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Original Article

Experimental observation of vitro pigs' hearts with bipolar radiofrequency ablation

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Abstract: Bipolar ablation is an innovative direction of catheter ablation technology. The aim of this study was to investigate the damaged area of bipolar radiofrequency ablation in vitro pigs' hearts under different conditions and to evaluate the effectiveness and safety. The bipolar radiofrequency ablation was performed in vitro pigs' hearts with a 4 mm bipolar electrode under different conditions at various combinations of the parameters (Distance: from 12 mm to 17 mm; Power: 30 w or 40 w; Time: from 20 s to 90 s; Temperature: 45°C or 60°C; Saline Perfusion: 0 ml/h, 1000 ml/h or 1500 ml/h). We measured the length, width, depth, connection rate and blasting rate of the connective ablation lesion and then evaluated the effectiveness and safety of connective ablation lesion. Numerical analysis showed that there was a positive correlation between the time, temperature and the length, depth, connection rate, blasting rate. There was a negative correlation between the power, perfusion and the depth, while other indexes were positively correlated with the power, perfusion. Distance and length were positively correlated, while other indexes were negatively correlated with the distance. Regression analysis showed that the infusion was not significantly correlated with the depth, connection rate, blasting rate. The temperature was not significantly correlated with the length, connection rate. Power and depth's correlation was not significant. When the parameter combination was 12 mm, 20 s, 30 w, 60°C, 1500 ml/h, the effectiveness and safety was optimum, with the mean lesion length being 19.89 ± 3.02 mm, the depth of an average being 3.50 ± 0.63 mm, the connection rate and the blasting rate being 100% and 13.9% respectively. The bipolar ablation in vitro pigs' hearts could form the most stable continuous damage.

Keywords: Bipolar ablation, isolated pigs' hearts, cold saline perfusion, connective ablation

Introduction

The focus of atrial fibrillation (AF) ablation is on ablating pulmonary vein and isolating pulmonary vein potentials. Ablation could form anatomical obstacles to eliminate the potentials of the pulmonary vein, block the pulmonary vein-atrial bidirectional conduction, and subsequently stop AF [1]. The ablation endpoint should be the completion of the ablation lines, the termination of atrial fibrillation during ablation procedures and the atrial fibrillation is no longer induced after ablation.

The targets of the present radiofrequency catheter ablation are independent unipolar ablation points formed by the electrode's moving point-by-point. Each ablation point can cause a range of tissue injury. These ablation targets could achieve the final completion of a continuous electrical anatomical isolation. In recent years, as bipolar ablation becoming a surgical treatment of atrial fibrillation, its effect has been highly profiled. Bipolar radiofrequency ablation could form a current loop between the two electrodes, and the heat is confined to the tissue between the two electrodes. Hence, an effective continuous damage could be formed after the coagulation and necrosis of the tissue. It is an innovative new direction of catheter ablation technology, which surgical bipolar ablation strategy is applied to internal medicine catheter ablation of AF. We intended to ablate isolated pig hearts, using bipolar ablation mode made by analog bipolar connections. The effectiveness and safety of bipolar radiofrequency ablation were evaluated by investigating the distance, time, temperature, power, perfusion flow

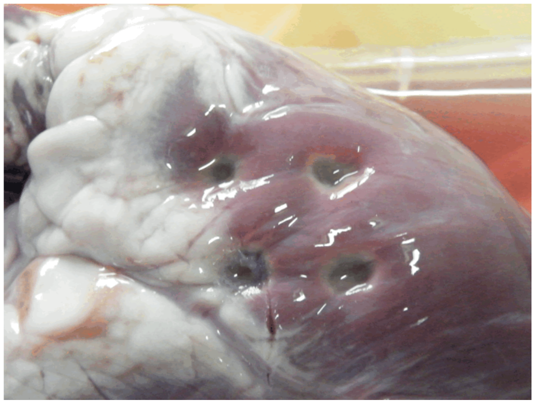

Figure 1. The outside view of vitro pigs' hearts with bipolar radiofrequency ablation.

Figure 2. The inside view of vitro pigs' hearts with bipolar radiofrequency ablation.

of the formation of continuous damage and their change rules under the vitro bipolar ablation condition.

