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LASER CATHETER ABLATION OF ATRIAL ZONES WITH GANGLIONATED PLEXI: IMPACT ON ATRIAL FIBRILLATION INDUCIBILITY AND THE RISK OF ESOPHAGEAL DAMAGE IN EXPERIMENTAL SETTINGS

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Aim. To study the potential applicability of transcatheter laser ablation for the destruction of atrial ganglionated plexi (GP) zones and the safety of this technique in relation to inadvertent esophageal damage.

Methods. This was a two-stage investigation: (1) *ex vivo* experiments: the risk of esophageal damage during ablation on the dorsal (posterior) left atrial (LA) wall was assessed; three swine organ complexes were used, which included the heart, lungs and esophagus; (2) *in vivo* experiments assessing the effects of laser catheter ablation of GP zones on the inducibility of atrial fibrillation (AF) and changes in atrial effective refractory period - included 13 landrace pigs (average weight 38.8±1.2 kg).

Ex vivo: laser catheter ablations were performed from the endocardial surface of the LA towards the esophagus with a power of 15 watts of varying duration; ablation was performed under thermal scanning of the LA and esophagus; then a macroscopic examination of the myocardial and esophageal walls was performed.

In vivo: before and after catheter laser ablation (15 W) of the GP zones in the right atrium and atrial septum, atrial ERP was assessed with programmed stimulation, and AF induction with high-frequency (33 Hz, 2 min) stimulation was evaluated. At the end of the experiment, the animals were euthanized, and the heart and lungs were collected in a single unit.

Results. *Ex vivo* experiments: in two cases, damage to the endocardium of the LA was detected at an exposure time of 30 s. Damage to the esophagus was observed with a longer exposure time (> 30 seconds) with a 11.3-15.4°C increase in temperature. In the *in vivo* experiments, 78 laser applications (6±1 in one swine) were delivered to the posterior wall of the right atrium and atrial septum.

Atrial effective refractory period was not altered after ablation (183±20 ms vs 186±18 ms, P=0.99). At the baseline, AF was induced in 12 out of 13 animals (92%). After ablation, AF was induced in 7 animals (54%) (P=0.03). There was a trend toward a decrease in the duration of AF after laser ablation of GP zones (18 [5; 141] vs. 2 [0; 14] s after ablation, P=0.06). Transmural damage was observed in 46% of the hearts. No damage to extra-cardiac structures was detected.

Conclusion. *Ex vivo*, laser ablation on the dorsal (posterior) wall of the LA with a power of 15 W and duration <30 s does not lead to visible damage to the esophagus. Laser ablation of atrial GP zones is feasible and reduces the inducibility of AF. No change in atrial effective refractory period is detected following GP zones ablation, when performed from the right atrium.

Key words: atrial fibrillation; radiofrequency ablation; laser ablation; experimental study

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Disbalance of the autonomic nervous system contributes significantly to the pathogenesis of cardiovascular disease. In hypertension, ischemic heart disease, and chronic heart failure, pathophysiological mechanisms involve the excessive activation of the sympathetic nervous system alongside a reduction in parasympathetic activity [1]. Alterations in parasympathetic nerve activity significantly contribute to the development and maintenance of cardiac arrhythmias, including atrial fibrillation, sinus node dysfunction, and atrioventricular (AV) junction dysfunction [2].

Ganglionic plexuses (GP), primarily situated on the epicardial surface within the fat pads of the left and

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right atria, play a crucial role in the pathophysiology of atrial fibrillation (AF). The destruction of these plexuses has been proposed as a potential method to prevent the recurrence of this arrhythmia [3]. In 2011, L. Calò et al. conducted a clinical study on patients with "vagal" paroxysmal AF, performing ablation of right atrial GP without pulmonary vein isolation. The study demonstrated efficacy in 70% of the patients [4].

Increased parasympathetic tone, which depresses sinus node automaticity and AV conduction, can be counteracted at the organ level by destroying GP and nerves [5]. Attempts at targeted correction of parasympathetic influences using catheter-based radiofrequency interventions are known as cardiac neuroablation [6]. Currently, cardiac neuroablation lacks formal indications for use. However, its potential role in preventing recurrent atrial fibrillation, correcting sinus node dysfunction, treating AV block, and managing vasovagal syncope is being intensively studied [5, 7].

