; Priori et al., 2015). ICDs detect and terminate malignant, potentially fatal ventricular arrhythmias, but they do not prevent recurrence of further life-threatening arrhythmias. One of the most common reasons for arrhythmic events is the progression of ischemic heart disease (IHD) (Bunch et al., 2007). It has been documented that long-term mortality risk among ICD patients with IHD is correlated with the time elapsed from last coronary revascularization (Barsheshet et al., 2011). Similarly, it is proven that patients implanted with an ICD longer after the myocardial infarction have a higher chance of developing ventricular tachyarrhythmias (Boriani et al., 2012).

Ischemic events are established to cause ST-segment deviations in intracardiac electrocardiograms (EGMs) both in animals and in humans (Fischell et al., 2005; Mendenhall et al., 2012; Williams et al., 2008). Some ICDs manufactured by St. Jude Medical (now Abbott) enable constant beat-to-beat monitoring of the intracardiac ST segment using implanted ICD leads. Similar systems have demonstrated that this approach might be a reliable method of identifying ischemic events (Fischell et al., 2010). However, the predictive value of the ST monitoring feature in identifying pending arrhythmic events remains unknown.

The inSight study was designed to determine the prevalence of ischemic changes as recorded by ICD ST deviations over the 24 hours preceding malignant ventricular arrhythmias treated by ICD, and to define their temporal relationship to these events. We reasoned that prediction of worsening ischemia could play an important part in allowing physicians to identify ICD patients with greater mortality risk and enabling them to intervene with appropriate therapy.

METHODS

The inSight study was a prospective, non-randomized, exploratory, international multicenter investigation in patients with recently implanted single- or dual-chamber ICD equipped with an ST monitoring feature and ShockGuard™ algorithm (Ellipse™/Fortify Assura™, St. Jude Medical). Implantation details are summarized in Table 1. Other inclusion criteria included the following: age ≥18 years, the projected burden of ventricular pacing of not more than 20% of the time, diagnosed coronary artery disease (CAD), or high risk of future development of CAD in investigators’ opinion. Patients were excluded in case of electrocardiographic abnormalities that could interfere with ST-segment analysis, including long-standing persistent or permanent atrial fibrillation/atrial flutter (AF/AFI), complete heart block, uncontrolled ventricular bigeminy or trigeminy (premature ventricular contractions on regular basis), severe left ventricular hypertrophy resulting in inter-ventricular conduction delay (IVCD), and intermittent bundle branch block (BBB). Other exclusion criteria were pregnancy (ongoing or planned) or declared non-compliance with control visit schedule.

Patients were prospectively enrolled between December 2012 and August 2014 by 49 centers in 14 countries (Australia, Canada, Finland, France, Germany, Hong Kong, India, Italy, Japan, Korea, the Netherlands, Poland, Saudi Arabia and the United Kingdom). Each participating site’s Institutional Review Board (IRB) or ethics committee accepted the study protocol. The study was registered in ClinicalTrials.gov (NCT01685047). All participating subjects signed written informed consent.

The ST monitoring feature allows reviewing diagnostic data of the ST segment, including ST deviation trend, ST histogram data, and ST episode log. A detailed description of the ST monitoring feature capabilities can be found in Table 2. ShockGuard™ algorithm prevents inappropriate therapy delivery in case of noise generated by ICD lead damage. All devices were programmed according to the algorithm as shown in Figure 1.

Follow-up for all subjects was continued until the last enrolled subject completed their 12-month follow-up visit. Patients were assigned to two groups, depending on physicians’ preference to use a remote control system (Merlin.net; SJM) or not. The only