Materials and methods

Bipolar radiofrequency ablation device and electrode

Comparing with U.S. AtriCure Company's bipolar radiofrequency ablation clamp system, each of the two head electrodes is 4 mm thermostat catheter with 90% platinum and 10% iridium, and contains 6 perfusion holes. We improved the radiofrequency ablation model, by using the IBI-1500T8 radiofrequency device and Keli ZNB-XG intelligent infusion pumps, which was configured with circulating constant temperature water bath unit. Two electrodes were connected to the radio frequency device with one connected to the ablation catheter by a 1641 cable and the other connected to the back plate interface by an improved 1910 cable. During ablation, the formation of the current loop between the two electrodes was to imitate bipolar ablation. We used a digital vernier caliper (ASIMETO Germany, the resolution ratio of 0.01 mm, allows the error ± 0.03 mm/150 mm) to fix the distance between the two ablation electrodes, with the distance from 12 mm to 14 mm and increment by 1 mm. The head electrodes were embedded with temperature sensors. The material of the catheter body and catheter handle was PebaxTM polyester thermoplastic elastomer and polycarbonate respectively. The head of the catheter was adjustable in order to meet the requirements of tissue fit closely.

Bipolar ablation with isolated pig heart

Panama minipigs' fresh isolated hearts (Huaxin special animal breeding base, LaoGang town, Pudong new area, Shanghai) were placed in the Langendorff heart perfusion system with water bath at 37°C. Factors controlled mode was executed during ablation. We chose one level from five factors respectively and combined them into one group. These five factors included: distance (from 12 mm to 17 mm, increment by 1 mm), power (30 w or 40 w), time (from 20 s to 90 s, increment by 10 s), temperature (45°C or 60°C), and saline perfusion (1000 ml/h or 1500 ml/h). Each group was performed six times. There were (6×2×8×2×2) 384 groups and the bipolar ablation had been implemented (384×6) 2304 times (**Figures 1**, **2**) .

Data were analyzed after ablation with perfusion, and ablation was performed without perfusion under the fixed power at 30 w and temperature at 60°C then. We chose one level from two factors (time and distance) respectively, and combined them into one group. The bipolar ablation was also performed six times in each group. There were (1×1×8×6) 48 groups and the bipolar ablation had been implemented (48×6) 288 times.

The average temperature, power and impedance were observed during ablation, while the morphology of the lesion was observed after ablation. Indicators of intersection area, such as length, width, depth with a digital vernier caliper (ASIMETO Germany, resolution ratio is 0.01 mm, allowing error ± 0.03 mm/150 mm) and the number of explosion were measured to

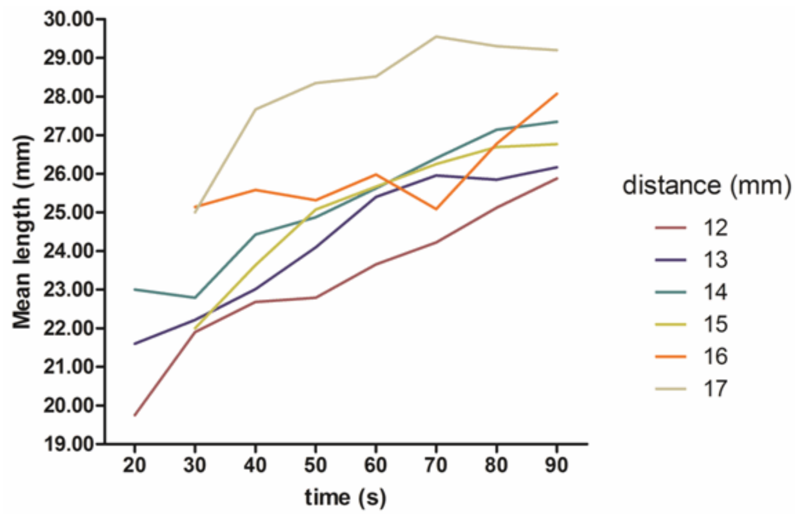

Figure 3. With perfusion, different distances, the ablation length with time. There was a positive correlation between the time, distance and the ablation length.

