Cardiovascular Innovations and Applications

Vol. 8 (2023) 52
ISSN 2009-8618
DOI 10.15212/CVIA.2023.0066

RESEARCH ARTICLE

Left Bundle Branch Ablation Guided by a Three-Dimensional Mapping System: A Novel Method for Establishing a Heart Failure Animal Model

Pengkang He[1,a], Han Jin[1,a], Yiran Hu[2], Sixian Weng[3], Sijing Cheng[4] and Hao Huang[4]

[1]Department of Cardiology, Institute of Cardiovascular Disease, Peking University First Hospital, Beijing 100034, China
[2]Department of Cardiology and Macrovascular Disease, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[3]Department of Cardiology, The Key Laboratory of Geriatrics, Beijing Institute of Geriatrics, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital, National Center of Gerontology of National Health Commission, Beijing, China
[4]Center of Arrhythmia, Fuwai Hospital, State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China

Received: 3 June 2023; Revised: 18 July 2023; Accepted: 5 September 2023

Abstract

Objective: Few studies have been conducted to establish animal models of left bundle branch block by using three-dimensional mapping systems. This research was aimed at creating a canine left bundle branch block model by using a three-dimensional mapping system.
Materials and Methods: We used a three-dimensional mapping system to map and ablate the left bundle branch in beagles.
Results: Ten canines underwent radiofrequency ablation, among which left bundle branch block was successfully established in eight, one experienced ventricular fibrillation, and one developed third-degree atrioventricular block. The maximum HV interval measured within the left ventricle was 29.00 ± 2.93 ms, and the LBP-V interval at the ablation site was 20.63 ± 2.77 ms. The LBP-V interval at the ablation target was 71.08% of the maximum HV interval.
Conclusion: This three-dimensional mapping system is a reliable and effective guide for ablation of the left bundle branch in dogs.

Keywords: left bundle branch block; heart failure; animal model; canine; three-dimensional mapping; ablation

Background

Complete left bundle branch block (LBBB) is a common ECG abnormality, particularly in people with cardiac insufficiency [1, 2]. LBBB is indicative of left ventricular electrical activity asynchrony. According to guidelines, cardiac resynchronization therapy is the first line treatment for people with heart failure and reduced ejection fraction accompanied by LBBB [3]. However, in practice, the efficacy of cardiac resynchronization therapy in such cases is not always satisfactory,

[a]Pengkang He and Han Jin contributed equally to this work.
Correspondence: **Pengkang He**,
E-mail: vampire_c@126.com

and a substantial number of patients show either poor or absent treatment response [4]. Thus, the role of complete LBBB in heart failure is not fully understood.

Animal models provide an effective means of studying certain medical problems. Currently, the most frequently used animal models of heart failure involve rapid right ventricular pacing, ligation of coronary arteries and artificial establishment of valve regurgitation [5–7]. These models cannot accurately simulate the mechanism of synchronized left ventricular heart failure. Therefore, the establishment of an animal model of LBBB combined with cardiac insufficiency is important to support further research. Early attempts to establish such a model involved ablation of the left bundle branch (LBB) under two-dimensional fluoroscopic guidance. Although this method has yielded some success, it is also prone to inaccuracy, which can lead to third-degree atrioventricular block in experimental animals [8]. This drawback might be addressed by using three-dimensional mapping technology, which is widely applied in ablation of complex arrhythmias clinical settings, to facilitate LBB mapping and ablation, and create a left ventricular dyssynchrony model. Thus, this study used a three-dimensional mapping system to establish an LBBB model.

Materials and Methods

This study was conducted on nine beagles weighing 12–15 kg. All experimental procedures were approved by the Ethics Committee of the State Key Laboratory of Fuwai Hospital (ethical approval number 0104-3-8-ZX(X)-21).

Equipment

The 3D mapping and LBB ablation procedures used a CARTO3 (Biosense Webster, Inc., Diamond Bar, CA) system. The 12-lead ECG and intracardiac ECG were recorded with a multichannel electrophysiological recording system (GE CardioLab EP Recording system, USA). The fluoroscopic mode was CARDIO EP, Extremely Low, 3.75 f/s (General Electric Medical System, MA, USA). The mapping catheter was a SmartTouch ablation catheter (Biosense Webster, Inc., Diamond Bar, CA).

Animal Preparation

Beagles were anesthetized with propofol (0.5 mg/kg), tracheally intubated, and given positive pressure ventilation and 1–3% isoflurane to maintain anesthesia. The right femoral artery was exposed, and an 8 F sheath was placed in the artery. A SmartTouch ablation catheter (Biosense Webster, Inc., Diamond Bar, CA) was subsequently introduced through the artery sheath.

