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CLINICAL RESEARCH

Impact of COVID-19 on the incidence of cardiac arrhythmias in implantable cardioverter defibrillator recipients followed by remote monitoring[☆]

Impact de la pandémie de COVID-19 sur l'incidence des arythmies cardiaques chez les patients implantés d'un défibrillateur automatique implantable et suivis en télé-cardiologie

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Abbreviations: ATP, antitachycardia pacing; COVID-19, coronavirus disease 2019; ICD, implantable cardioverter defibrillator; OHCA, out-of-hospital cardiac arrest; VA, ventricular arrhythmia.

[☆] Tweet: An increase in ventricular arrhythmia incidence has been observed in the 2 weeks before the lockdown order whereas a dramatic drop of ventricular arrhythmia occurred during the lockdown period.

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KEYWORDS

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Summary

Background. – The coronavirus disease 2019 (COVID-19) has been a fast-growing worldwide pandemic.

Aims. – We aimed to investigate the incidence of cardiac arrhythmias among a large French cohort of implantable cardioverter defibrillator recipients over the first 5 months of 2020.

Methods. – Five thousand nine hundred and fifty-four implantable cardioverter defibrillator recipients were followed by remote monitoring during the COVID-19 period (from 01 January to 31 May 2020). Data were obtained from automated remote follow-up of implantable cardioverter defibrillators utilizing the Implicity® platform. For all patients, the type of arrhythmia (atrial fibrillation, ventricular tachycardia or ventricular fibrillation), the number of ventricular arrhythmia episodes and the type of implantable cardioverter defibrillator-delivered therapy were recorded.

Results. – A total of 472 (7.9%) patients presented 4917 ventricular arrhythmia events. An increase in ventricular arrhythmia incidence was observed after the first COVID-19 case in France, and especially during weeks #10 and #11, at the time of major governmental measures, with an increase in the incidence of antitachycardia pacing delivered therapy. During the 11 weeks before the lockdown order, the curve of the percentage of live-stream television coverage of COVID-19 information matched the ventricular arrhythmia incidence. During the lockdown, the incidence of ventricular arrhythmia decreased significantly compared with baseline (0.05 ± 0.7 vs. 0.09 ± 1.2 episodes per patient per week, respectively; $P < 0.001$). Importantly, no correlation was observed between ventricular arrhythmia incidence and the curve of COVID-19 incidence. No changes were observed regarding atrial fibrillation/atrial tachycardia episodes over time.

Conclusions. – An increase in ventricular arrhythmia incidence was observed in the 2 weeks before the lockdown order, at the time of major governmental measures. Ventricular arrhythmia incidence decreased dramatically during the lockdown.

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MOTS CLÉS

Épidémie du
COVID-19 ;
Arythmies
ventriculaires ;
Défibrillateur
automatique
implantable ;
Télé-cardiologie

Résumé

Contexte. – Le COVID-19 est une épidémie mondiale de croissance rapide.

Objectifs. – Nous avons étudié l'incidence des arythmies cardiaques dans une cohorte française de patients implantés de défibrillateur automatique implantable (DAI) pendant les cinq premiers mois de 2020.

Méthode. – Cinq milles neuf cent cinquante quatre patients implantés d'un DAI suivis en télé cardiologie ont été analysés pendant la première partie de l'épidémie de COVID-19 (du 1er janvier au 31 mai 2020). Les données ont été automatiquement extraites en utilisant la plateforme de télé-cardiologie Implicity. Pour l'ensemble des patients, le type d'arythmie (fibrillation atriale, tachycardie ventriculaire ou fibrillation ventriculaire), le nombre d'épisodes d'arythmie ventriculaire, et le type de thérapie délivrée par le DAI ont été recueillis.

Résultats. – Au total, 472 (7,9 %) patients ont présenté 4917 épisodes d'arythmie ventriculaire. Une augmentation de l'incidence des arythmies ventriculaires a été observée après le premier cas de COVID-19 en France et particulièrement pendant les semaines 10 et 11, au moment des principales mesures gouvernementales. Une élévation de l'incidence de stimulation antitachycardique délivrée par le DAI a également été observée pendant cette période. Pendant la semaine numéro 11, avant le début du confinement, on met en évidence une corrélation entre le pourcentage d'information dédié au COVID-19 sur les chaînes d'information télévisée et l'incidence des arythmies ventriculaires. Pendant le confinement, l'incidence des arythmies ventriculaires a diminué de façon significative comparée à la période avant

confinement ($0,05 \pm 0,7$ vs $0,09 \pm 1,2$ épisodes par patient par semaine, $p < 0,001$). Aucune corrélation n'est observée entre l'incidence des arythmies ventriculaires et l'incidence de nombre de cas de COVID-19. Aucun changement n'a été observé concernant l'incidence des arythmies supraventriculaires pendant cette période.