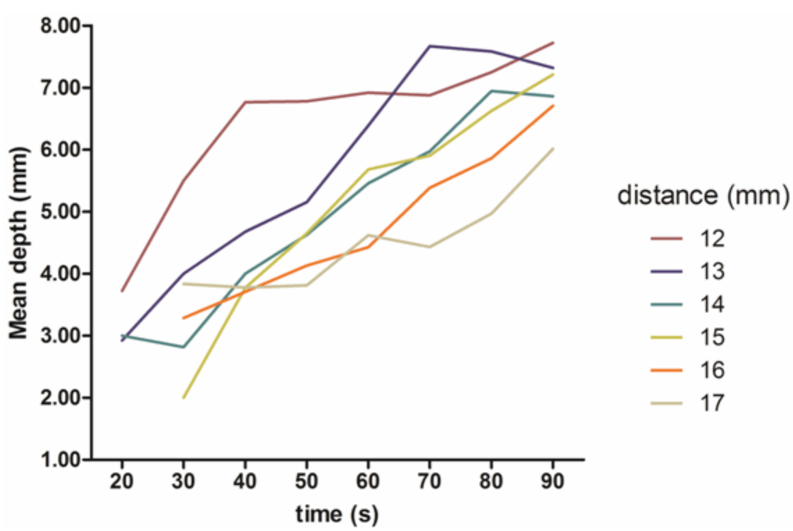

Figure 4. With perfusion, different distances, the ablation depth with time. There was a positive correlation between the time and the ablation depth. There was a negative correlation between the distance and the depth.

evaluate the effectiveness and safety of bipolar ablation in different ablation conditions.

Statistical analysis

Quantitative data were expressed as mean ± SD. Means were compared using t-test or analysis of variance. Count data were expressed as rates, using the Pearson chi-square or continuity-corrected chi-square test. Data on connection rate and burst rate were examined using logistic regression analysis. Data on the length and depth were analyzed using multiple regression analysis. We analyzed the correlation and regression between the connection rate and the burst rate. The data analyses were performed with the statistical software SPSS 16.0, and P value < 0.05 were considered statistically significant.

Results

With perfusion, logistic regression analysis for connection rate

The independent variables included time, distance, power, temperature and perfusion, while the dependent variable was connection rate. LogitP = 8.470 - 1.225X (distance) + 0.146X (power) + 0.132X (time). The influence of time, distance and power on connection rate were significantly different, RR (power) = 1.157, RR (time) = 1.141, RR (distance) = 0.294, respectively. It indicated that the connection rate of 40 w was 115.7% of 30 w. Beginning with 20 s, the connection rate increased to 114.1% of former level as time increased 10 s each time. In addition, with the distance starting at 12 mm, the connection rate decreased to 29.4% of former level as the distance increased 1 mm each time.

With perfusion, logistic regression analysis of burst rate

The independent variables included time, distance, power, temperature and perfusion, while the dependent variable was burst rate. LogitP = -6.677 – 0.395X (distance) + 0.189X (power) +

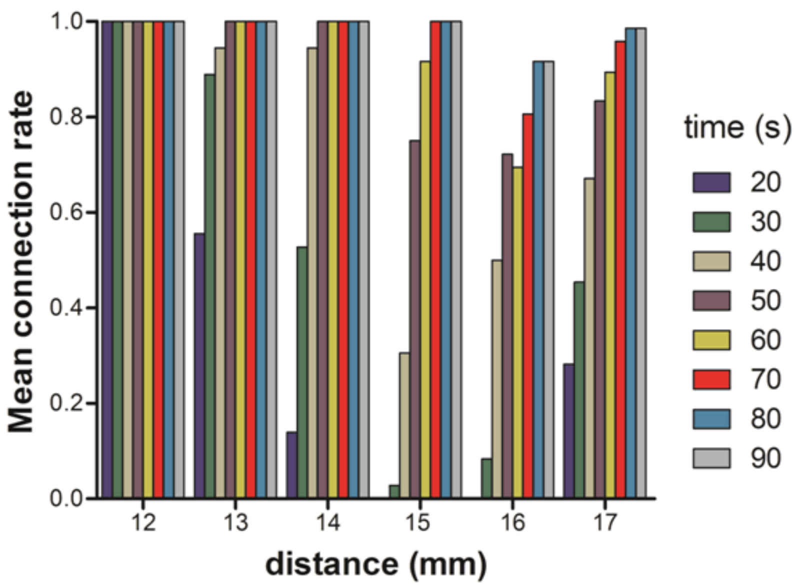

Figure 5. With perfusion, different distances, the connection rate with time. There was a positive correlation between the time and the connection rate. There was a negative correlation between the distance and the connection rate.