| TABLE 1  | Implantation details |
|-----------|----------------------|
| **Implantation details, n (%)** | |
| **Device model, n (%)** | |
| 1259 (Fortify Assura VR) | 54 (11.25) |
| 1359 (Fortify Assura VR) | 60 (12.5) |
| 1277 (Ellipse VR) | 102 (21.25) |
| 1377 (Ellipse VR) | 54 (11.25) |
| 2259 (Fortify Assura DR) | 59 (12.29) |
| 2359 (Fortify Assura DR) | 48 (10.00) |
| 2277 (Ellipse DR) | 65 (13.54) |
| 2377 (Ellipse DR) | 37 (7.71) |
| Fortify ST | 1 (0.21) |
| **Implantation side, n (%)** | |
| Left side | 470 (97.92) |
| Right side | 10 (2.08) |
| **System position, n (%)** | |
| Sub-pectoral | 104 (21.67) |
| Subcutaneous | 375 (78.13) |
| Data missing | 1 (0.21) |
| **RV lead position, n (%)** | |
| RV apex | 381 (79.38) |
| RV outflow | 12 (2.50) |
| RV septum | 82 (17.08) |
| Other | 5 (1.04) |

Abbreviation: RV, right ventricle.
difference between the groups was the follow-up schedule. In Group 1, alert events, including ST-segment changes, were collected via a remote control system, and in-clinic follow-up visits were scheduled every 6 months. Group 2 did not use a remote control and had alert events reviewed during device interrogation every 3 months.

Device session records were collected during each in-clinic follow-up. In patients with recorded ventricular tachycardia (VT) or ventricular fibrillation (VF) episodes, the ST-segment deviation over the 15 min prior to the event, each relative to the pre-P-wave level, was compared using Student’s t test with those from a period of 23–24 h prior to the event. All events with significant ST-segment changes (p < .05) were further visually inspected to confirm they were evaluable; additional criteria for exclusion from further analysis included inappropriate therapy or known non-ischemic cause of ST-segment changes, for example, aberrant conduction or occurrence of another VT/VF episode within 24 h prior to the analyzed event. Statistical analysis was performed to determine whether there were any demographic or medical factors that could be linked with higher odds of the characteristic ST-segment changes preceding VT/VF episode.

The study protocol also included dobutamine stress echocardiography (DSE) in every patient after confirmed VT/VF episode, unless previous DSE had been performed not later than 6 months before the arrhythmic event and no new symptoms of IHD were present.

Statistical analysis was performed using Statistica software, version 13.3 (StatSoft, Inc.) with statistical significance set at p < .05. ST-segment deviation prior to VT/VF event was compared with the baseline using Student’s t test. A logistic regression model was applied to determine whether there were any demographic and clinical characteristics in the group that displayed the characteristic ST-segment changes.

The study was supported by grants from St. Jude Medical/Abbott.

3 | RESULTS

3.1 | Clinical characteristics

A total of 481 participants were enrolled (mean age was 64 ± 11 years, 83% of subjects were men). Mean time of follow-up was 15 ± 5 months. One of the patients was withdrawn from the study after enrollment due to protocol deviation (the patient was implanted with ICD not containing ST Management Feature). Detailed baseline characteristics of the studied population are described in Table 3.
Out of the 480 followed subjects, 26 (5.4%) died during the study. Nine deaths (34.6%) were related to cardiac causes, the remaining deaths were non-cardiac (n = 6; 23%), or the cause of death remained unknown (n = 11; 42.3%). There were 235 all-cause hospitalizations that occurred in 140 subjects during the follow-up. The mean duration of all-cause hospitalization was 9.29 ± 15.90 days.

Only 11 hospitalizations in 9 subjects occurred due to ICD shocks. The mean duration of hospitalization due to this cause was 4.18 ± 2.99 days.