Conclusion. — Une augmentation de l'incidence des arythmies ventriculaires est observée dans les deux semaines avant le confinement, au moment des principales mesures gouvernementales. Pendant le confinement, l'incidence des arythmies ventriculaires a significativement diminué.

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Background

The coronavirus disease 2019 (COVID-19), initially reported in Wuhan, China, in December 2019, has been a fast-growing worldwide pandemic. In several countries, daily life has been deeply and suddenly impacted by the closure of shops and the shutdown of schools and universities, and most citizens have been confined at home for several weeks. As a consequence, this situation has significantly increased the risk of experiencing stress in the overall population [1]. Additionally, the confinement period has been associated with considerable lifestyle changes, especially eating habits and physical activity [2].

It is well established that environmental stress (such as earthquakes, war or sporting events) may increase the risk of cardiovascular events [3,4]. Similar results have been reported with the COVID-19 pandemic. Indeed, a transient two-fold increase in out-of-hospital cardiac arrest (OHCA) was observed in Paris, France, during the 6 weeks following the lockdown order [5]. Similarly, the incidence of OHCA in Italy in 2020 has been strongly associated with the cumulative incidence of COVID-19 cases [6]. However, the impact of the COVID-19 pandemic on the occurrence of ventricular arrhythmia (VA) among patients implanted with an implantable cardioverter defibrillator (ICD) has not been investigated so far.

In this work, we aimed to retrospectively evaluate the impact of the COVID-19 pandemic and lockdown order on the occurrence of cardiac arrhythmias, whether atrial or ventricular, in a unique and large population of ICD recipients followed prospectively by remote monitoring.

Methods

Study population

For the purpose of this multicentre study, we retrospectively included all patients previously implanted with an ICD before 01 January 2020, and followed them continuously until 31 May 2020, using the Implicity® remote monitoring platform (Paris, France). A total of 30 tertiary centres were enrolled. Of note, Abbott (Chicago, IL, USA), Biotronik (Berlin, Germany), Boston Scientific (Marlborough, MA, USA), Medtronic (Minneapolis, MN, USA) and MicroPort (Shanghai, China) devices were included.

Among the overall population, the following variables were obtained from automated remote follow-up of ICDs utilizing the Implicity® platform: age category, sex category, the occurrence of sustained VA, type of VA (i.e. ventricular tachycardia or ventricular fibrillation), number of ICD-delivered therapies (i.e. antitachycardia pacing [ATP] or ICD shock), the occurrence of supraventricular tachycardia (i.e. atrial fibrillation or atrial tachycardia episodes), heart rate and mean activity level per day. Notably, the Implicity® platform used the definition of the device's manufacturer for classifying the VA event. However, non-sustained VA events were not defined as VA episodes. Patients with incomplete follow-up or missing data during the 6-month study were not included in this work. The study received the proper ethical oversight and ethics committee approval. All patients gave their consent to the use of their clinical data.

Study objectives

During the 22-week study period, the occurrences of cardiac arrhythmias and ICD-delivered therapies were described and compared with the media-related COVID-19 evolution in France. The main timeline of events was: 11 January, first COVID-19 death in Wuhan, China; 24 January, first case in France; 26 February, first death in France; 12 March, first French presidential television allocution; 14 March, epidemic stage 3; and 16 March, lockdown order. Notably, the confinement period extended from week #12 to week #20 (from 16 March to 11 May 2020). We also compared the incidence of VA with the television live-stream coverage of the COVID-19 pandemic. Additionally, the incidence of VA during the 22 weeks was compared with the COVID-19 pandemic progression in France (i.e. the number of new COVID-19 cases per week in France). These data were collected from the Audiovisual National Institute and the French Public Health websites, respectively [7,8].