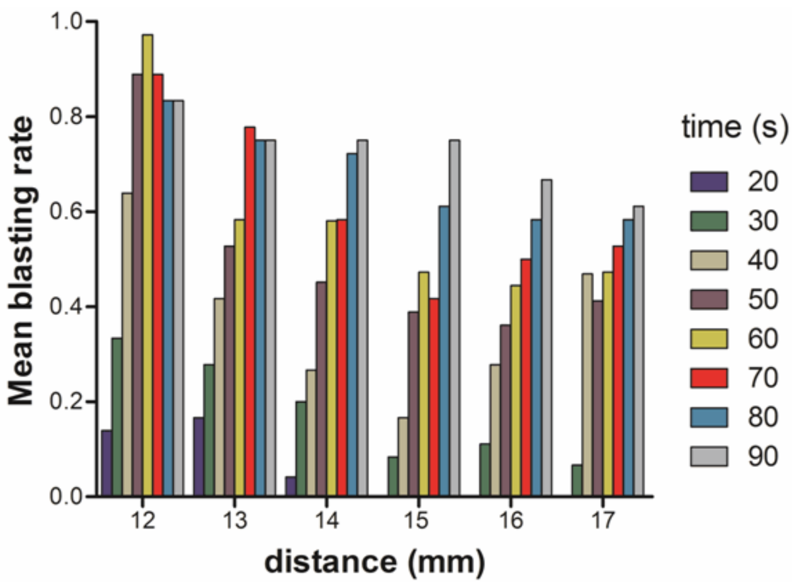

Figure 6. With perfusion, different distances, the blasting rate with time. There was a positive correlation between the time and the blasting rate. There was a negative correlation between the distance and the blasting rate.

0.058X (time) + 0.043X (temperature). The influence of time, distance, power and temperature on burst rate were significantly different, RR (power) = 1.208, RR (time) = 1.060, RR (distance) = 0.673, RR (temperature) = 1.044, respectively. It meant that the burst rate of 40 w was 120.8% of 30 w and of 60°C was 104.4% of 45°C. Beginning with 20 s, the burst rate increased to 106.0% of former level as time increased 10 s each time. Plus, the distance was started at 12 mm, the burst rate decreased to 67.3% of former level as the distance increased 1 mm each time.

With perfusion, multiple regression analysis for ablation length

The independent variables included time, distance, power, temperature and perfusion, while the dependent variable was ablation length. F examination shows a highly significant relatively for regression equation. F = 397.612, P = 0, Y = 8.218 + 0.739X (distance) + 0.041X (power) + 0.063X (time) + 0.001X (perfusion).

With perfusion, multiple regression analysis for ablation depth

The independent variables included time, distance, power, temperature and perfusion, while the dependent variable was ablation depth. F examination showed a highly significant relativity for regression equation. F = 228.599, P = 0, Y = 8.037 – 0.474X (distance) + 0.018X (temperature) + 0.058X (time).

With perfusion, descriptive statistical analysis for length, depth, connection rate and burst rate

Figures 3-6 showed that the time and temperature were positively correlated with the length, depth, connection rate, blasting rate. Whereas, the depth was negative correlated with the power, perfusion, while other indexes were positively correlated with the power, perfusion. Distance and length were positively correlated, while other indexes were negatively correlated with the distance (**Figures 3**-**6**).

With perfusion, regression analysis for connection rate and burst rate

Connection rate was independent variable and burst rate was dependent variable. F examination showed a highly significant relativity for regression equation. F = 77.094, P = 0, Y = 0.626X (connection rate).

Without perfusion, logistic regression analysis for connection rate

The independent variables included time and distance, while the dependent variable was connection rate. LogitP = -0.868X (distance) + 0.214 (time). The influence of time and distance on connection rate were significantly different, RR (time) = 1.238, RR (distance) = 0.420, respectively. Beginning with 20 s, the connection rate increased to 123.8% of former level as time increased 10 s each time. With the distance starting at 12 mm, the connection rate decreased to 42.0% of former level as the distance increased 1 mm each time.