| Group's characteristic | Study group (n = 480) |
|------------------------|-----------------------|
| Age, mean ± SD         | 63.95 ± 11.29         |
| Men, n (%)             | 400 (83.33)           |
| Height (cm), mean ± SD | 170.46 ± 8.48         |
| Weight (kg), mean ± SD | 79.22 ± 18.46         |
| Baseline medical data  |                       |
| Baseline EF (%), mean ± SD | 33.97 ± 11.98   |
| NYHA class, n (%)      |                       |
| Class I                | 140 (29.17)           |
| Class II               | 241 (50.21)           |
| Class III              | 94 (19.58)            |
| Class IV               | 3 (0.63)              |
| Indication for implant, n (%) |             |
| Primary prevention     | 296 (61.67)           |
| Secondary prevention   | 184 (38.33)           |
| VF                     | 112 (60.87)           |
| VT                     | 72 (39.13)            |
| Medical history, n (%) |                       |
| Ischemic cardiomyopathy| 366 (76.3)            |
| Non-ischemic cardiomyopathy| 105 (21.8)   |
| Hypertrophic cardiomyopathy| 9 (1.9)      |
| Atrial arrhythmia, n (%)|                        |
| Atrial fibrillation    | 76 (15.83)            |
| Atrial flutter         | 14 (2.92)             |
| Ventricular arrhythmia, n (%) |              |
| Premature ventricular contractions | 27 (5.63)       |
| Non-sustained ventricular tachycardia | 24 (88.89)  |
| Ventricular bigeminy   | 2 (7.41)              |
| Ventricular trigeminy  | 1 (3.70)              |
| Monomorphic ventricular tachycardia | 107 (22.29)  |
| Ventricular fibrillation| 79 (16.46)           |
| Polymorphic ventricular tachycardia | 10 (2.08)    |
| Other                  | 23 (4.79)             |
| Relevant comorbidities, n (%) |                |
| Chronic obstructive pulmonary disease | 42 (8.75)       |
| Neurovascular (TIA or CVA) | 24 (5.00)        |
| Other                  | 204 (42.50)           |
| Baseline pharmacological treatment, n (%) |       |
| ACE inhibitors         | 312 (65.00)           |
| ARBs                   | 74 (15.42)            |
| Adrenergic block       | 1 (0.21)              |
| Aldosterone antagonists| 180 (37.50)           |
| Antiplatelet medication| 343 (71.46)           |
| Anti-arrhythmic        | 98 (20.42)            |
| Anticoagulants         | 125 (26.04)           |
| Beta-blockers          | 422 (87.92)           |

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; ARVD, arrhythmogenic right ventricle dysplasia; CVA, cerebrovascular accident; EF, ejection fraction; SD, standard deviation; TIA, transient ischemic attack; VF, ventricular fibrillation; VT, ventricular tachycardia.

### 3.2 | Follow-up events

Out of the 480 followed subjects, 26 (5.4%) died during the study. Nine deaths (34.6%) were related to cardiac causes, the remaining deaths were non-cardiac (n = 6; 23%), or the cause of death remained unknown (n = 11; 42.3%). There were 235 all-cause hospitalizations that occurred in 140 subjects during the follow-up. The mean duration of all-cause hospitalization was 9.29 ± 15.90 days. Only 11 hospitalizations in 9 subjects occurred due to ICD shocks. The mean duration of hospitalization due to this cause was 4.18 ± 2.99 days.

### 3.3 | ICD-documented ventricular tachyarrhythmias

In total, 245 ICD therapies (appropriate and inappropriate) in 117 subjects (24%) were observed, as illustrated in the Graphical Abstract. Further analysis led to the exclusion of 80 events due to missing EGM data (n = 70), occurrence of event prior to enrollment (n = 2), or inappropriate therapy (n = 8). Out of 165 confirmed VT/VF episodes with complete EGM data, 93 (58%) episodes in 69 subjects were preceded by significant ST-segment changes. Further 22 events were excluded due to known, non-ischemic causes of ST changes (aberrant conduction (n = 16), or another ventricular arrhythmia episode within 24 h prior to analyzed event (n = 6)). Ultimately, 71 ventricular events (43% of confirmed VT/VF episodes) in 56 subjects (12% of the study population and 34% of all patients with ventricular arrhythmias) were confirmed as preceded by characteristic ST-segment changes. Out of the 71 episodes, 54 (76%) were monomorphic VTs, while the remaining 17 episodes (24%) were polymorphic VTs or VF.

### 3.4 | Model predicting ST-segment changes

None of the analyzed demographic and clinical factors proved to be associated with greater odds of presenting with ST-segment changes prior to VT/VF episode (Table 4).
Demographic and medical characteristics of patients with arrhythmias preceded by ST-segment changes and those with no ST-segment changes prior to arrhythmic events were not significantly different, as summarized in Table 5.

