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Signa Vitae

ORIGINAL RESEARCH

Electrocardiogram changes during the induction of ventricular fibrillation and resuscitation in a rabbit cardiac arrest model induced by esophageal electrodes

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Abstract

Background: Although the ventricular fibrillation (VF) cardiac arrest (CA, VFCA) rabbit model is very widely used, research on electrocardiogram (ECG) changes during the establishment of the VFCA model remains scarce. This study aimed to explore the impact of stimulation time and pattern on VF occurrence during the VFCA rabbit model establishment and to examine ECG characteristics alongside real-time dynamic blood pressure (BP) throughout the stimulation and resuscitation phases. **Methods**: VFCA was induced in male New Zealand rabbits using a transesophageal-chest wall electrode with 50 V 30 Hz alternating current. Rabbits were subjected to electrical stimulation for durations of 30 s, 45 s or 60 s. If initial stimulation failed to induce 3-min CA, rabbits were reassigned to either intermittent or continuous stimulation until a 3-min CA was achieved. **Results**: The study conducted 88 electrical stimulations on 42 male New Zealand rabbits to induce 3-min CA, with 32 rabbits (76.2%) requiring one or two stimulations to achieve this. Of the 88 stimulations, 77 (87.5%) successfully induced CA, including 73 (83.0%) cases of VF. An analysis of 42 initial stimulations revealed 35 VFs, with 13 instances leading to a 3-min CA. The 30 s and above-30 s of stimulation time groups exhibited 8 and 27 VF occurrences ($\chi^2 = 1.890$, $p = 0.169$) and 2 and 11 3-min CA events ($\chi^2 = 0.805$, $p = 0.370$), respectively. Except for the initial stimulation, 46 stimulations were given, including 20 intermittent stimulations and 26 continuous stimulations, which resulted in 17 and 21 VFs ($\chi^2 = 0.000$, $p = 1.000$) and 13 and 16 3-min CA events ($\chi^2 = 0.058$, $p = 0.809$), respectively. In addition, a significant difference in stimulation time was observed between the intermittent and continuous stimulation groups. **Conclusions**: Our results provide important insights that could be used to improve the success rate of establishing VFCA rabbit models.

Keywords

Ventricular fibrillation; Cardiac arrest; Esophageal-chest; Electrocardiogram; Rabbits

1. Introduction

Cardiac arrest (CA) is defined as the cessation of cardiac mechanical activity, confirmed by the absence of a detectable pulse [1]. Despite advancements in cardiopulmonary resuscitation (CPR), overall survival rates continue to be unsatisfactory [2–4]. In China, only 1.8% of patients who experience out-of-hospital cardiac arrest (OHCA) survive until they are discharged from the hospital [5].

Ventricular fibrillation cardiac arrest (VFCA) and asphyxia cardiac arrest (ACA) are the most commonly used animal CA models [1, 2]. To date, most studies have focused on VFCA, revealing significant differences in outcomes compared to those observed using ACA models [1, 2, 6]. The VFCA model is extensively applied in rabbit studies [7, 8]. Despite the widespread use of the VFCA rabbit model, investigations into electrocardiogram (ECG) alterations during VF induction and subsequent resuscitation are scarce. Current research primarily examines VF waveform following electrical stimulation, and ECG modifications due to effective electrical stimulation [2, 7–11]. Additionally, most previous studies provide unclear axis variables on the ECG and blood pressure (BP) graphs, rendering them unsuitable for educational purposes in ECG interpretation. Furthermore, there is an absence of standardized criteria for stimulation duration and pattern across animal studies, with reported stimulation times ranging from 5 s to 180 s [1–4, 6–17].

Considering the substantial differences between human and rabbit ECGs, our present study aimed to improve the success rate of establishing VFCA rabbit models using a transesophageal-chest wall electrode with a 50 V 30 Hz alternating current by examining the ECG alterations and the

association between the duration and pattern of stimulation and the induction of VF.

2. Materials and methods

2.1 Experimental animals

The study was conducted in Room B709 at the Basic Experimental Laboratory, Wenzhou Medical University. Experimental subjects, consisting of 42 clean-grade, healthy adult male New Zealand rabbits (weighing 1.7–3.0 kg, aged 12–18 weeks), were purchased from the Hangzhou Fuyang Hongfeng Rabbit Farm. These rabbits were randomly divided to undergo electrical stimulation for 30 s, 45 s or 60 s according to the results after the researcher opened the sealed, opaque envelope containing the results of randomization by one of the investigators. If the initial stimulation (step 1) failed to induce CA for a period of 3 min, the rabbits were randomly subjected to either intermittent stimulation or continuous stimulation (step 2) until a 3-min CA was induced.