Induction of LBBB

Retrograde Crossing of the Aortic Valve

Care must be taken when in operations near the aorta in beagle dogs, because excessive force during the operation can damage the aortic valve. A “bend in and straight out” catheter motion was used to cross the aortic valve. However, because the diameter of the canine aortic sinus is small, the catheter could not fully bend into a U-shape. Therefore, the surgeon slightly curved the catheter at the bottom of the Valsalva sinus to point the tip of the catheter toward the aortic valve. Through gentle forward delivery, the catheter was advanced across the valve at the time of valve opening. The surgeon monitored the pressure value during valve crossing to avoid high pressure (exceeded 30 g) and damage to the aortic valve.

Mapping of LBB Potential

For mapping LBB potential (LBBP), electroanatomic reconstructions of the aortic root and LV chamber were first made with a TC ablation catheter and CARTO3 system (Biosense Webster, Inc., Diamond Bar, CA). An attempt was subsequently made to record the His potential in the aortic sinus, and the HV interval was measured. After the ablation catheter crossed the aortic valve, the catheter tip was steered toward the left ventricular septum. The LBB potential under the aortic sinus from the back to the front of the septum was carefully monitored and mapped point by point on the Carto system.

Determination of the Ablation Target Site

Two methods were used to determine the ablation target site. First, the target was often located at the intersection of the left front branch and the

left rear branch beneath the aortic valve (always at the right coronary cusp). Second, the HV intervals were measured in each animal. We identified an HV interval at the target location of 15–20 ms, or 50–60% of the maximal HV interval at the LV region (Figures 1 and 2). The potential at the target point was mainly V wave, with no A wave or only minimal far field A wave. Simultaneously, a clear and sharp near field beam branch potential was recorded. Most targets were found under the aortic valve; however, some were found above the valve within the aortic sinus. Ablation at the fascicular level should be avoided in choosing ablation sites, to avoid incomplete LBBB and subsequent induction of ventricular arrhythmias (Figure 3).

Ablation Procedure

After determination of the ablation target site, the catheter was placed at the target location before