The current approach to transcatheter cardiac neuroablation involves targeting nerves and atrial ganglia in both the right atrium (in accumulation sites - posterior septal region of the right atrium, fat pad in the area between the atria) and the left atrium (LA) (near the mouth of the pulmonary veins and in the interatrial sulcus) [3].

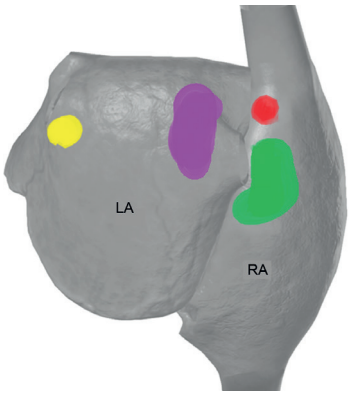

Fig. 1. Schematic representation of the location of the ganglionic plexuses (GPs) of the heart in pigs [11], where LA, left atrium; RA, right atrium; yellow, left atrial GP; purple, posterior GP; red, ventral right atrial GP; green, right atrial GP.

In addition to the commonly used radiofrequency ablation, other methods of myocardial and nerve element destruction, such as ultrasound, chemical ablation, and electroporation, are currently under investigation. Laser exposure is also a promising method of thermal ablation. The main advantages of laser energy include its ability to focus energy precisely, generate the highest temperature at a depth beyond the application surface, and effectively target deeper structures. This approach minimizes collateral damage to the endocardium or vascular intima [8, 9].

The aim of this experimental work was to investigate the feasibility of using laser catheter exposure for cardiac neuroablation and to evaluate the safety of laser ablation on the dorsal (posterior) wall of the LA, particularly concerning the risk of esophageal injury.

Esophageal thermal injury is the most threatening complication of ablations in the LA due to the risk of atrial-esophageal fistula formation, with a mortality rate of 85% [10]. Therefore, one of the objectives of the study was to determine the potential risk of damage to the esophageal wall during laser applications in the atria near its course. In pigs, the esophagus is in close proximity to the dorsal wall of the LA, as in humans. However, *in vivo* ablations in the LA are significantly hampered due to anatomical features. Performing an *ex vivo* study allows for standardized assessment of thermal damage, as well as application in the atrium directly opposite the ventral esophageal wall.

METHODS

Ex vivo laser myocardial ablation experiment

The *ex vivo* experiment entailed simulating transcatheter ablation in the LA on the dorsal wall (equivalent to the posterior wall in humans) with an evaluation of the potential risk of esophageal injury.

Three pig organ complexes, comprising the heart, lung, and esophagus, sourced from an agricultural facility, were utilized to examine the temperature effects of laser applications on the endocardial side of the left atrium myocardium and to assess potential collateral damage to the esophagus during laser ablation on the dorsal wall of the left atrium. The organocomplexes were placed in a container for the experimental procedure. For the experiment, a laser energy source (wavelength 1064nm; Medilas D, Dornier Medtech, Wessling, Germany) and a prototype guided laser irrigated catheter (SMTS, Moscow, Russia) with a diameter of 8.5 Fr were utilized. The inferior and superior vena cava were secured on the bench, and a vertical incision was made through the anterior wall of the left atrium for direct visualization of the dorsal wall. The esophagus was positioned behind the dorsal wall of the LA in its typical

Fig. 2. Example of high-frequency stimulation (B 1-2) and induction of atrial fibrillation, where standard surface ECG leads are shown in green and endograms from a ten-pole diagnostic electrode placed in the proximal part of the coronary sinus are shown in white.

Table 1.

Temperature measurement during laser ablation and evaluation of esophageal lesions