2.2 Preparation and processing of animal models

2.2.1 Surgical operation

After weighing the male New Zealand rabbits, a 24G closed intravenous catheter was inserted into the ear marginal vein. Anesthesia was induced by injecting 25% and 4 mL/kg urethane (C14988772, MacLean Biochemical Technology Co., Ltd, Shanghai, China) into the catheter. After the confirmation of effective anesthesia, the animal was placed in a supine position, and their limbs were fixed to the operating table, and their chest hairs were removed for electric stimulation and defibrillation. Subcutaneous 3-lead ECG was inserted into limb leads, and a 22G closed intravenous catheter was inserted into the femoral artery and flushed intermittently with saline containing 5 U/mL heparin to prevent clotting. The end of the subcutaneous 3-lead ECG was connected to an RM6240 transducer (Chengdu Instrument Factory, Chengdu, Sichuan, China), and the ECG and BP were monitored on a computer screen. Blind intubation was performed using a No. 2.5 uncuffed tracheal tube (Shaodai Medical Device Co., Ltd, Nanchang, China). The duration time of this step was 30–40 min, and the anesthesia dose was 13.21 $\pm$ 2.01 mL.

2.2.2 Induction of VF and CPR

An esophageal electrode was positioned to a depth of 17 cm, and a one-and-a-half-inch acupuncture needle was inserted subcutaneously at the site where cardiac activity was most audibly distinct, establishing a current pathway. Subsequently, a 50 V 30 Hz alternating current was applied for continuous electrical stimulation. After the onset of electrical stimulation, the artery pulse waveform disappeared, and the arterial BP dropped rapidly below 25 mmHg. After electrical stimulation for 30–60 s, the ECG and BP are observed. In the absence of VF on the ECG, either random intermittent or continuous stimulation was used until VF was evident on the ECG. Upon confirmation of VF on the ECG, the rabbit was left unattended for 3 min. If CA did not occur within this period, the procedure was repeated as previously described to induce a 3 min duration of CA. Subsequent to this phase, resuscitation efforts were initiated, involving tracheal intubation, chest compression, defibrillation, and the administration of adrenaline [12, 18, 19]. Tracheal intubation with assisted ventilation was given using an HX-300 animal ventilator (Taimeng Technology Co., Ltd, Chengdu, China) set to 45 breaths per min and a tidal volume of 15 mL/kg. Chest compression were immediately started at a rate of 200 per min, compressing to a depth of one-third the chest wall thickness and maintaining a 1:1 compression-to-relaxation ratio (Fig. 1A). In cases of VF, defibrillation was performed using a SHINOVA DM8A-II animal defibrillator (SHINOVA, Shanghai, China) at 5–10 J/kg using a biphasic waveform, followed by continued chest compression (Fig. 1B). Adrenaline was administered intravenously through the ear vein at a dose of 20 μg/kg. Each resuscitation cycle lasted 2 min and continued until either successful resuscitation was achieved (Fig. 1C,D) or attempts were ceased. Rabbits that survived until the end of the observation period were euthanized via lethal injection of urethane. The experimental protocol is summarized in Fig. 2.

2.3 Collection of ECG indicators and methods

The ECG and BP were monitored using limb leads and femoral arterial catheterization, respectively. The end of the arterial catheter was connected to an RM6240 biological signal acquisition and processing system. Pulse rate and invasive BP parameters (systolic, diastolic and mean) were recorded directly from the monitoring system onto a standardized data collection template. The recording speed for both ECG and BP waveforms was set at 20 milliseconds per division (ms/div).

2.4 Definition of terms

CA was identified by the absence of an arterial pulse, accompanied by a BP decrease to below 25 mmHg [7, 9, 10]. Return of spontaneous circulation (ROSC) was characterized by the establishment of a self-sustaining rhythm, with a mean arterial pressure (MAP) of 60 mmHg or higher, and successful resuscitation persisting for more than 10 min [3, 9, 11]. The initial stimulation refers to the first instance of electrical stimulation applied immediately following the preparation of animal models. Intermittent stimulation occurs when an initial stimulation fails to induce CA, with subsequent stimulation commencing 30 min after vital signs have stabilized [9, 18]. Continuous stimulation was applied when an initial stimulation did not result in CA, with the following stimulation initiated without delay. Abandonment of rescue was considered when resuscitation extended beyond 10 min, the BP fell below 20 mmHg, pulseless electrical activity (PEA) was observed on the ECG, and there was no response to chest compression and adrenaline administration [2, 9, 18, 19].