Statistical analysis

Data are summarized as number (percentage) for categorical variables, and as mean \pm standard deviation or median (interquartile range), as appropriate, for continuous variables. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Categorical variables were compared using the χ^2 test or Fisher's exact test, whereas quantitative data were compared using Student's

t-test or the Mann–Whitney *U* test, as appropriate. To compare the incidence of cardiac arrhythmias per patient before and after the lockdown order we used a linear general model analysis with repeated measures. Statistical analysis was performed with the use of the Statistical Package for Social Sciences, version 22 (SPSS, Chicago, IL, USA).

Results

A total of 5954 ICD recipients were included in the study. Among this population, 4694 (78.8%) were male and 2748 (46.1%) were aged > 70 years. The distribution of sex and age categories within the cohort is illustrated in Fig. 1. Of note, half of the patients were implanted with a single- or double-chamber ICD (2989, 50.2%), whereas 2379 (40.0%) and 586 (9.8%) received a cardiac resynchronization therapy defibrillator or a subcutaneous ICD, respectively. The study population was followed for 22 weeks (from 01 January to 31 May 2020). The lockdown was ordered in France from 16 March to 11 May 2020.

Evolution of daily activity and heart rate during the pandemic

Initially, the mean activity per day was stable at around $12.0 \pm 6.2\%$ and $12.2 \pm 6.5\%$ in January and February, respectively, and decreased significantly to $10.9 \pm 6.1\%$ and $10.7 \pm 5.8\%$ in March and April, respectively ($P < 0.001$), once the lockdown was ordered in France. Similarly, a mild, but significant decrease in mean heart rate in March and April compared with January and February was observed (69.3 ± 7.1 and 69.1 ± 7.3 vs 69.8 ± 7.6 and 69.9 ± 7.4 beats/min, respectively; $P < 0.001$) (Fig. 2A and Fig. 2C). Additionally, the mean activity level per day and the mean heart rate suddenly decreased after the lockdown order (Fig. 2B and Fig. 2D)

Evolution of the occurrence of cardiac arrhythmias

During the 22 weeks of follow-up, a total of 4917 VA events occurred among 472 (7.9%) patients [i.e. 4698 (95.5%) and 219 (4.5%) ventricular tachycardia and fibrillation episodes, respectively]. The incidence of VA episodes per patient per week among the overall population is illustrated in Fig. 3A. Interestingly, increased VA incidence was observed after the first COVID-19 case in France was declared, and especially during weeks #10 and #11, at the time of the two major governmental measures: the first French President television allocution (12 March) and the transition to epidemic stage 3 (14 March). After the lockdown order (16 March) and during the 11 following weeks, the incidence of VA dropped significantly compared with the 11 weeks before the lockdown order (0.05 ± 0.7 vs. 0.09 ± 1.2 VA episodes per patient per week, respectively; $P < 0.001$). The analysis of the incidence of ATP delivered therapy showed a similar evolution, with a sudden increase in ATP delivered at weeks #10 and #11 (Fig. 3B). However, the incidence of ICD shocks remained unchanged during the 22-week study period (Fig. 3C). Additionally, we observed no relationship between the curve of new French COVID-19 cases in France and the

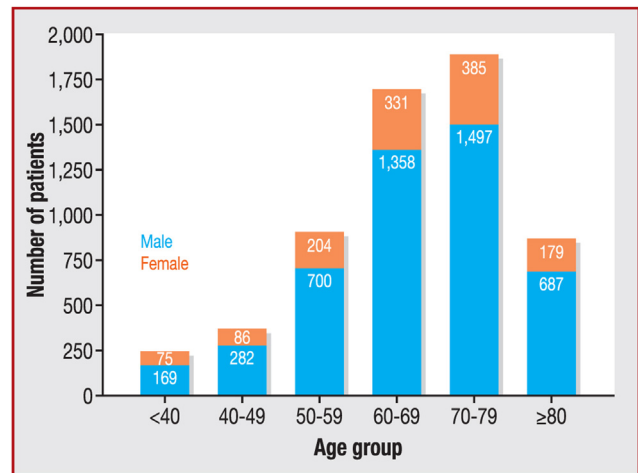


Figure 1. Cohort characteristics depending on age and sex category.

incidence of VA (Central illustration, blue curve). However, during the 11-weeks before the lockdown order, the curve of the percentage of live-stream television coverage of COVID-19 matched the incidence of VA (Central illustration, red curve). Lastly, as illustrated in Fig. 3D, no changes were observed regarding atrial fibrillation/tachycardia episodes.