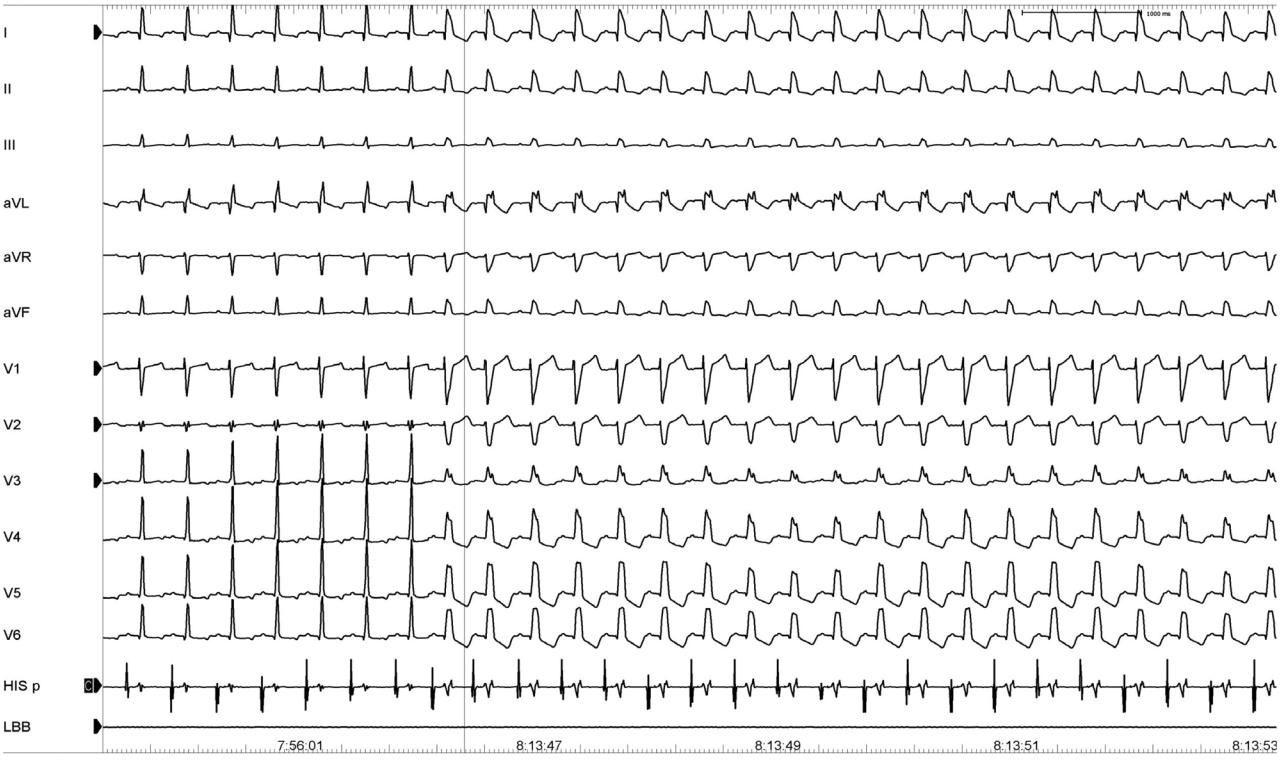

Figure 1 Changes in ECG Before and After Ablation.

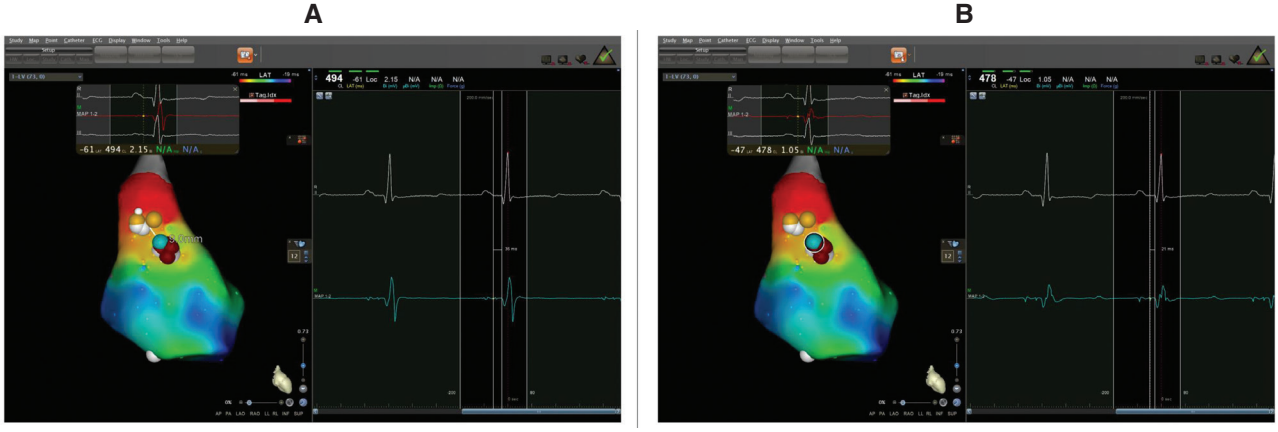

Figure 2 The Ablation Target Locations on the Mapping System.
Ablation procedure is depicted in this figure through three-dimensional mapping, with the max H-V interval being 36 ms (A) and the LBP-V interval at the ablation site being 21 ms (B), and the distance between the two points being 9.1 mm (A).

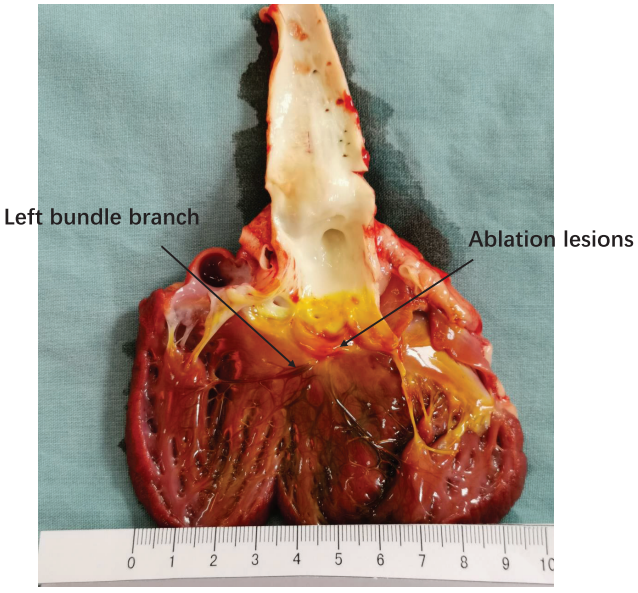

Figure 3 The Locations of Ablation Targets on the Gross Specimen.