3.5 | Relation between ST-segment changes and confirmed ischemia

Only 6 episodes of the acute coronary syndrome were observed in the study population during the follow-up: 2 myocardial infarctions with ST-segment elevation myocardial infarction (STEMI) and 4 episodes of unstable angina. Five patients underwent coronary revascularization: 4 subjects by percutaneous coronary intervention and 1 by coronary artery bypass grafting.

A total of 230 VT/VF episodes in 112 subjects were classified as requiring a DSE test according to study protocol, including 71 events with confirmed significant ST-segment changes. Unfortunately, only 15 DSE tests in 14 subjects were performed. The results of DSE tests are summarized in Table 6.

4 | DISCUSSION

To our knowledge, this is the first study designed not only to investigate the possibility of detection of EGM ST-segment changes related to ischemia but also to assess the prevalence of ischemic changes as recorded by ICD ST deviations over the 24 h preceding malignant ventricular arrhythmias treated by ICD, and to define their temporal relationship to these events. The principal finding of the study is that a relatively high number of ventricular events (43%) were preceded by significant ST-segment changes. Most of these episodes were monomorphic VTs (n = 54; 76%).

The concept of analyzing ST-segment changes in EGMs in order to diagnose ischemic events was previously investigated both in animals and in humans. Early studies included transcutaneous insertion of an electrode to the right ventricle in pigs or in human patients undergoing transcutaneous coronary angioplasty to record ST-segment changes during balloon inflation in the coronary arteries (Fischell et al., 2005; Mendenhall et al., 2012; Williams et al., 2008). Intracardiac electrograms proved to be more sensitive in detecting ST-segment changes than surface ECG (Fischell et al., 2005; Siegel et al., 1982; Theres et al., 2002). The next stage of studies included implantation of dedicated devices in order to continuously monitor ST segment, first in animals, then in human patients (Fischell et al., 2006, 2010). The first human study by Fischell et al. reported 4 cases (among 37 observed patients) in which ST-segment changes related to coronary artery occlusion and/or ruptured arteriosclerotic plaque were detected by an implantable intracardiac ischemia detecting device. The system used in this study showed promising sensitivity and specificity; however, it did not have a functionality of cardioversion and/or defibrillation. The reported median time from ST-segment alarm to hospital medical contact was as short as 19.5 minutes (Fischell et al., 2010). All those facts led to the development of ICDs featuring the ability of constant beat-to-beat monitoring of the intracardiac ST segment.

In this study, a total of 245 ICD interventions (appropriate and inappropriate) in 117 subjects (24%) were observed during a mean follow-up time of 15 ± 5 months. This incidence is comparable with the rate described in real-life ICD patients (Lelekovski et al., 2012; Proclemer et al., 2013; Wasiak et al., 2020; Wilkoff et al., 2004).

The majority of episodes with significant ST-segment changes were monomorphic VTs, that is, 54 episodes (76%). However, in groups of patients with arrhythmic episodes preceded and not preceded by ST-segment changes, the proportion of VTs was almost the same (51/71 vs 52/72, respectively). Interestingly, ST-segment changes prior to VT/VF events were present with comparable frequency in patients with ischemic cardiomyopathy and in those with non-ischemic cause of heart failure (but at the risk of developing CAD in investigators’ opinion) (Table 5). The mechanism in which VT occurs in survivors of myocardial infarction is well established to be related to re-entry circuits involving scar tissue (Bolli, 1986). In some patients after myocardial infarction, the development of new ongoing ischemia can create a zone of slow conduction or block that, together with preexisting scar, can be a trigger for VT. In this setting, the ST-segment changes characteristic for ischemia can precede VT episodes. Occurrence of monomorphic VT during early phase (72 h) of the first myocardial infarction is also possible, although it is reported to be rare, not exceeding 3% of cases, according to data from a study by Hatzinikolaou-Kotsakou et al. (2007). There are many suggested mechanisms of VT induction during an early phase of the first acute ischemic event (with no scar-related substrate). Most studies highlight a possible role of intramural re-entry or triggered