	Organocomplex 1						Organocomplex 2						Organocomplex 3					
Ablation duration, s	0	15	30	45	60	75	0	15	30	45	60	75	0	15	30	45	60	75
Left atrial temperature, °C	17	32.2	30	26.4	36.3	36.5	10.8	22.8	33.7	41.4	44.3	40.3	14.2	28.2	35.2	39.2	29.1	48.6
Temperature in the inner part of the esophagus, °C	-	26.9	25.8	29.5	30.8	32.8	-	23.7	25.6	30.7	33.5	27.6	-	19.5	28.1	26.4	33.8	36.5
Temperature in the outer part of the esophagus, °C	18.4	21	38.5	28	39.7	41.8	20	28.1	32.6	36.4	34.3	32.3	15	24.2	34	32.5	32.1	39.8
Left atrial damage	-	No	No	No	No	Yes	-	No	Yes	Yes	Yes	Yes	-	No	Yes	Yes	Yes	Yes
Transmural damage to the left atrium	-	No	No	No	No	Yes	-	No	Yes	Yes	Yes	Yes	-	No	No	No	No	Yes
Collateral damage to the esophagus	-	No	No	No	No	Yes	-	No	No	Yes	Yes	Yes	-	No	No	No	No	Yes

Table 2.

Electrophysiologic parameters before and after laser ablation of ganglionic plexuses

Animal #	Weight, kg	EARP before ablation, ms	AFD before ablation, s	EIT	SRRT before ablation, s	Number of ablations, n	EARP after ablation, ms	AFD after ablation, s	EIT	SRRT after ablation, s
1	39.2	170	300	Yes	-	6	190	-	-	-
2	37	150	5	No	6	6	150	5	No	6
3	37.3	190	-	-	-	6	180	60	No	61
4	39.6	160	28	No	29	5	170	-	-	-
5	39	170	20	No	21	7	190	-	-	-
6	38.8	150	300	Yes	-	6	150	100	No	101
7	40.8	200	141	No	142	6	200	7	No	8
8	37.9	200	300	Yes	-	6	200	300	No	-
9	39.5	200	4	No	5	6	200	2	No	3
10	40.8	200	14	No	15	6	200	14	No	15
11	39.5	200	3	No	4	6	200	-	-	-
12	37.6	200	5	No	6	6	200	-	-	-
13	37.5	200	18	No	19	6	200	-	-	-

Note: EARP, effective atrial refractory period; AFD, atrial fibrillation duration; EIT, electroimulsive therapy; SRRT, sinus rhythm recovery time.

anatomical location. A longitudinal incision was made along the dorsal wall of the esophagus, extending from the upper third to the lower third, to facilitate observation and temperature measurement at the surface of the ventral esophageal mucosa. To measure the temperature, a Flir E6 thermal imaging camera (Flir, Sweden) was mounted at 30 cm. The ablation protocol included 15 W exposure, irrigation at a rate of 40 ml/min, and applications of 15, 30, 45, 60, and 75 seconds. The ablation parameters were selected based on previous studies in the experiment [12, 13]. At the beginning and end of each application, thermal scanning of the LA, inner and outer parts of the esophagus was performed using a thermal imaging camera, and macroscopic assessment of atrial myocardial damage, transmural damage, and esophageal damage assessment were performed.

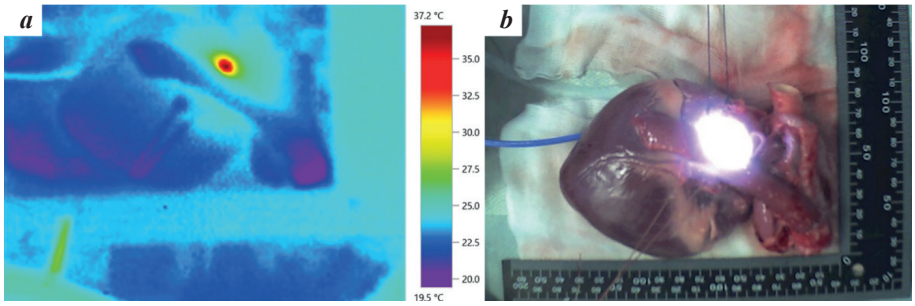

Fig. 3. Thermographic registration of temperature changes in a pig heart preparation during laser energy application using a thermal imaging camera, where the maximum temperature at the contact point is 37.2 °C (a - thermographic image of laser catheter contact with a pig heart preparation, b - application of laser action on the posterior wall of the left atrium).