Without perfusion, logistic regression analysis of burst rate

The independent variables included time and distance, while the dependent variable was burst rate. LogitP = -4.277 + 0.067X (time). The influence of time on burst rate was significantly different, RR (time) = 1.069. It indicated that beginning with 20 s, the burst rate increased to 106.9% of former level as time increased 10 s each time.

Without perfusion, multiple regression analysis for ablation length

The independent variables included time and distance, while the dependent variable was ablation length. F examination showed a highly significant relativity for regression equation. F = 203.971, P = 0, Y = 2.872 + 1.161X (distance) + 0.052X (time).

Without perfusion, multiple regression analysis for ablation depth

The independent variables included time and distance, while the dependent variable was ablation depth. F examination showed a highly significant relativity for regression equation. F = 65.662, P = 0, Y = 3.562 − 0.134X (distance) + 0.055X (time).

Without perfusion, descriptive statistical analysis for length, depth, connection rate and burst rate

Analysis showed that there was a positive correlation between the time and the length, depth, connection rate, blasting rate, respectively. There was a positive correlation between the distance and the length, while other indexes were negatively correlated with the distance. Length, depth, connection rate and burst rate both decreased when compared with ablation with perfusion.

Without perfusion, regression analysis for connection rate and burst rate

Connection rate was independent variable and burst rate was dependent variable. F examination shows a highly significant relativity for regression equation. F = 62.080, P = 0, Y = 0.461X (connection rate).

Discussion

AF is the most commonly repeated, sustained arrhythmia. Treatment strategies on AF include heart rate control and rhythm control. Rhythm control, using drugs, electrical cardioversion and radiofrequency ablation, can significantly improve the patients' symptoms and quality of life with reduction of anticoagulants use. Heart rate control strategy functions as controlling ventricular rate, preventing and reducing the formation of blood clots. It is known that rhythm control is the ideal goal of the treatment of AF. However, as the arrhythmogenic effect of antiarrhythmic drugs, recurrence and bleeding risk of anticoagulant drugs, rhythm control is considered less safe and effective than heart rate control. The emergence of radiofrequency ablation is a kind of revolutionary treatment for AF and is expected to maintain sinus rhythm with the help of catheter ablation.

Currently ablation mainly uses radiofrequency as energy, and experts do not recommend the best radiofrequency energy delivery system and catheter in consensus. Circumferential pulmonary vein ablation procedure is currently used mainly for paroxysmal and persistent AF with good effect [2]. 4 mm temperature control catheter with cold saline infusion, is commonly used in clinical radiofrequency ablation. About 40 targets on each side of the pulmonary veins were needed to achieve circumferential pulmonary vein ablation. Demazumder etc. have tested in vitro the minimum inter-electrode distance of 4 mm unipolar head electrode catheter causing the injury intersection [3]. In their study, the parameters on distance were 2 mm without liquid flow and 5 mm with liquid flow. This distance will shorten while placed in the body, which means adjacent ablation distance should be less than 5 mm in order to form an effective continuous damage. The tissue damaged size (length and depth) is an indicator of ablation efficacy and safety. The greater range of the tissue damage caused by the unipolar electrode ablation, the longer distance of inter-electrode distance caused the injury intersection, and the fewer number of the required ablation targets. Increasing the size of the head electrode can expand the electrode-tissue contacting area and make the head electrode cool easily. Strengthening the radio frequency power, temperature and time can augment the range of tissue damage, but also increase the risk of the tissue burned and forming scab. The perfusion electrode can be more rapidly cooled than non-perfusion electrode and produce a wider range of tissue injury.