| Analyzed factor                      | p-value | Odds ratio | Lower 95% confidence limit for odds ratio | Upper 95% confidence limit for odds ratio |
|--------------------------------------|---------|------------|------------------------------------------|------------------------------------------|
| No anti-arrhythmic medication        | .8372   | 1.098      | 0.449                                    | 2.689                                    |
| No beta-blockers                     | .2735   | 1.856      | 0.614                                    | 5.617                                    |
| No statins                           | .4740   | 0.682      | 0.240                                    | 1.943                                    |
| Non-ischemic cardiomyopathy          | .4320   | 0.655      | 0.229                                    | 1.880                                    |
| Ischemic cardiomyopathy              | .1891   | 0.490      | 0.169                                    | 1.420                                    |
| Monomorphic ventricular tachycardia  | .8737   | 0.935      | 0.407                                    | 2.145                                    |
activity related to the high sympathetic drive or mechanical stretch (Gantenberg & Hageman, 1992; Pogwizd & Corr, 1987).

All the analyzed demographic and clinical factors fail to prove to be associated with greater odds of presenting with ST-segment changes prior to VT/VF episode. Also, the use of beta-blockers, well known for their anti-ischemic activity, did not have an impact on reducing odds of ST-segment changes preceding arrhythmic event (Dézsi & Szentes, 2017).

Despite the study protocol, only 15 DSE tests (in 14 subjects) were performed. Moreover, only 6 episodes of acute coronary syndrome were observed in the study population during follow-up: 2 STEMI and 4 episodes of unstable angina. This resulted in a lack of data to confirm a likely relation of ST-segment changes with ongoing ischemia, which is the most important limitation of our study.

Predictive value of ST-segment changes detected by ICD was investigated by Watanabe et al. (2018). In this study, 173 patients after implantation of ICD with the ST-segment monitoring function were followed for a mean of $23.3 \pm 7.7$ months. Significant ST changes were observed in 15 patients (8.7%), most of which were asymptomatic. Patients were tested for coronary artery stenosis using coronary angiography and/or for ischemia with myocardial perfusion imaging. The sensitivity, specificity, and negative predictive values of the ST monitoring feature to detect ischemia were 75.0%, 72.5%, and 93.5%, respectively, and to predict stenosis were 76.9%, 83.5%, and 97.5%, respectively.

The prevalence of the significant ST-segment changes prior to VT/VF episodes in our study was relatively high (43% of all

| TABLE 5 | Comparison between demographic and medical characteristics of patients with and without ST-segment changes prior to arrhythmic events |
|---|---|
| Parameter | ST changes ($N = 56$) | No ST changes ($N = 50$) |
| Age, mean ± SD | 63.5 ± 13.3 | 65.8 ± 11 |
| Gender—male, n (%) | 50 (89.3) | 41 (82) |
| Height (cm), mean ± SD | 169.6 ± 8.4 | 170.6 ± 7.7 |
| Weight (kg), mean ± SD | 74.9 ± 16.3 | 82.8 ± 22.4 |
| Baseline medical data | | |
| LV ejection fraction (%), mean ± SD | 34.3 ± 13.1 | 33.2 ± 12.4 |
| NYHA class, n (%) | | |
| Class I | 18 (32.1) | 13 (26.0) |
| Class II | 26 (46.4) | 25 (50.0) |
| Class III | 11 (19.6) | 11 (22.0) |
| Class IV | 0 (0) | 1 (2.0) |
| Indication for implant, n (%) | | |
| Primary prevention | 23 (41.1) | 26 (52) |
| Secondary prevention | 33 (58.9) | 24 (48) |
| Etiology, n (%) | | |
| Ischemic cardiomyopathy | 33 (58.9) | 33 (66) |
| Non-ischemic cardiomyopathy | 18 (32.1) | 18 (28) |
| Hypertrophic cardiomyopathy | 2 (3.6) | 1 (2) |
| Hypertrophic cardiomyopathy | 2 (3.6) | 1 (2) |
| History of atrial arrhythmia, n (%) | | |
| Paroxysmal atrial fibrillation | 9 (16.1) | 9 (18) |
| Paroxysmal atrial flutter | 2 (3.6) | 1 (2) |
| History of ventricular arrhythmia, n (%) | | |
| Premature ventricular contractions | 5 (8.9) | 6 (12) |
| Monomorphic ventricular tachycardia | 24 (43.2) | 21 (42) |
| Ventricular fibrillation | 11 (19.6) | 7 (14) |
| Polymorphic ventricular tachycardia | 0 (0) | 2 (4) |
| Other ventricular arrhythmia | 1 (1.8) | 3 (6) |
| Relevant comorbidities, n (%) | | |
| Chronic obstructive pulmonary disease | 5 (8.9) | 7 (14) |
| Neurovascular | 2 (3.6) | 0 (0) |
| Previous TIA | 1 (50) | 0 (0) |
| Previous CVA | 1 (50) | 0 (0) |
| Other comorbidities | 26 (46.8) | 20 (40) |