Impact of sex and age on the incidence of VA

Interestingly, a difference in the incidence of VA during the study period was observed between males and females. Indeed, the incidence of VA was unchanged for females during the pandemic, whereas males exhibited an increased incidence of VA at weeks #10 and #11 (Fig. 4A), explaining the increase observed in the overall population. Conversely, there was no impact of patient age on the incidence of VA (Fig. 4B).

Discussion

The main results of this study, focusing on ICD recipients observed with remote monitoring during the COVID-19 pandemic, are as follows: (1) ICD recipients, especially men, presented a sudden increase in VAs, especially ventricular tachycardia events, during the 2 weeks before the lockdown order; (2) once confinement was ordered, a significant decrease in VA incidence was observed, returning to its baseline values; (3) mean heart rate and mean activity level per day were significantly reduced during the 11 weeks of confinement; and (4) no changes were observed regarding the occurrence of atrial arrhythmias during the study period.

The occurrence of VA during the COVID-19 pandemic has been mainly investigated through the incidence of OHCA. Indeed, in a French analysis, the occurrence of OHCA during the pandemic period (16 March to 26 April 2020) was compared with an equivalent time period in the years before the pandemic [5]. The authors observed a transient two-fold increase in OHCA incidence, coupled with a reduction in survival during the COVID-19 pandemic. However, only 9.2% of these patients had a shockable rhythm (i.e. ventricular tachycardia or fibrillation) at the time of emergency