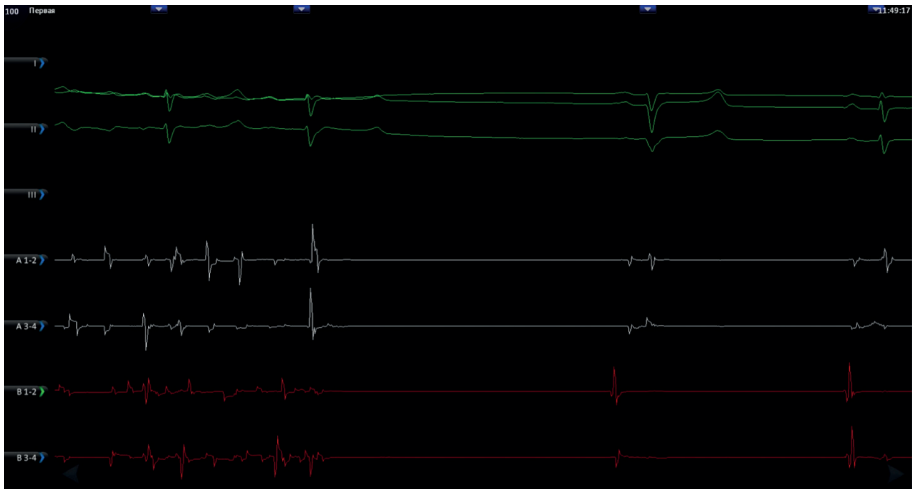

Fig. 4. Restoration of sinus rhythm after induction of atrial fibrillation in pig #1 using high-frequency electrocardiostimulation after laser cardiac neuroablation, where A 1-2 and A 3-4 are endogram recordings from the diagnostic electrode placed in the coronary sinus; abl 1-2 are endogram recordings from the ablation electrode.

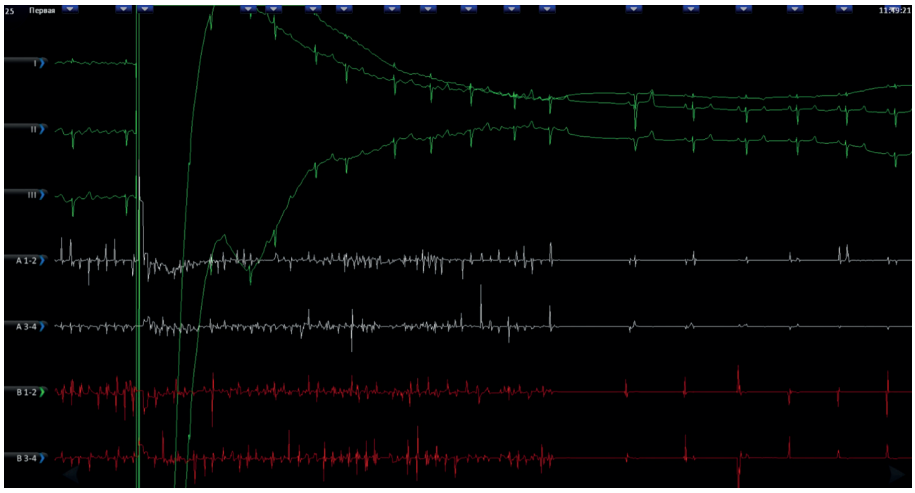

Fig. 5. Attempt to restore sinus rhythm using electrical cardioversion in a sustained paroxysm of atrial fibrillation caused by high-frequency electrical cardiac pacing, where A 1-2, A 3-4 are endogram recordings from the ablation electrode, B 1-2 and B 3-4 are endogram recordings from the diagnostic electrode placed in the coronary sinus.

In vivo laser ablation of pigs myocardium

Under previous experimental conditions, transseptal puncture and manipulation of the left atrium in pigs have been demonstrated to be significantly restricted and associated with a high risk of complications. This limitation arises due to the small distance between the interatrial septum and the posterior (dorsal) wall of the left atrium [14]. In our study, during catheter ablation of GP areas *in vivo*, we were constrained to performing exposures solely in the right atrium, targeting anatomical regions with a concentration of ganglionic plexuses. A schematic representation of the location of the areas of highest atrial GP concentration in pigs is presented in Fig. 1 [11].