2.5 Statistical methods

SPSS 20.0 (International Business Machines Corporation, Armonk, NY, America) was used for data analysis. Numerical data are expressed as mean $\pm$ standard deviation, and categorical data are expressed as n (%). A student's *t*-test was

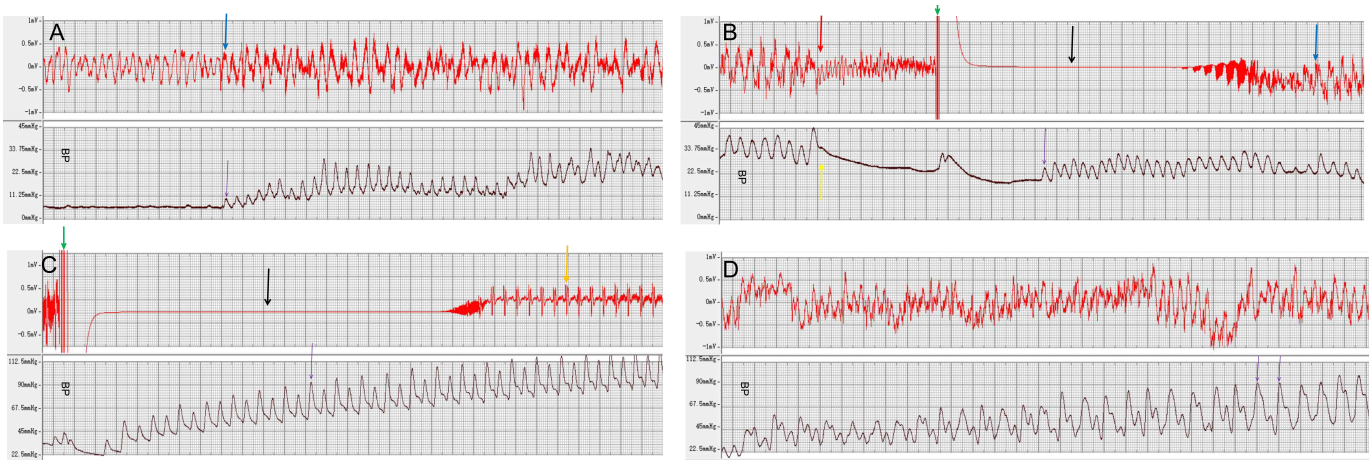

FIGURE 1. ECG wave and arterial pulse wave during CPR and ROSC. (A) When compression started, the ECG displayed a compression waveform (indicated by a blue arrow), accompanied by an increase in blood pressure (BP, purple arrow). (B) Ceasing compression resulted in the disappearance of the BP waveform (yellow arrow), while the ECG indicated VF (red arrow). Subsequently, defibrillation commenced (green arrow). Following defibrillation, compression was promptly resumed (purple arrow), and ECG exhibited a transient blank area (black arrow) before returning to a compression waveform (blue arrow). (C) ROSC after defibrillation. After defibrillation (green arrow), BP increased rapidly above 90 mmHg (purple arrow). The ECG showed a blind area (black arrow) and then showed a self-maintained rhythm (orange arrow). (D) ROSC after compression. BP slowly increased above 90 mmHg with continuing compression (purple arrow). Abbreviations: ECG, electrocardiogram; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; ROSC, return of spontaneous circulation; BP, blood pressure.