**Abbreviations:** ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; ARVD, arrhythmogenic right ventricle dysplasia; CVA, cerebrovascular accident; EF, ejection fraction; SD, standard deviation; TIA, transient ischemic attack; VF, ventricular fibrillation; VT, ventricular tachycardia.
confirmed VT/VF episodes). Nevertheless, the predictive value of the ST monitoring feature in identifying pending arrhythmic events has to be established yet.

The study has an important limitation, which is a lack of information whether conversion of arrhythmia by device was similarly effective in both groups. Such analysis could shed light on a possible mechanism of analyzed ventricular arrhythmias.

5 | CONCLUSIONS

In this exploratory study, ST-segment changes preceding VT/VF episodes, likely representative of ischemic events, were observed in more than 1 of 3 of all patients with VT/VF episodes and in 12% of all the patients enrolled in the study. ST-segment changes were observed with similar frequency in patients with known coronary artery disease and those with a non-ischemic cause of heart failure.

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CONFLICT OF INTEREST

Jerzy Krzysztof Wranicz has received lecturer fees from St. Jude Medical/Abbott. Dirk Bastian has received lecturer fees from St. Jude Medical/Abbott and Medtronic. Christof Kolb has received travel support and lecture honoraria from Abbott, Biotronik, Boston Scientific, Bristol Myer Squibb, Medtronic, MicroPort, and Novartis; study compensation to the employer from Abbott, Biotronik, Boston Scientific, MicroPort, and ResMed Foundation; and advisory board fees from MicroPort. Edgar Zitron has received lecturer fees from St. Jude Medical/Abbott and Medtronic. Krzysztof Kaczmarek has received travel grants and lecturer fees from St. Jude Medical/Abbott. Michał Kałowski, Aparna Jaswal, and Iwona Cygankiewicz declared no conflict of interest.

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REFERENCES

Al-Khatib, S. M., Stevenson, W. G., Ackerman, M. J., Bryant, W. J., Callans, D. J., Curtis, A. B., Deal, B. J., Dickfeld, T., Field, M. E., Fonarow, G. C., Gillis, A. M., Granger, C. B., Hammill, S. C., Hlatky, M. A., Joglar, J. A., Kay, G. N., Matlock, D. D., Myerburg, R. J., & Page, R. L. (2017). 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Heart Rhythm: the Official Journal of the Heart Rhythm Society, 72, e91–e220. https://doi.org/10.1016/j.hrthm.2017.10.036

Barshehset, A., Goldenberg, I., Moss, A. J., Huang, D. T., Zareba, W., McNITT, S., Klein, H. U., & Guetta, V. (2011). Effect of elapsed time from coronary revascularization to implantation of a cardioverter defibrillator on long-term survival in the MADIT-II trial. Journal of Cardiovascular Electrophysiology, 22, 1237–1242. https://doi.org/10.1111/j.1540-8167.2011.02096.x