Experimental operations were performed on 13 pigs of the Landrace line (mean animal weight was 38.8±1.2 kg). The experimental study was approved by the Committee for the control of the maintenance and use of laboratory animals of the FSBI «Almazov NMRC» of the Ministry of Health of Russia. The procedures were acute, that is, the animals were withdrawn from the experiment at the end of surgery. All procedures were performed in an experimental operating room equipped with a mobile fluoroscopic unit (BV Endura, Philips, the Netherlands) and the Biotok Unity

non-fluoroscopic navigation system (Biotok, Tomsk, Russia). Sedation was performed by intramuscular injection of 1.5 ml of Zoletil 100 solution (Virbac, France), followed by peripheral venous access to the subcutaneous auricular vein. Then tracheal intubation was performed and invasive ventilation was performed (WATO EX-35 device, Mindray, China) with the following parameters: FiO_2 - 0.3, respiratory volume - 10 ml/kg, positive end-expiratory pressure - 6 cm of water column. Anesthesia was maintained using 1% isoflurane (Baxter, Puerto Rico). Puncture and cannulation of the right femoral artery and right femoral vein were performed. A 12 F diameter Flexcath multi-purpose steerable intraducer (Medtronic, Ireland) and a 7 F diameter hemostatic intraducer (Avanti, Cordis, USA) were placed in the femoral vein region. A 7 F diameter hemostatic intraducer (Avanti, Cordis, USA) was placed in the right femoral artery. After performing vascular accesses, heparin solution was administered intravenously (B. Braun, Germany) at a dose of 300 U/kg. The level of activated clotting time was monitored every 30 minutes, with a target level of ≥250 seconds.

The Biotok system (Tomsk, Russia) with built-in programmable pacemaker was used for endocardial electrophysiologic study. A 10-pole unguided Webster electrophysiology catheter (Biosense Webster, USA) was inserted into the region of the right femoral vein through a short 7 F hemostatic intraducer and positioned into the coronary sinus region under fluoroscopic control. The effective refractory period (ERP) of the atria was assessed using a technique commonly accepted in clinical practice. This involved placing a ten-pole diagnostic electrode in the coronary sinus and delivering a series of eight electrical impulses with identical amplitude and frequency to the atrial myocardium. The ninth pulse is then applied with a gradually decreasing time interval until no atrial myocardial response to the pulse is recorded. The cycle of an additional, ninth pulse in which the atrial myocardium has not responded to the electrical impulse is considered an atrial ERP. Atrial stimulation was then performed for 2 minutes using high-frequency electrical atrial stimulation (33 Hz) to induce AF (Figure 2). When stimulation was turned off, the fact of AF induction was recorded and the time for which AF continued was measured. In case if AF did not resolve on its own within 5 minutes, sinus rhythm was restored using external biphasic electrical cardioversion (200 J).

Transvascular laser ablation of right atrial GP

After restoration of sinus rhythm, a prototype fiber-optic catheter for laser ablation (SMTS, Russia) was inserted into the right atrial cavity through a steerable intraducer placed in the right femoral vein and connected to a laser energy generator (Medilas D, Germany). Under the guidance of the nephluoroscopic navigation system "Biotok," the catheter was positioned in the transition area between the dorsal wall of the right atrium and the interatrial septum. Subsequently, a series of laser applications were administered with 4-6 mm between ablation points, employing the following parameters: 15 Watts of power, 30 seconds duration per application, and an irrigation rate of 40 ml/min. Ablation was performed using continuous wave laser energy with a wavelength of 1064 nm. After laser myocardial ablation, a repeat of the AF induction protocol was performed.

Pathomorphological study

At the end of the experiment, the animals were euthanized by intravenous injection of a lethal dose of potassium chloride solution. After the onset of biological death, heart and lungs were harvested in a single block. The preparation was fixed in 10% buffered formalin solution for further macroscopic and histologic examination. Histologic examination was performed according to standard protocols using hematoxylin and eosin staining of paraffin sections. Morphometric analysis was performed using LeicaApplicationSuite V 4.5.0 image analyzer and LeicaScope (Germany).

Statistical analysis

The database was created in MS Excel program. Statistical analysis was performed using the STATISTICA 12 statistical package (StatSoft Inc., Tulsa, Oklahoma, USA). Categorical measures are represented by frequencies and percentages of the total number of observations. Quantitative data were tested for normality using the Kolmogorov-Smirnov criterion. Data are described as mean ± standard deviation (M±SD) in case of a normal distribution; median, 25% and 75% quartiles in case of a distribution other than Gaussian. The Mann-Whitney or Wilcoxon test was used to analyze the differences of indicators with such distribution, and t-test was used for indicators with normal distribution. Chi-square analysis was performed for categorical variables. Differences were considered significant at $P<0.05$.