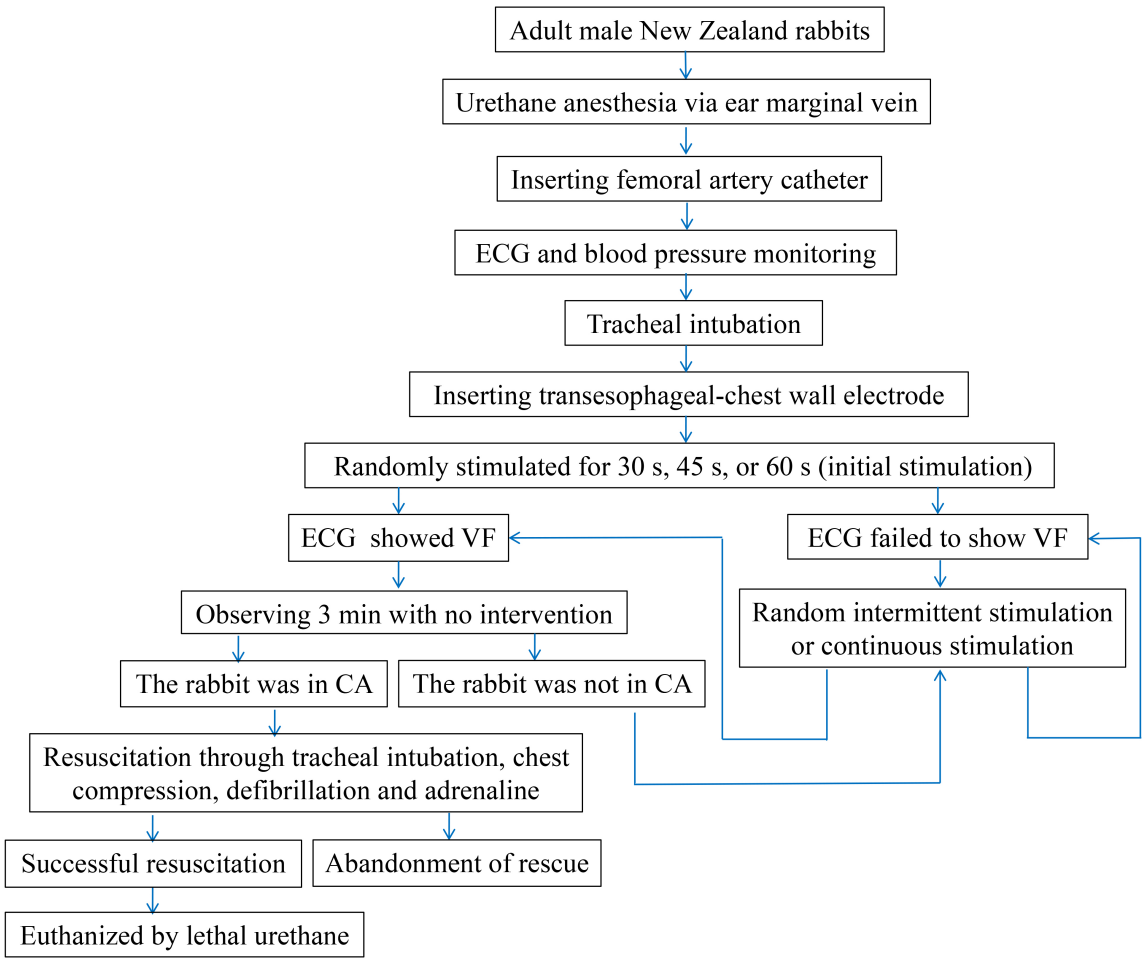

FIGURE 2. The diagram of the experimental protocol. Abbreviations: ECG, electrocardiogram; VF, ventricular fibrillation; CA, cardiac arrest.

used to compare the continuous variables between the 30 s and above-30 s groups in the initial stimulation. The chi-square test (all theoretical frequencies $\geq$5), continuity-adjusted chi-square test (1 $\leq$ minimum theoretical frequency $<$ 5), and Fisher's exact test (minimum theoretical frequency $<$1) were used to evaluate and compare the 30 s and above-30 s groups in the step 1 and the intermittent stimulation and continuous stimulation groups in the step 2. Differences with a $p < 0.05$ were considered statistically significant.

3. Results

3.1 Basic information

The study involved 42 New Zealand male white rabbits, with an average weight of 2546.14 $\pm$ 235.28 g. After the induction of full anesthesia, the measured invasive systolic BP was 115.24 $\pm$ 12.48 mmHg, diastolic BP was 86.33 $\pm$ 10.59 mmHg, and the heart rate was 298.79 $\pm$ 25.90 beats per min. To induce a 3-min duration CA, a total of 88 electrical stimulations were administered to all rabbits (Fig. 3). Among these, 32 rabbits (76.2%) underwent one or two stimulations (with 13 rabbits receiving a single stimulation and 19 rabbits receiving two stimulations). The remaining 10 rabbits required three or more stimulations to achieve the desired outcome (5 received three stimulations, 3 received four stimulations and 2 received five stimulations).

3.2 ECG manifestation after electrical stimulation

Of the 88 electrical stimulations, 77 (87.5%) successfully induced CA, while 11 (12.5%) did not (Fig. 4). Of the successful CA inductions, ECG monitoring identified 73 (83.0%) instances of VF (Fig. 5A), which included 68 initial rhythm VFs and 5 cases of pulseless ventricular tachycardia (VT, Fig. 5B). Additionally, there were 3 instances of PEA (Fig. 5C), and 1 instance of asystole (Fig. 5D). Among the non-CA cases, there were 5 instances of sinus bradycardia (Fig. 5E), 2 instances of escape rhythm (Fig. 5F), 2 instances of premature beats (Fig. 5G), and 2 instances of normal rhythm. All non-CA instances were a result of electrical stimulations that lasted for 30 s.

3.3 Relationship between electrical stimulation and VF

Among the forty-two rabbits subjected to a total of 88 electrical stimulations, there were 73 instances (83.0%) of VF. Relationship between stimulation time and VF is shown in Table 1. During the initial round of stimulation applied to all 42 rabbits, 35 experienced VF, leading to 13 occurrences of a 3-min CA (Fig. 3). Analysis between the groups subjected to 30 s and above-30 s of stimulation time revealed 8 versus 27 VFs (χ^2 = 1.890, p = 0.169) and 2 versus 11 3-min CA events (χ^2 = 0.805, p = 0.370), respectively (Table 2).

Excluding the initial stimulation, 46 additional stimulations were administered, comprising 20 intermittent and 26 continuous stimulations. These led to VFs 17 and 21 times (χ^2 = 0.000, p = 1.000) and resulted in 3-min CAs 13 and 16 times (χ^2 = 0.058, p = 0.809), respectively (Fig. 3). Of the 38 stimulations resulting in VF, the distribution was as follows: 8 from 30 s of intermittent stimulation, 5 from 45 s of intermittent stimulation, 4 from 60 s of intermittent stimulation, 14 from 30 s of continuous stimulation, 7 from 45 s of continuous stimulation, and none from 60 s of continuous stimulation (χ^2 = 7.116, p = 0.029). Comparisons of different stimulation patterns in step 2 are shown in Table 3.