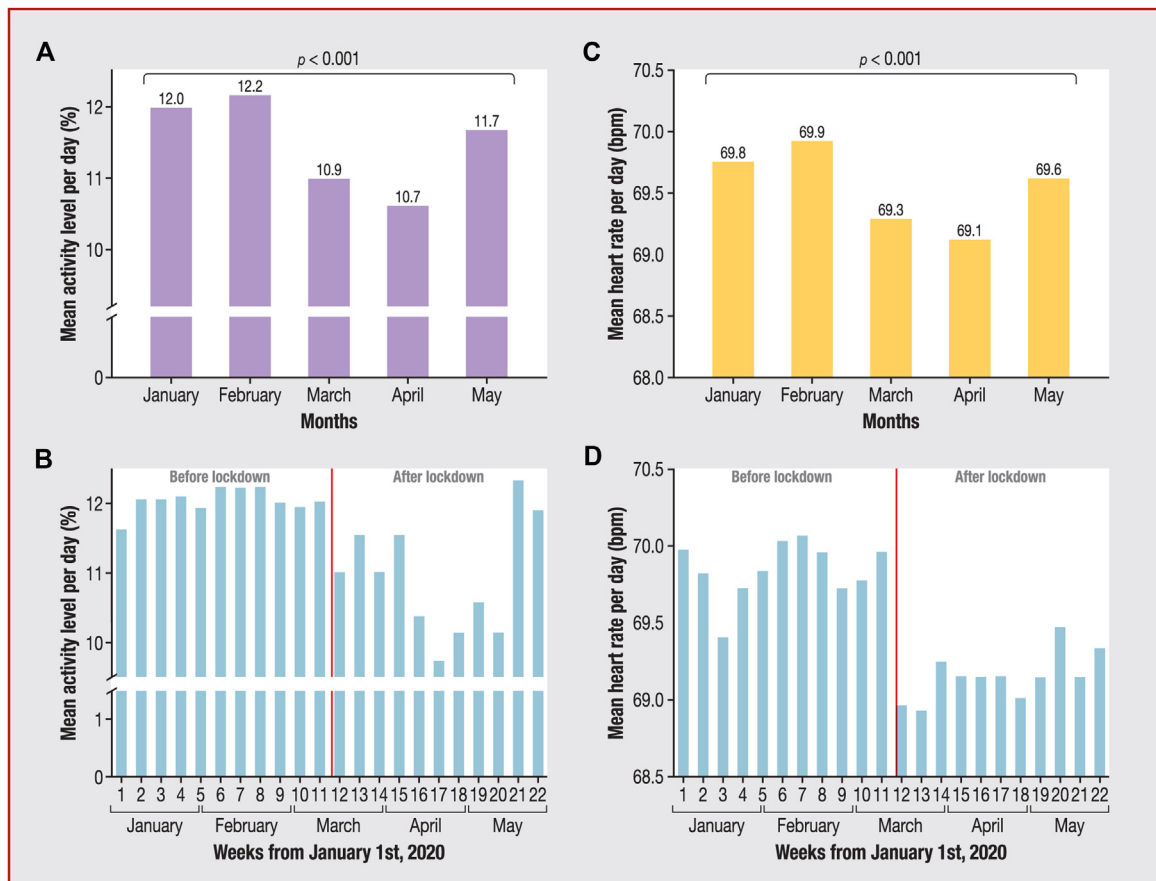


Figure 2. A. Mean activity level per month. B. Mean activity level per week. C. Mean heart rate per month. D. Mean heart rate per week.

medical service arrival, significantly less than the years before, and, consequently, most of these OHCA presented with non-shockable rhythms. Similarly, in the Lombardy region of Italy, the cumulative incidence of OHCA has been strongly correlated to the cumulative incidence of COVID-19 [9]. However, the causes of OHCA were not reported by authors. Recently, the outcomes of 278 OHCA have been investigated in the USA during the COVID-19 pandemic, and shockable rhythm (ventricular tachycardia or fibrillation) was rarely the cause of OHCA, being seen only in 23% of the cases [10]. In these studies, the authors suggested that these findings could be directly related to the COVID-19 infection itself, as well as indirectly, through the lockdown behaviour changes, overwhelming of emergency medical services or clinical visit rescheduling [5]. Nonetheless, these results highlight that the increased incidence in OHCA observed during this period was not related to a higher incidence of VA events, but more to non-shockable rhythms (i.e. as a result of OHCA occurring in hypoxaemic patients with COVID-19 or pulseless electrical activity in patients with acute myocarditis and advanced cardiac injury).

Our study specifically focused on the incidence of cardiac arrhythmias in ICD recipients during the COVID-19 period. Importantly, our study retrospectively analysed a large ICD population, and all manufacturers with a remote monitoring system were included, representing real-world data. We found a sudden increase in the incidence of VA during the 2 weeks before the lockdown order, followed by a significant

decrease in VA events during the confinement period. One may hypothesize that this variation in VA incidence could be related to the stress generated by the outbreak experience. Indeed, the 2 weeks before the lockdown order were specifically associated with stressful media coverage of the pandemic in France, including the first COVID-19 death in the country, the epidemic stage 2 and then stage 3, the first televised presidential allocation, followed by a high number of COVID-19 cases and deaths. These events could potentially have led to a stressful situation, increasing the incidence of VA in ICD recipients. This hypothesis may be supported by the increased incidence of VA in parallel with the sudden rise in the percentage of live-stream television coverage of COVID-19 information. These data potentially suggest the stressful impact of massive media information on ICD recipients. Of note, almost 75% of the study cohort were aged > 60 years, a population known to be at risk of contracting severe COVID-19, especially those with underlying cardiac disease [11]. These characteristics could potentially increase the stress of contracting the infection in this population, resulting in a higher incidence of VA. Indeed, chronic and acute psychosocial stresses are associated with cardiac arrhythmic risk [12], and a recent analysis clearly showed that during the outbreak, patients at risk were extremely worried about contracting COVID-19 [13]. Lastly, we did not observe any relationship between the incidence of VA and the increased number of COVID-19 cases, suggesting that the occurrence of VA is not related to the infection itself.