RESULTS

Results of ex vivo laser ablation

A total of 15 applications were made on the dorsal wall of the LA. No visible myocardial damage was observed after 15-second applications, but 30-second applications revealed atrial wall damage in samples #2 and #3 (Table 1). Transmural myocardial damage and esophageal damage were achieved in organ complex #2 after 30, 45, 60, and 75 seconds with temperatures that ranged from 32.3 °C to 36.4 °C on the external side of the esophagus (an 11.3-15.4 °C increase in temperature during ablation

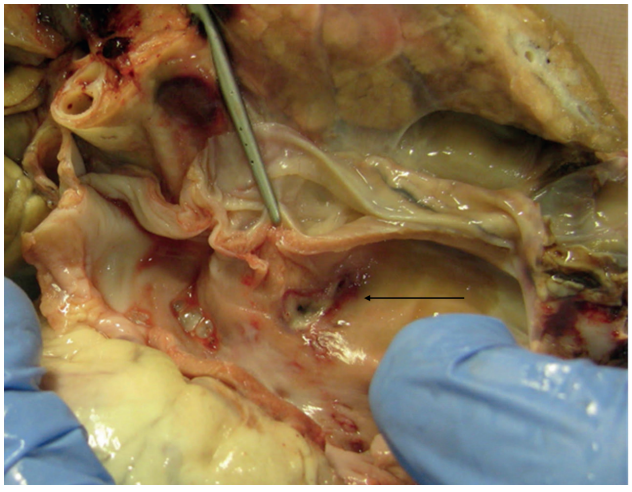

Fig. 6. Ablation point after laser application along the posterior wall of the right atrium with black necrosis in the center (marked with an arrow).

over baseline was recorded); and in organ complex #3, transmural myocardial damage and esophageal damage were observed only after 75 seconds of application with a temperature reaching 39.8 °C on the external ventral side of the esophagus (18.8 °C temperature increase). During ablation of the left atrium wall, the mean maximum temperature increase was 27.8°C at 75 seconds of exposure, while the minimum increase was 13°C at 15 seconds of exposure. Significant temperature increases were observed at 15 (P=0.004), 30 (P=0.025), and 75 (P=0.024) seconds of exposure. However, there was no statistically significant temperature increase at 45 (P=0.076) and 60 (P=0.057) seconds. A significant increase in esophageal surface temperature was observed at the end of each laser application at seconds 30 (P=0.018), 45 (P=0.028), 60 (P=0.013), and 75 (P=0.036). There was no statistically significant increase in temperature at 15 seconds (P=0.083). The maximum temperature increase was +20 °C at the 75th second (Fig. 3).

Induction of AF, transvascular laser ablation of GP

With high-frequency atrial stimulation, induction of AF was achieved in 92% of cases, in 12 of 13 experimental animals (Table 2). The shortest duration of inducible AF was 4 seconds (animal #11, Fig. 4). The maximum duration of the AF episode >300 seconds was observed in three animals (animals #1; 6; 8) (Fig. 5), and was terminated by electrical cardioversion (200 J). In nine animals, the time to independent recovery of sinus rhythm ranged from 4 to 142 seconds (15 [6; 21]). The mean atrial ERP was 183±20 ms. During laser ablation of atrial GP zones, all animals had persistent sinus rhythm. A total of 78 laser exposures (6±1 laser applications per 1 animal) were performed on the dorsal wall of the right atrium and in the interatrial septum. When induction was attempted again, AF was not induced in 6 experimental animals (46%) (P=0.03 versus initial induction). Seven (53%) had provoked AF; in six of them sinus rhythm recovered on its own. In one pig (#8), the duration of AF was 300 seconds, followed by electrical cardioversion. There was a trend toward a decreased duration of AF after ablation of atrial GP zones (18 [5; 141] seconds before ablation versus 2 [0; 14] seconds after ablation, P=0.06). Atrial ERP after laser ablation was 186±18 ms, with no statistically significant difference compared with baseline (P=0.99).