3.4 ECG manifestation during CPR

During CPR, ECG monitoring revealed that 36 rabbits (85.7%) exhibited VF, 1 rabbit presented with pulseless VT, 3 rabbits demonstrated PEA, and 2 rabbits were found in asystole.

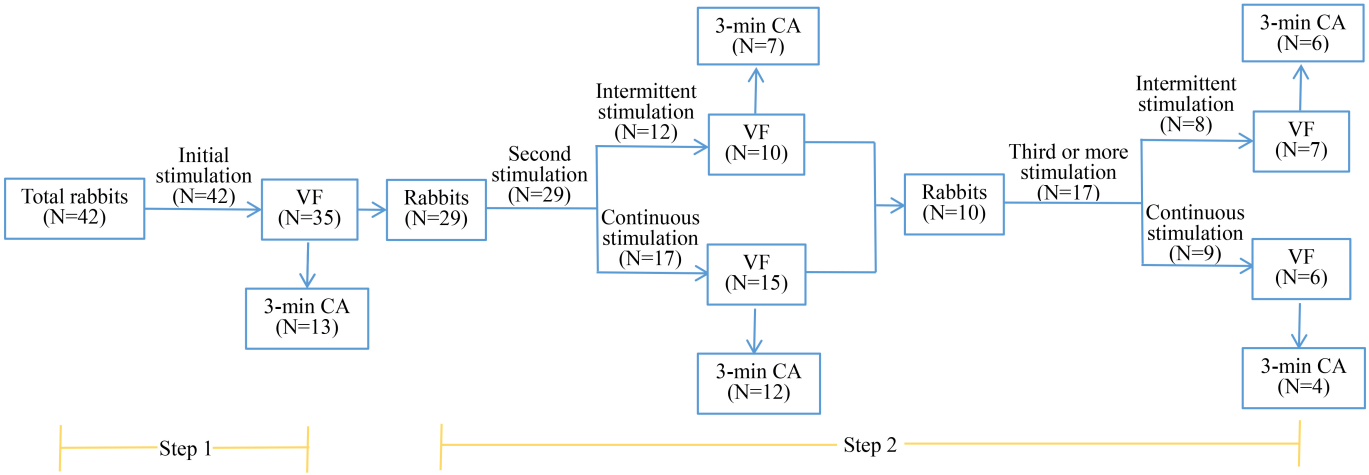

FIGURE 3. Relationship between the rabbits and the events. Forty-two rabbits were subjected to an initial round of stimulation, resulting in 35 instances of VF and 13 cases experiencing CA for 3 min. Of the remaining 29 rabbits (42 initially minus the 13 with 3-min CA), a second stimulation was applied. This led to 25 additional instances of VF and 19 cases (7 from intermittent stimulation plus 12 from continuous stimulation) experiencing CA for 3 min. Abbreviations: VF, ventricular fibrillation; CA, cardiac arrest.