ablation with a pressure of 5–10 g. Sustained and rapid ventricular tachycardia or a prolonged PR interval in the surface ECG were monitored; if identified, the position and pressure of the ablation catheter were readjusted to avoid inducing ventricular fibrillation and AV conduction block during ablation. The ablation was generally performed in cold saline perfusion mode (15 mL/min) at 35 W, and the LBBB pattern was observed after 5–10 s of ablation. Subsequently, continuous ablation was performed for 60 s. If no LBBB pattern was observed after 15 s of ablation, the target point was reconsidered and remapped. During ablation, sustained ventricular tachycardia and a prolonged PR interval were monitored; if present, the ablation procedure was stopped immediately, and the target location was adjusted. After successful ablation, re-ablation was performed for 30–60 s to avoid recovery of LBB conduction. After successful ablation, animals were typically observed for 30 minutes. If no recovery of LBB conduction was observed, the ablation was considered successful. If recovery of LBB conduction was found, the ablation was repeated at the ablation target for another 60 s.

Implantation of Pacemakers

A dual chamber pacemaker was implanted after placement of an atrial lead (model 5076-52, Medtronic, Minneapolis, MN, USA). The animals were then returned to the care facility after the procedure.

After LBB ablation and implantation of the pacing lead, each animal received a dual-chamber pacemaker. Subsequently, the pacemaker was programmed to AOO 200 ppm for 3 weeks to induce dyssynchronous heart failure.

Follow-up

Echocardiography, 12-lead ECG, pacing parameters and procedure-associated complications were recorded at a 6-week follow-up. All animals were then euthanized for anatomical research. After the animals were euthanized with a high concentration potassium solution, the hearts were isolated, and specimens were prepared to observe the ablation lesions.

Results

LBBB models were successfully established in eight of ten canines. One animal died because of ventricular fibrillation during the ablation process, and a second animal experienced third-degree atrioventricular block after ablation.

Among the eight animals with successfully established LBBB, the maximum HV interval measured within the left ventricle was 29.00 ± 2.93 ms, and the LBP-V interval at the ablation site was 20.63 ± 2.77 ms. The maximum HV interval of animals causing third degree conduction block was 22 ms, and the LBP-V interval at the ablation site was 18 ms. The distance between the position of the maximum HV interval and the ablation site was 8.51 ± 2.19 mm in the animals with successful model establishment. On average, the LBP-V interval at the ablation target was 71.08 ± 8.10% of the maximum HV interval (Table 1).

The average intrinsic QRS duration was 45.25 ± 4.17 ms. LBB ablation significantly prolonged the QRS duration (45.25 ± 4.5 ms vs 105.50 ± 7.35 ms, $P < 0.001$). The baseline PR interval was 88.50 ± 15.08, and the post ablation PR interval was 93.50 ± 16.55 ($P = 0.001$). After 6 weeks' follow-up, the LBBB duration (105.50 ± 7.35 to 108.36 ± 6.88 ms; $P = 0.824$) did not differ from that in the acute phase (Table 2).

Table 1 Electrical Characteristics of Ablation Sites and ECG Parameters Before and After Ablation[a].

Ablation sites	MHV (ms)	LBP-V (ms)	Distance (mm)	LBP-V/MHV
Successfully ablated animals	29.00 ± 2.93	20.63 ± 2.77	8.51 ± 2.19	71.08 ± 8.10%
3° AVB animal	22	18	12.1	81.8%
VF animal	26	14	7.0	53.84%

[a]The table shows the maximum HV interval and the LBP-V interval at the ablation target, with the latter being 71% of the MHV interval.
MHV: maximum HV interval; AVB: atrioventricular block; VF: ventricular fibrillation.

Table 2 ECG Parameters Before and After Ablation[a].

ECG parameters	Before ablation	After ablation (acute)	P value	After ablation (6 weeks)	P value
QRS duration	45.25 ± 4.17	105.50 ± 7.35	<0.001	108.36 ± 6.88	0.824
PR interval	88.50 ± 15.08	93.50 ± 16.55	0.001	94.08 ± 12.88	0.928

[a]Ablation resulted in a significant increase in the QRS duration, with a slight increase in the PR interval. This difference was maintained after 6 weeks.

Discussion

Our research established a canine model of LBBB by using a three-dimensional mapping system, thus achieving efficient and safe ablation of the LBB and lasting LBBB, and avoiding ablation-induced ventricular arrhythmias and third-degree atrioventricular block.