Pathomorphological examination

In 12 of 13 experimental animals, endocardial lesions were observed, which were presented as irregularly shaped brown spots or hemorrhages located along the dorsal wall of the right atrium and interatrial septum (Fig. 6, Table 3). Transmural damage was observed in 46% of the cardiac organ complexes examined (Table 3). No collateral damage of other organs was detected. Microscopic examination was performed in 10 experimental animals, and a total of 107 atrial wall fragments were analyzed. In animal #4, coagulation necrosis of the ganglionary plexus with intramural location was observed, while in the remaining experimental animals, ganglionary plexuses and nerve fibers appeared visually intact. The observed damage in the atrial myocardium ranged from hemorrhage with fibrin and coagulation necrosis to intramural coagulation changes in cardiomyocytes, characterized by vacuolization and “lumpy” decomposition of cytoplasm accompanied by hemorrhages (Fig. 7).

DISCUSSION OF FINDINGS

Our study unveiled that at an application power of 15 W on the posterior (dorsal) wall of the left atrium, the risk of esophageal injury escalates notably for exposures of 30 seconds or longer. However, we hypothesize that shorter exposures might be comparatively safer, given the absence of esophageal wall heating and limited heating of the epicardial surface of the atrium. However, these findings warrant cautious interpretation since thermometry was conducted at

Table 3.

Macro- and microscopic picture after laser ablation of ganglionic plexuses

#	NOD	MDS, mm	DT	NGD	Microscopic characterization
1	No	2x2	No	-	-
2	No	1x2	No	-	-
3	No	10x6	Yes	No	Coagulation necrosis, transmyocardial edema
4	No	5x5	No	Yes	Coagulation necrosis of the endothelium
5	No	2x1	No	No	Myocardial damage, pitting necrosis.
6	No	-	No	No	Intramural coagulation damage of cardiomyocytes
7	No	3x2	No	No	Transmural injuries: coagulation necrosis of CMCs with hemorrhage, foci of fibrin deposition
8	No	5x4	Yes	No	Intramural coagulation damage of CMCs with massive hemorrhage
9	No	12x4	Yes	No	Coagulation necrosis of endocardium and subendocardial CMCs
10	No	3x2	Yes	No	Endocardial fibrin overlay, intramyocardial hemorrhage with small-focal necrosis of muscle fibers
11	No	3x3	Yes	-	-
12	No	4x2	No	No	Intramural coagulation changes in CMCs
13	No	1x1	Yes	-	-

Note: NOD - neighboring organs damage; MDS - myocardial damage size, mm; DT - damage transmurality; NGD - nerve ganglia damage; CMCs, cardiomyocytes.

room temperature, which differs from the tissue temperature experienced during actual clinical conditions of catheter ablation. We also assessed thermal injury under acute experimental conditions without analyzing potential delayed effects on esophageal wall microcirculation. These delayed effects may lead to secondary trophic damage of the esophageal wall in the long term [15].

In this work, the use of laser technology for cardiac neuroablation with the effect of reducing the inducibility of AF is demonstrated for the first time. The possibility of modification of autonomous nervous regulation by radiofrequency endocardial ablation has been repeatedly demonstrated previously. Radiofrequency current applications in the region of atrial GP location resulted in acceleration of sinus rhythm as well as improvement of AV conduction [16].

To accurately delineate the location of GP high-frequency stimulation from a mapping electrode was employed to evaluate the deceleration of sinus rhythm following electrical activation of the ganglia. However, this approach often resulted in induction of AF during stimulation and was not highly specific. Therefore, an approach to ablate atrial anatomical areas with the highest concentration of GP has been proposed [17-19].

Laser energy sources are widely used in medicine as exposure techniques for various therapeutic and diagnostic approaches [8]. It is now possible to produce small diameter optical fibers capable of conducting sufficient power for medical transvascular interventions [9]. Fiber lasers are potentially applicable for ablation and have advantages over other ablation techniques. Firstly, fiber lasers with high average power (>40 W) are available, and the laser flux can be focused as well as collimated for selective exposure. The exposure may be better titrated and the total time required may be shorter than with radiofrequency or ultrasound ablation. Secondly, laser exposure enables the creation of a substantial temperature gradient that extends significantly deeper than the application surface. This capability facilitates the induction of necrosis in deeply located structures, such as the fat pads on the epicardial surface of the atria. Moreover, the laser wavelength used in our work has sufficient penetrating power to ablate structures on the subepicardial surface. The selectivity of tissue damage using different wavelengths of the laser source has been investigated previously [20]. Nevertheless, the nature of the damage in exposure and the reaction of the surrounding tissues remain insufficiently studied.