Bolli, R., Fisher, D. J., & Entman, M. L. (1986). Factors that determine the occurrence of arrhythmias during acute myocardial ischemia. American Heart Journal, 111, 261–270. https://doi.org/10.1016/0002-8703(86)90138-9

Boriani, G., Botto, G., Lunati, M., Proclemer, A., Schmidt, B., Erdogan, A., Rauhe, W., Biffi, M., Santi, E., Becker, D., Messier, M., & Santini, M. (2012). Influence of time between last myocardial infarction and prophylactic implantable defibrillator implant on device detections and therapies. ' Routine Practice' data from the SEARCH MI registry. BMC Cardiovascular Disorder, 12, 72. https://doi.org/10.1186/1471-2261-12-72

Bunch, T. J., Hohnloser, S. H., & Gersh, B. J. (2007). Mechanisms of sudden cardiac death in myocardial infarction survivors: Insights from the randomized trials of implantable cardioverter-defibrillators. Circulation, 115, 2451–2457. https://doi.org/10.1161/CIRCULATIONAHA.106.683235

Dézsi, C. A., & Szentes, V. (2017). The real role of β-blockers in daily cardio vascular therapy. American Journal of Cardiovascular Drugs, 17, 361–373. https://doi.org/10.1007/s40256-017-0221-8

Fischell, T. A., Fischell, D. R., Avezum, A., John, M. S., Holmes, D., Foster, M., Kovach, R., Medeiros, P., Piegs, L., Guimaraes, H., & Gibson, C. M. (2010). Initial clinical results using intracardiac electrogram monitoring to detect and alert patients during coronary plaque rupture and ischemia. Journal of the American College of Cardiology, 56, 1089–1098. https://doi.org/10.1016/j.jacc.2010.04.053

Fischell, T. A., Fischell, D. R., Fischell, R. E., Baskerville, S., Hendrick, S., Moshier, C., Harwood, J. P., & KrucOFF, M. W. (2005). Potential of an intracardiac electrogram for the rapid detection of coronary artery occlusion. Cardiovascular Revascularization Medicine, 6, 14–20. https://doi.org/10.1016/j.carrev.2005.05.002

Fischell, T. A., Fischell, D. R., Fischell, R. E., Virmani, R., DeVries, J. J., & KrucOFF, M. W. (2006). Real-time detection and alerting for acute ST-segment elevation myocardial ischemia using an implantable, high-fidelity, intracardiac electrogram monitoring system with long-range telemetry in an ambulatory porcine model. Journal of the American College of Cardiology, 48, 2306–2314. https://doi.org/10.1016/j.jacc.2006.07.058

Gantenberg, N. S., & Hageman, G. R. (1992). Enhanced induction of ventricular arrhythmias during sympathetic stimulation before and...
during coronary artery occlusion. *International Journal of Cardiology*, 34, 75–83. https://doi.org/10.1016/0167-5273(92)90085-h

Hatzipanagou-Kotsakou, E., Tzakas, D., Hotidis, A., Stakos, D., Floros, D., Mavridis, A., Papanas, N., Chalikias, G., Maltezos, E., & Hatseras, D. I. (2007). Could sustained monomorphic ventricular tachycardia in the early phase of a prime acute myocardial infarction affect patient outcome? *Journal of Electrocardiology*, 40, 72–77. https://doi.org/10.1016/j.jelectrocard.2006.02.004

Lelakowski, J., Piekarz, J., Rydlewska, A., & Majewski, J., Senderek, T., Ząbek, A., & Małecka, B. (2012). Factors predisposing to ventricular tachyarrhythmia leading to appropriate ICD intervention in patients with coronary artery disease or non-ischaemic dilated cardiomyopathy. *Kardiologia Polska*, 70, 1264–1275

Mendenhall, G. S., Zahr, F., Bhattacharya, S., Toma, C., & Saba, S. (2012). Effect of coronary occlusion on intracardiac electrogram morphology. *Europace*, 14, 1524–1531. https://doi.org/10.1093/europace/eus098