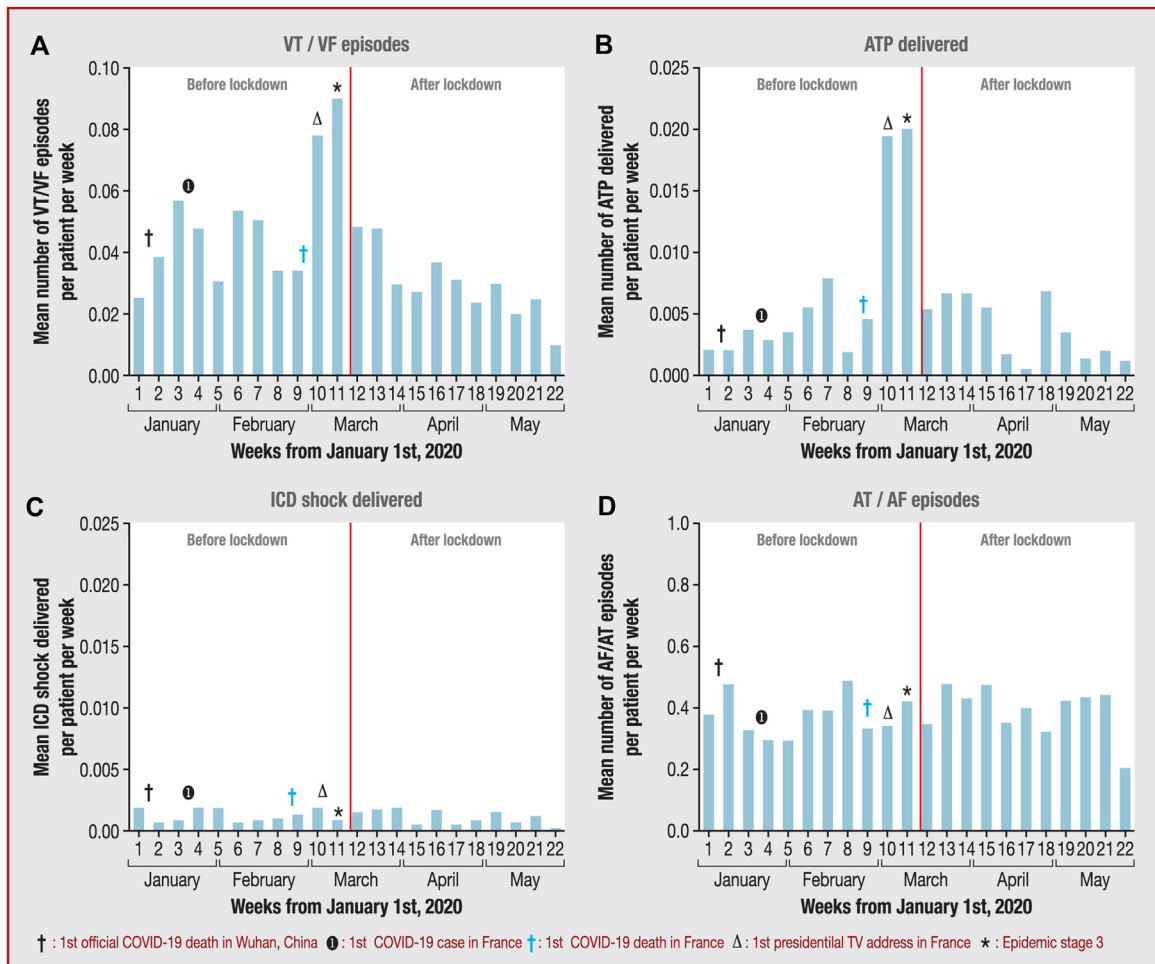


Figure 3. A. Incidence of ventricular arrhythmias during the 22-week follow-up. B. Incidence of implantable cardioverter defibrillator (ICD)-delivered therapy (antitachycardia pacing [ATP]) per week. C. Incidence of ICD-delivered therapy (shock) per week. D. Incidence of atrial fibrillation (AF)/atrial tachycardia (AT) episodes per week. COVID: coronavirus disease 2019; TV: television; VF: ventricular fibrillation; VT: ventricular tachycardia.

Similar results have been published recently in a large ICD population in the USA. Authors demonstrated a 32% reduction in VA needing ICD therapies following implementation of lockdown measures. Interestingly, compared with a control period, significantly fewer VA events occurred during the COVID-19 pandemic. These data implicate a potential role for real-life stressors in VA burden in patients with ICD [14]

Interestingly, we also observed a significant decrease in VA incidence during the lockdown period. It has previously been found that patients significantly modified their daily habits during the confinement. Indeed, among an Italian cohort of 24 ICD recipients, a statistically significant reduction of physical activity was recorded during home quarantine [15]. Similarly, we showed that patients decreased their daily activity level, associated with a significant reduction of their mean heart rate, potentially suggesting a less “proarrhythmogenic” sympathetic nervous system during the confinement. It is well established that the autonomic nervous system plays a crucial role in the pathogenesis of VA, and sympathetic overstimulation

may trigger VA episodes [16]. Based on this data, one may hypothesize that the lifestyle change, with lower physical activity levels, could directly impact the occurrence of VA, with a reduction of sympathetic tone. Additionally, the lockdown period generated a sizable reduction in social activities, limiting the risk of COVID-19 infection and potentially decreasing the anxiety of being infected. Our cohort was specifically at risk of severe COVID-19 disease, and the stress and anxiety of contracting the virus may have been reduced during the quarantine, thereby limiting the occurrence of VA.