Another method of inactivating nerve impulse transmission in the parasympathetic nerve ganglia of the atria is the administration of botulinum toxin. The clinical application of the drug appears promising, but studies have yet to demonstrate reproducible results [21-23].

A new method of exposure is the use of pulse electric field, which leads to electroporation and death of myocardial cells in exposure. The potential advantage of this technique in comparison with traditional methods (radiofrequency, laser ablation, cryoablation) is the absence of serious thermal damage to adjacent structures, primarily the esophagus and diaphragmatic nerve. A recent study investigated the effect of electroporation on the duration of atrial ERP as a method of atrial GP injury in a chronic experiment [24]. ERP was measured before and after ablation with stimulation from the region of the coronary sinus orifice. It was found that GP ablation caused a mean acute prolongation of the atrial ERP by 80 ms. However, 4 months after ablation, atrial ERP shortened, which may be explained by reinnervation [25]. Similar results were obtained in another chronic experimental study in dogs where GP ablation was performed in the right atrium [26]. In our study, given the absence of pronounced damage to the GPs themselves on microscopic examination, this effect may be related to functional disruption of the ganglia, as well as probable damage to nerve outgrowths in the myocardial thickness.

Laser energy is an alternative to radiofrequency ablation, this approach is able to induce deeper damage compared to other ablation methods [13]. Given the small distance between the esophagus and the posterior (dorsal in the case of experimental animals) wall of the LA, the risk of thermal damage to the esophagus due to radiofrequency ablation with subsequent development of atrial-esophageal fistula is up to 0.4% [10]. In *in vivo* experiments, we did not observe any damage to the surrounding structures, and there were no cases of tamponade development after laser exposure.

Study limitations

Limitations of this study include the absence of a delayed analysis of nerve damage, as the study was acute in nature, focusing primarily on the electrophysiologic parameters of the atrial myocardium. Additionally, the sample size of *ex vivo* preparations was limited; however, it was adequate to determine the application duration necessary to pose a significant risk of thermal damage to the esophagus. It should be noted that intramural temperature monitoring using thermosensors in the atrial wall, adipose tissue, and esophageal wall was not performed. However, esophageal surface temperature was continuously measured during and after exposure using a thermal imaging camera, and the maximum temperature values were included in the analysis. Also, limitations of the study included the absence of electrophysiologic mapping of nerve ganglia, we used an anatomic approach in determining the target ablation zones; also, physiologic parameters of autonomic nervous system activity were not analyzed.

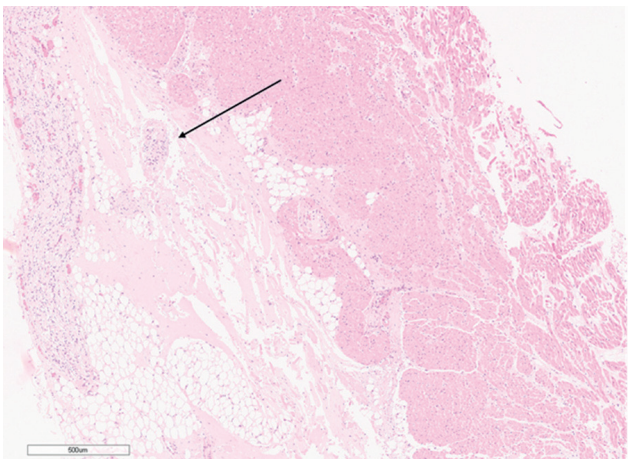

Fig. 7. Coagulation necrosis of the nerve ganglion in the ablation zone in pig #4 (arrow).

CONCLUSION

In the experiment on animals' catheter laser applications in the projection zones of atrial GP lead to a decrease in AF inducibility. In an *ex vivo* experiment, laser applications on the dorsal (posterior) wall of the LA with a power of 15 W and a duration of more than 30 seconds can lead to a significant increase in temperature on the esophageal surface, but shorter exposures do not lead to a change in esophageal temperature in the projection of the applications.

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