Pogwizd, S. M., & Corr, P. B. (1987). Reentrant and nonreentrant mechanisms contribute to arrhythmogenesis during early myocardial ischemia: Results using three-dimensional mapping. *Circulation Research*, 61, 352–371. https://doi.org/10.1161/01.RES.61.3.352

Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G. F., Coats, A. J. S., Falk, V., González-Juanatey, J. R., Harjola, V.-P., Jankowska, E. A., Jessup, M., Linde, C., Nihoyannopoulos, P., Parissis, J. T., Pieske, B., Riley, J. P., Rosano, G. M. C., Ruipope, L. M., Ruschitzka, F., ... van der Meer, P. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *European Heart Journal*, 37, 2129–2200. https://doi.org/10.1002/euhf.592

Priori, S. G., Blomström-Lundqvist, C., Mazzanti, A., Blom, N., Borggrefe, M., Camm, J., Elliott, P. M., Fitzsimons, D., Hatala, R., Hindricks, G., Kirchhof, P., Kjeldsen, K., Kuck, K.-H., Hernandez-Madrid, A., Nikolau, N., Norekval, T. M., Spaulding, C., & Van Veldhuisen, D. J.; ESC Scientific Document Group (2015). 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *European Heart Journal*, 36, 746–837. https://doi.org/10.1093/eurheartj/ehv316

Proclemer, A., Muser, D., Campana, A., Zoni-Berisso, M., Zacchin, M., Locatelli, A., Brieda, M., Gramegna, L., Santarone, M., Chioldi, L., Mazzone, P., Rebellato, L., & Facchin, D. (2013). Indication to cardioverter-defibrillator therapy and outcome in real world primary prevention. Data from the IRIDE [Italian registry of prophylactic implantation of defibrillators] study. *International Journal of Cardiology*, 168, 1416–1421. https://doi.org/10.1016/j.ijcard.2012.12.042

Siegel, S., Brodman, R., Fisher, J., Matos, J., & Furman, S. (1982). Intracardiac electrode detection of early or subendocardial ischemia. *Pacing Clinical Electrophysiology*, 5, 892–902. https://doi.org/10.1111/j.1540-8159.1982.tb00028.x

Theres, H., Stadler, R. W., Stylos, L., Glos, M., Leuthold, T., Baumann, G., Nelson, S. D., & Krucoff, M. W. (2002). Comparison of electrocardiogram and intrathoracic electrogram signals for detection of ischemic ST segment changes during normal sinus and ventricular paced rhythms. *Journal of Cardiovascular Electrophysiology*, 13, 990–995. https://doi.org/10.1046/j.1540-8167.2002.00990.x

Wasiak, M., Tajstra, M., Pyka, Ł., & Gasiór, M. (2020). Long-term clinical outcomes after placement of an implantable cardioverter-defibrillator: does the etiology of heart failure matter? *Kardiologia Polska*, 78, 318–324. https://doi.org/10.33963/KP.15242

Watanabe, T., Hirooka, K., Furukawa, Y., Yabuki, M., Hirata, A., Kashiwase, K., Shotta, R., Mine, T., Mizuno, H., Tanaka, T., Doi, T., Yoshida, A., Okuyama, Y., & Nanto, S. (2018). Continuous ST-monitoring function of implantable cardioverter defibrillator detects silent ischemia in patients with coronary artery disease. *Journal of the American Heart Association*, 7, e009332. https://doi.org/10.1161/JAHA.1118.009332

Wilkoff, B. L., Hess, M., Young, J., & Abraham, W. T. (2004). Differences in tachyarrhythmia detection and implantable cardioverter-defibrillator therapy by primary or secondary prevention indication in cardiac resynchronization therapy patients. *Journal of Cardiovascular Electrophysiology*, 15, 1002–1009. https://doi.org/10.1111/j.1540-8167.2004.03625.x

Williams, J. L., Stuart Mendenhall, G., & Saba, S. (2008). Effect of ischemia on implantable defibrillator intracardiac shock electrograms. *Journal of Cardiovascular Electrophysiology*, 19, 275–281. https://doi.org/10.1111/j.1540-8167.2007.01042.x

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