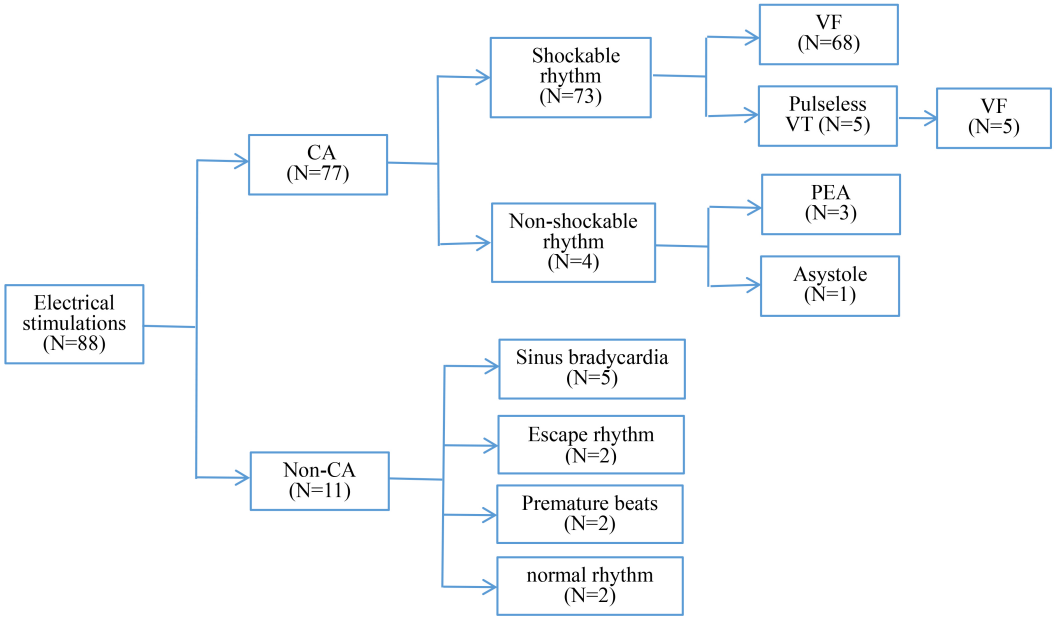

FIGURE 4. ECG manifestations after electrical stimulation. Of the 88 electrical stimulations, 77 (87.5%) induced CA, while 11 (12.5%) did not. ECG monitoring in the CA cases revealed 73 (83.0%) instances of VF, including 68 initial rhythms and 5 pulseless VTs. Abbreviations: ECG, electrocardiogram; CA, cardiac arrest; VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity.

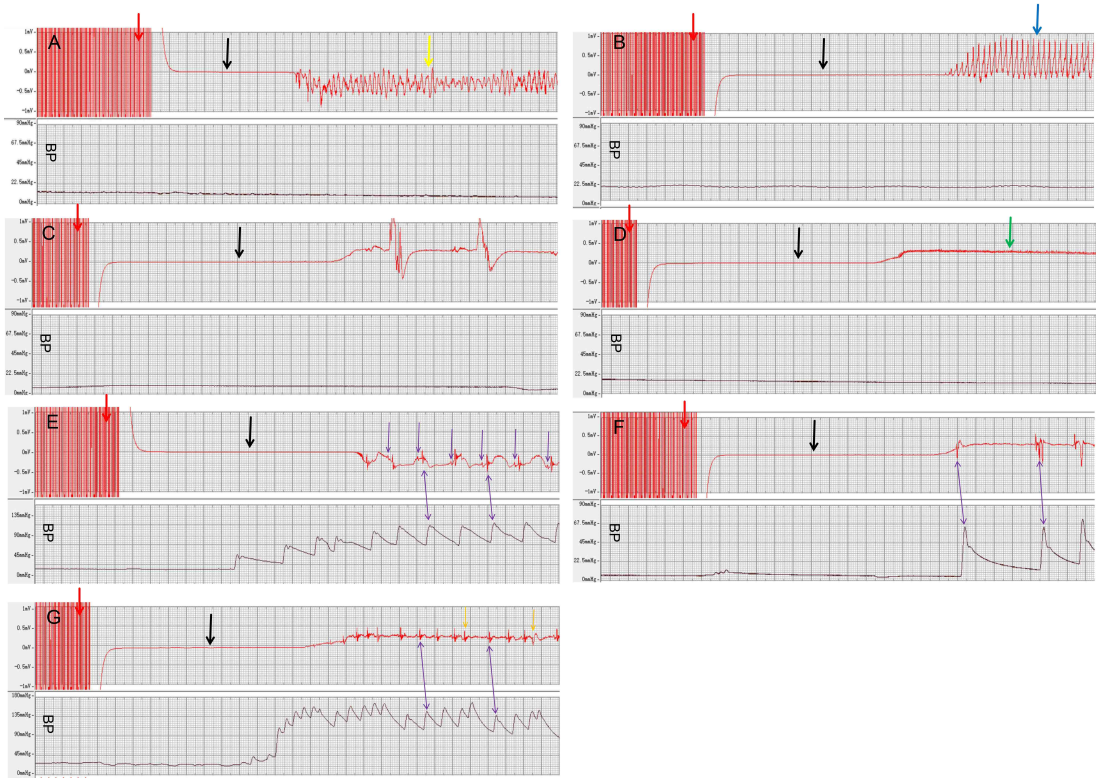

FIGURE 5. ECG wave and arterial pulse wave after electrical stimulation. Following the cessation of electrical stimulation (red arrow), an ECG blind period lasting approximately 5 s was observed (black arrow). Subsequently, the ECG demonstrated various arrhythmias: (A) VF (yellow arrow), (B) pulseless VT (blue arrow), (C) PEA, (D) asystole (green arrow), (E) sinus bradycardia, (F) escape rhythm, and (G) premature beats (orange arrow). (A–D) were occurring with blood pressure (BP) below 25 mmHg, while (E–G) were occurring with BP above 60 mmHg. The purple arrow represents the P wave, and the double purple arrow represents that the QRS wave peak is related to systolic pressure. Abbreviations: ECG, electrocardiogram; VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity; BP, blood pressure.

TABLE 1. Relationship between stimulation time and VF.