The His bundle has a direct anatomical connection to the LBB, which extends from it. The LBB in dogs is usually located at the junction of the RCC and the NCC, and has a width of 3–5 mm [9]. Subsequently, it is divided into the left anterior branch and the left posterior branch in the interventricular septum. The LBB in dogs has a similar location to that in humans; however, its position beneath the endocardium is shallower and therefore more vulnerable to damage, thereby increasing the success rate of ablation. Notably, the main trunk of the LBB is relatively thick, and multiple ablations may be required to achieve complete block.

In this research, we observed that the aortic sinus and left ventricle in dogs were smaller than those in adult humans and similar to those in children. Initially, we used an orange-grip catheter, which could not easily pass through the aortic valve into the left ventricle. Excessive manipulation could potentially damage the aortic valve and lead to aortic valve regurgitation. After switching to a blue-grip catheter (ThermalCool SmartTouch D curve with a smaller bending radius of 47 mm), this aspect improved, and the process was akin to treating pediatric patients. However, the technique of crossing valves in human hearts cannot be directly applied to canine hearts. Therefore, we developed a new valve crossing method by slightly bending the bottom of the aortic sinus so that the tip of the catheter pointed to the rear side, and bending it when the aortic valve opened, so that the catheter was pushed into the left ventricle. The three-dimensional mapping system was able to trace the catheter's progress through the aorta, thereby creating a map of the aorta's shape, and enabling the catheter to move in and out of the aortic valve with ease.

The LBP-V interval at the ablation target was usually 65–70% of the mapped maximum HV interval time and therefore was an ideal ablation indicator. Ablation within this range is both safe and effective. Animals with third-degree atrioventricular block had a value of 81.8%, whereas one successfully ablated animal had a value of 80%. Moreover, the spatial distance from the ablation point to the maximum HV value is a useful reference for selecting ablation targets.

A previous study has suggested that an LBP-V interval less than 20 ms and an A/V potential ratio less than 1/10 at the ablation target can effectively prevent the occurrence of third-degree atrioventricular block [10]. Thus, the closer the ablation target is to the ventricular side, the safer the procedure. However, our study indicated that, except in one

animal, the LBP-V interval at all ablation targets exceeded 20 ms, and a small number of ablation points (one or two times) could be achieved, thus resulting in LBBB. Previous studies suggested that the ablation target was located at the root of the LBB, where the LBB branches near the ventricular side and is connected by the reticular bundle branch. Our findings also revealed that the ablation target location was too low, thus hindering LBBB and causing LBB conduction block. Research conducted in the early stages also showed that ablation at sites with LBP-V intervals of less than 10 ms required higher power and a longer duration to block the LBB, and was also associated with a higher occurrence of complete atrioventricular block [11]. Blocking the LBB through ablation too close to the ventricle side is challenging, and prolonged high-power ablation has the potential to cause undesired damage, as supported by our findings. The three-dimensional mapping system enabled precise identification the LBB and its branches, thus allowing for the selection of safe and effective ablation targets. Furthermore, the ventricles of canines are highly sensitive, and ventricular arrhythmias can easily occur through catheter contact or ablation. Lower ablation targets can cause ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation. Our findings do not support ablation targets situated beyond 13 mm from the maximum HV interval. Thus, our method for mapping was effective in locating the ablation target.

We found no significant difference in QRS wave duration immediately after ablation versus 6 weeks after ablation, thus indicating that our ablation technique caused lasting LBBB and provided a strong basis for further rapid pacing induced cardiac dysfunction (Table 2). Additionally, after 3 weeks of rapid right atrial pacing, the left ventricular ejection fraction of the experimental animals was markedly below that at baseline.

In contrast to the two-dimensional X-ray fluoroscopy used in previous studies, this study used a three-dimensional mapping system, which decreased the radiation dose and operation time, while protecting operators. This mapping system enabled intuitive and precise visualization of the intracardiac structure. Additionally, the utilization of catheters able to detect tip pressure helped ascertain the catheter's contact with tissue, thus increasing the success rate of ablation. By using a single ablation catheter, we achieved diminished vascular puncture complications and research costs, as well as a simpler operation process.