Study limitations

Our study has several limitations. First, we did not know the proportion of patients infected with the COVID-19 and the potential correlation between the occurrence of VA and having COVID-19 itself. However, all patients regularly transmitted remote monitoring ICD information, suggesting that a large part of the cohort was at home and not hospitalized during the study period. Second, we did not collect

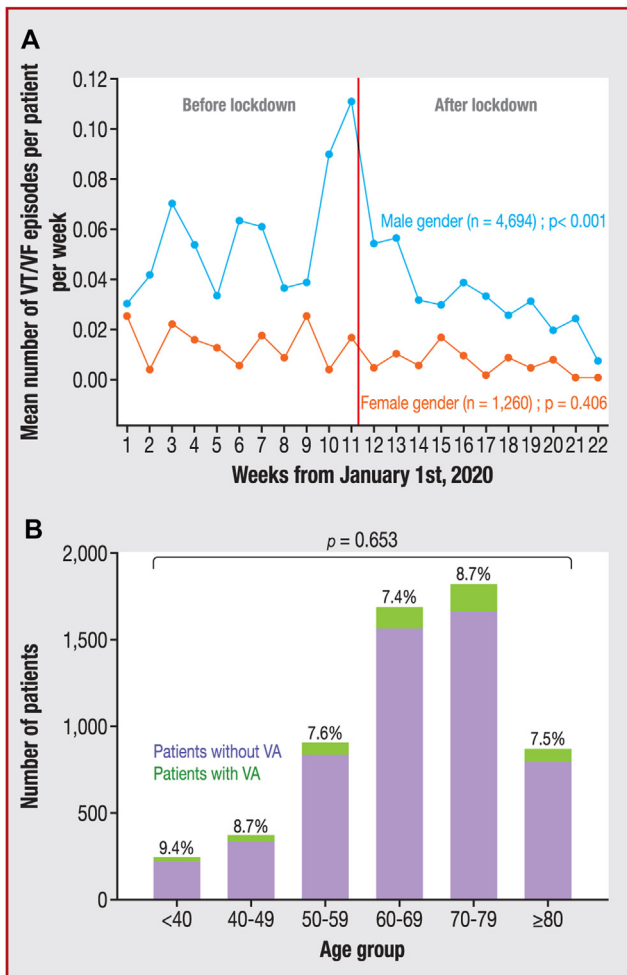


Figure 4. A. Incidence of ventricular arrhythmia (VA) episodes during the 22-week follow-up, depending on sex category. B. Proportion of patients with VA in each age category. VF: ventricular fibrillation; VT: ventricular tachycardia.

the ICD device programming, and were unable to obtain data regarding VA detection/treatment zones. Nonetheless, we assumed that device programming was left unchanged during the study period and, consequently, each patient was their own control over the 22 weeks of follow-up. Furthermore, in patients with a unique ventricular fibrillation detection zone, some VAs may have been undiagnosed, somehow underestimating the real incidence of VA. Third, only 2020 data were available and unfortunately, we cannot compare the incidence of VA observed during the pandemic with previous years. Lastly, additional clinical data were not available for confidentiality reasons (such as the underlying cardiomyopathy, cardiovascular risk factors and history of previous VA), limiting an extensive description of the population.

Conclusions

The COVID-19 pandemic had an impact on the occurrence of VA in ICD recipients: an increase in the incidence of VA during the 2 weeks before the lockdown order was observed, followed by a significant reduction during the following 11

weeks of confinement. No changes were observed for atrial arrhythmias. Intense stress generated at the beginning of the pandemic and changes in daily habits, with decreased physical activity, may explain such variation.

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None.

Disclosure of interest

The authors declare that they have no competing interest.

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