Events	Total stimulation that led to VF (N = 73)			Initial stimulation that led to VF (N = 35)			The second stimulation that led to VF (N = 25)			The third or more stimulation that led to VF (N = 13)		
	30 s (N = 30)	45 s (N = 36)	60 s (N = 7)	30 s (N = 8)	45 s (N = 24)	60 s (N = 3)	30 s (N = 12)	45 s (N = 11)	60 s (N = 2)	30 s (N = 10)	45 s (N = 1)	60 s (N = 2)
<20 s VF	6	8	1	2	7	1	1	1	0	3	0	0
20–39 s VF	4	5	1	3	5	1	1	0	0	0	0	0
40–59 s VF	2	2	0	1	2	0	1	0	0	0	0	0
≥60 s VF	18	21	5	2	10	1	9	10	2	7	1	2
3-min CA	17	20	5	2	10	1	8	9	2	7	1	2

VF, ventricular fibrillation; CA, cardiac arrest.

TABLE 2. Comparisons of different stimulation time in step 1 (initial stimulation).

Variables	30 s (N = 12)	Above-30 s (N = 30)	t/χ^2	p
Basic information				
Body weight (g)	2487.17 ± 250.98	2569.73 ± 228.81	−1.028	0.310
Systolic BP (mmHg)	116.08 ± 14.22	114.90 ± 11.97	0.274	0.785
Diastolic BP (mmHg)	81.67 ± 10.41	88.20 ± 10.24	−1.859	0.070
Heart rate (beats per min)	296.33 ± 26.91	299.77 ± 25.88	−0.384	0.703
VF	8 (66.7%)	27 (90.0%)	1.890	0.169
<20 s VF	2 (16.7%)	8 (26.7%)	0.082	0.775
20–39 s VF	3 (25.0%)	6 (20.0%)	0.000	1.000
40–59 s VF	1 (8.3%)	2 (6.7%)	-	1.000
≥60 s VF	2 (16.7%)	11 (36.7%)	0.805	0.370
3-min CA	2 (16.7%)	11 (36.7%)	0.805	0.370

BP, blood pressure; VF, ventricular fibrillation; CA, cardiac arrest.

TABLE 3. Comparisons of different stimulation patterns in step 2.

Parameters	All stimulations		χ^2	p	Stimulations that led to VF		χ^2	p
	Intermittent stimulation (N = 20)	Continuous stimulation (N = 26)			Intermittent stimulation (N = 17)	Continuous stimulation (N = 21)		
VF	17 (85.0%)	21 (80.8%)	0.000	1.000	-	-	-	-
Stimulation time								
30 s	11 (55.0%)	19 (73.1%)			8 (47.1%)	14 (66.7%)		
45 s	5 (25.0%)	7 (26.9%)	7.255	0.027	5 (29.4%)	7 (33.3%)	7.116	0.029
60 s	4 (20.0%)	0 (0.0%)			4 (23.5%)	0 (0.0%)		
3-min CA	13 (65.0%)	16 (61.5%)	0.058	0.809	13 (76.5%)	16 (76.2%)	0.000	1.000

VF, ventricular fibrillation; CA, cardiac arrest.

4. Discussion

CA remains a significant health challenge globally [4, 20]. The main cause of sudden cardiac death is malignant arrhythmias [21, 22]. The initial rhythm in 75–80% of CA cases is VF [7, 9, 21]. VFCA, a shockable CA, has a favorable prognosis, with a high rate of ROSC and positive neurological status at discharge, making it a focal point in clinical research [20–24]. VF can be easily replicated in experimental animals through electrical stimulation of the heart [3]. Compared to other methods, such as right ventricular endocardial stimulation, transesophageal-chest wall electrical stimulation is easier to perform, less invasive, and more reproducible [3, 7].

The VFCA model is commonly used in research involving rats, rabbits, and pigs due to its adaptability and the specific advantages each animal model offers [1–4, 6–17]. Among these animals, rabbits offer specific advantages [7, 8]. The application of the VFCA rabbit model is widespread, supporting a variety of research objectives [3, 7–9, 12–14, 19]. Boissady *et al.* [12] used a VFCA rabbit model to investigate the inhibitory

role of high-mobility group Box 1. Li *et al.* [13] used a VFCA rabbit model to study current-based defibrillation with biphasic waveforms. Our previous study [14] used a VFCA rabbit model to study cerebral protection of erythropoietin.

Arrhythmias and ECG parameters are extensively utilized across various rabbit models [25–31]. Azam *et al.* [25] examined the impact of Empagliflozin on VF using an ischemia-reperfusion rabbit model. Freeman *et al.* [26] applied a novel approach to study ECG parameters and arrhythmias in a myocardial infarction rabbit model. Research on ECG and CA-CPR is frequently interconnected [20, 22–24, 30, 32], with investigations into rabbit ECG and CA-CPR gaining significant interest. Dietrichs *et al.* [33] discovered a correlation between rabbit QRS interval/corrected QT-interval (QTc) values and the risk of VF, suggesting the potential of QRS/QTc as a novel biomarker for predicting CA.