Previous studies have indicated that models of heart failure induced by ligation of the aorta, occlusion of the coronary artery or rapid ventricular pacing cannot accurately replicate cardiac dysfunction after left ventricular asynchrony [12]. Performing open thoracic surgery on large animals carries a high risk of trauma and postoperative mortality. Furthermore, these methods can lead to inconsistent results because of uncontrollable myocardial thickening and death. Our study established an LBBB model with substantial broadening of the QRS with respect to that at baseline, thus indicating sufficient left ventricular dyssynchrony. Future research may use ventricular pacing to create a cardiac dysfunction model that better reflects clinical scenarios. After ablation of the LBB, mechanical activity in the left ventricle is no longer synchronized, and sustained rapid atrial pacing might lead to left ventricular enlargement and a decrease in left ventricular function. In comparison to other methods used to establish animal models of heart failure, the approach used in this study may be more representative of the pathophysiological mechanisms of heart failure in patients with dilated cardiomyopathy [13, 14].

Conclusion

Ablation of the LBB in dogs can be accomplished in a safe and effective manner with use of a three-dimensional mapping system, thereby establishing a canine LBB conduction block model. In selecting ablation targets, not only the local potentials but also the ratio of LBP-V time to maximum HV interval should be considered. This system can then be used to model left ventricular dyssynchrony heart failure.

Conflicts of interest

The authors have no conflicts of interest.

Data availability statement

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

Ethics statement

All experimental process were approved by the Ethics Committee of the State Key Laboratory of Fuwai Hospital (ethical approval number: 0104-3-8-ZX(X)-21).

Author contributions

Pengkang He and Han Jin engaged in experimental animal surgery, data processing, and article writing and revision. They contributed to this work equally.

Yiran Hu performed experimental implementation and data processing in this study.

Sixian Weng's primary focus was on performing surgical operations on experimental animals.

Sijing Cheng and Hao Huang were responsible primarily for experimental recording and data processing work.

Funding

This work was supported by the National Science Foundation for Young Researchers of China (grant Nos: 82000315, 82000325 and 82100325).

REFERENCES

1. Ponnusamy SS, Vijayaraman P. Left bundle branch block-induced cardiomyopathy: insights from left bundle branch pacing. JACC Clin Electrophysiol 2021;7(9):1155–65.
2. Elliott P, Andersson B, Arbustini E, Bilinska Z, Cecchi F, Charron P, et al. Classification of the cardiomyopathies: a position statement from the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J 2008;29(2):270–6.
3. Chung MK, Patton KK, Lau CP, Dal Forno ARJ, Al-Khatib SM, Arora V, et al. 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. Heart Rhythm 2023;20:e17–91.
4. Shanks M, Delgado V, Bax JJ. Cardiac resynchronization therapy in non-ischemic cardiomyopathy [J]. J Atr Fibrillation 2016;8(5):47–52.
5. Mitchell GF, Lamas GA, Pfeffer MA. Ventricular remodeling after myocardial infarction. Adv Exp Med Biol 1993;346:265–76.
6. Watanabe S, Fish K, Bonnet G, Santos-Gallego CG, Leonardson L, Hajjar RJ, et al. Echocardiographic and hemodynamic assessment for predicting early clinical events in severe acute mitral regurgitation. Int J Cardiovasc Imaging 2018;34(2):171–5.
7. Winslow RL, Rice J, Jafri S, Marbán E, O'Rourke B. Mechanisms of altered excitation-contraction coupling in canine tachycardia-induced heart failure, II: model studies. Circ Res 1999;84(5):571–86.
8. Liu L, Tockman B, Girouard S, Pastore J, Walcott G, KenKnight B, et al. Left ventricular resynchronization therapy in a canine model of left bundle branch block. Am J Physiol Heart Circ Physiol 2002;282(6):H2238–44.
9. Lazzara R, Yeh BK, Samet P. Functional anatomy of the canine left bundle branch. Am J Cardiol 1974;33(5):623–32.
10. Helguera ME, Trohman RG, Tchou PJ. Radiofrequency catheter ablation of the left bundle branch in a canine model. J Cardiovasc Electrophysiol 1996;7(5):415–23.
11. Sheng B, Du R, Hou Y, Chen A. Study of blocking of left bundle branch with radiofrequency catheter ablation in normal Canines. Chin J Cardiac Pacing Electrophysiol 2002;16(4):298–300.
12. Charles CJ, Rademaker MT, Scott NJA, Richards AM. Large animal models of heart failure: reduced vs. preserved ejection fraction. Animals (Basel) 2020;10(10):1906.
13. Shanks M, Delgado V, Bax JJ. Cardiac resynchronization therapy in non-ischemic cardiomyopathy. J Atr Fibrillation 2016;8(5):1362.
14. Aşkın L, Tanrıverdi O. The benefits of sacubitril-valsartan in low ejection fraction heart failure. Abant Med J 2022;11(3):337–336.