Currently, there is a shortcoming of research about applying the bipolar radiofrequency catheter ablation in circumferential pulmonary vein ablation. AtriCure bipolar radiofrequency ablation clamp system has advanced the surgical treatment of AF and prompted a new direction for internal medicine catheter treatment of AF. In fact, in radiofrequency ablation, the ablation target is unipolar ablation points independent of each other. Each ablation point can cause a range of tissue damage. Tissue damage can intersect as long as the distance is close enough, thus continuous anatomical obstacles are formed. AF catheter endocardia ablation (based on circumferential pulmonary vein ablation) is an important treatment for curing AF, restoring and maintaining sinus rhythm. The integrity of the linear ablation, which depends on thorough anatomical isolation, is the guarantee of bi-directional block. Every discharge of bipolar radiofrequency ablation can form a larger range of tissue injury than unipolar ablation. Additionally, it can increase the ablation length and reach a certain depth, which is more favorable for the formation of the anatomy of isolation. In recent years, the bipolar ablation AF with structural heart disease as surgical treatment strategies was favored and effective [4-6]. Because the bipolar ablation electrode could form a current loop between electrodes, the heat is confined between the two electrodes to cause tissue coagulation and necrosis. Anfinsen etc. have mentioned that under non-perfusion and 4 mm head electrode catheter bipolar ablation mode, the required minimum distance between the continuous damage was 9 mm in vitro, and 6-8 mm inside the body [7]. They also made a bipolar catheter by fixing the electrode distance of 5 mm, and then used it to perform endocardia ablation for right atrial free wall and the inferior vena cava - tricuspid of tricuspid isthmus of pigs' hearts. Finally, they confirmed that effective continuum damage could be formed through catheter bipolar radiofrequency ablation. However, they did not test under perfusion conditions.

We introduced the concept of surgical bipolar ablation and established bipolar ablation mode made by catheter. Our initial experiments ensured that the head electrode temperature was maintained at low levels to achieve a constant output preset power through cooling head electrode by the external circulation formed with an infusion of saline. This indicated that continuous damage could be formed in vitro until the inter-electrode distance was increased to 12 mm under perfusion conditions. If the inter-electrode distance was further increased, the efficiency of continuous damage formation would decline. It could be compensated by increasing the power, or (and) the temperature, time, perfusion.

With perfusion, there was no correlation between perfusion and depth, connection rate, burst rate. Temperature was not correlated with length or connection rate. Power was not correlated with depth. There was a positive correlation between the time, temperature and the length, depth, connection rate, blasting rate, respectively. There was a negative correlation between the power, perfusion and the depth, while other indexes were positively correlated with the power, perfusion. Distance and length were positively correlated, while other indexes were negatively correlated with the distance.

There was a linear regression relation between connection rate and burst rate. The mean ablation depth was set no greater than 4 mm, and we computed the maximum benefit value of connection rate and non-burst rate within the groups where the mean depth was no greater than 4 mm. When the distance, time, power, temperature, perfusion is 12 mm, 20 s, 30 w, 60°C, 1500 ml/h respectively, the benefit value increased to the maximum, indicating that the effectiveness and safety come to be the best. The mean length, depth, connection rate and burst rate were 19.89 ± 3.02 mm, 3.50 ± 0.63 mm, 100% and 13.9% respectively.

Without perfusion, distance was not correlated with burst rate. There was a positive correlation between the time and the length, depth, connection rate, blasting rate. There was a positive correlation between the distance and the length, while other indexes were negatively correlated with the distance. Length, depth, connection rate and burst rate both decreased compared with ablation with perfusion group. There was a linear regression relation between connection rate and burst rate. The mean ablation depth was also set no greater than 4 mm. When the distance, time was 12 mm, 50 s respectively, the benefit value increased to the maximum, where the mean length, depth, connection rate and burst rate were 16.00 ± 1.41 mm, 4.00 ± 1.05 mm, 80.6% and 13.9% respectively.

Comparing the optimal efficacy and safety of ablation with and without perfusion, the efficiency of ablation with perfusion is higher than that without perfusion, and the mean ablation length is higher and the depth is safer. It showed that ablation with perfusion could improve the efficiency of achieving linear ablation more during bipolar ablation. So the best parameters in our setting were 12 mm, 20 s, 30 w, 60°C, 1500 ml/h.

In conclusion, our research shows that heart bipolar ablation program is safe and feasible. This study displays the best values of distance, time, power, temperature and perfusion in Vitro Pigs' Hearts bipolar ablation. We also present the ablation data within different combinations of various factors, and their trends and statistical significance factors. Taken together, our study could provide references for further study of introducing bipolar ablation in vitro to in vivo.

Disclosure of conflict of interest

None.

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