Compared to previous studies, our research highlights that ECG changes during the induction of VF and resuscitation in the VFCA rabbit model are very rare. It is generally accepted that a thorough understanding of these changes is vital for improving modeling success rates. Our study presents several useful findings as follows: (1) At the onset of electrical stimulation, the arterial pulse waveform disappeared, and the arterial BP swiftly dropped below 25 mmHg. If these changes are not observed within 10 s after stimulation, the stimulation should be stopped and the needlepoint's position adjusted [10, 18]. (2) At the end of electrical stimulation, various ECG changes were observed (Fig. 5), the most common of which was VF [7, 19]. Additionally, some non-CA ECG changes were noted, such as sinus bradycardia (Fig. 5E), escape rhythm (Fig. 5F), and premature beats (Fig. 5G). These could be easily confused with PEA. The primary distinguishing features were the invasive artery pulse and its waveform. It is important to note that the QRS wave peak correlates with systolic pressure (Fig. 5E–G). (3) Attention should be paid to the differences between the normal VF waveform and the compression waveform. The compression waveform features thicker lines and darker colors compared to the VF waveform, with BP fluctuation evident during compression (Fig. 1A,B). (4) The increasing trend was more rapid and observable in BP at ROSC after defibrillation (Fig. 1C) than compression (Fig. 1D). Thus, understanding these changes is important for improving the success rate of establishing the model.

In the process of establishing the VFCA rabbit model, various studies have employed different stimulation methods and durations [3, 7, 9, 12]. In our approach, we utilized esophageal and chest wall electrical stimulation (50 V, 30 Hz alternating current) and determined that a longer initial stimulation duration is beneficial; we suggest that durations exceeding 30 s, such as 45 s, may be optimal for our model. If the initial stimulation does not induce 3-min CA, intermittent stimulation may be reapplied for the same or slightly longer duration than previously. Conversely, continuous stimulation could be applied for a slightly shorter duration (*e.g.*, 30 s) than the initial attempt, which may yield better outcomes. Notably, to minimize group differences in intervention studies, rabbits subjected to more than two stimulations should be excluded [10]. In our research, 32 rabbits (76.2%) successfully reached 3-min CA with one or two stimulations.

Regarding the incidence of VF in the VFCA rabbit model after electrical stimulation, Wang *et al.* [19] investigated transcutaneous electrical myocardial stimulation (50 Hz for 3 min) and reported VF in 15 cases (60.0%) after electrical stimulation. Huang *et al.* [7] utilized a transesophageal-chest wall electrode (35 mA, 50 Hz, 60 s) and observed VF in 15 cases (100.0%) after the initial ECG monitoring post-stimulation, and 11 cases (73.3%) exhibited VF at the start of CPR. In contrast, our study achieved 100.0% incidence of VF after electrical stimulation in 42 rabbits, with 36 (85.7%) showing VF at the onset of CPR. These findings suggest that a deeper understanding of ECG changes during VF induction and resuscitation could significantly improve outcomes in VFCA rabbit models.

There are several limitations to our study. First, the ECG exhibited a blind spot lasting approximately 5 s following electrical stimulation or defibrillation. Second, this experiment is inherently preliminary. The study did not sufficiently explore the differences in stimulation time between intermittent and continuous stimulation. Third, our study did not include the basal ECG parameters, such as QRS morphologies, QT intervals, and T wave features.

5. Conclusions

In establishing the VFCA rabbit model using a transesophageal-chest wall electrode, diverse ECG changes occur during VF induction and resuscitation. Enhancing the success rate of model establishment and the incidence of VF following electrical stimulation necessitates a comprehensive understanding of these ECG alterations. The key to this process is extending the initial stimulation duration beyond 30 s, with subsequent continuous stimulation periods being shorter than those for intermittent stimulation. This approach could be instrumental in improving both the VF occurrence rates post-stimulation and the overall success rate of the model's establishment.

ABBREVIATIONS

VF, ventricular fibrillation; CA, cardiac arrest; VFCA, ventricular fibrillation cardiac arrest; ECG, electrocardiogram; BP, blood pressure; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; ACA, asphyxia cardiac arrest; ROSC, return of spontaneous circulation; MAP, mean arterial pressure; PEA, pulseless electrical activity; VT, ventricular tachycardia; QTc, corrected QT-interval.

AVAILABILITY OF DATA AND MATERIALS

The datasets that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

JZC, WXS, HPL, WJH, SQC, ZPL and YLL—conception and design of the study. JZC, XRD and YLL—searched the literature, analysed the data, and wrote the manuscript.

JZC, WXS and YLL—drew the figures. JZC, WXS, QC and YLL—developed experimental protocol and participated in the experiments. All authors read and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All animal experiments were conducted according to the ARRIVE guidelines (https://arriveguidelines.org) for the reporting of animal experiments. The study protocol was approved by the experimental animal ethics committee of Wenzhou Medical University (approval no. wydw2022-0608). All methods were carried out in accordance with relevant guidelines and regulations.

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Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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