Controversial protamine in dealing with acute cardiac tamponade during radiofrequency ablation

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To the Editor: During radiofrequency catheter ablation (RFCA), acute cardiac tamponade is a common but life-threatening occurrence in which rapid blood accumulation in the pericardium cavity compresses the heart and causes the systemic circulation to deteriorate. Emergency percutaneous pericardiocentesis and immediate autologous blood transfusion are necessary. The administration of protamine for incessant bleeding is controversial, for pericardial blood clots may form spontaneously despite the neutralizing effects of heparin and may even necessitate thoracotomy. Our aim is to discuss the necessity and optimum time of protamine administration and to explore the means to prevent blood clot formation.

We retrospectively studied the medical history, procedural details, and imaging materials of 1826 patients who were admitted to our hospital for RFCA between April 2014 and June 2020. Before the procedure, all patients provided written informed consent for us to use their data. The study was approved by the local Institutional Committee on Human Research.

RFCA was recommended for atrial fibrillation (AF) and premature ventricular contraction, and the procedures were performed in accordance with the traditional standards of practice. A decapolar catheter was advanced into the right femoral vein or left subclavian vein and positioned in the coronary sinus, and a quadripolar catheter was, in general, positioned in the right ventricle or right atrium. Transseptal puncture was performed for AF under fluoroscopic guidance with or without intracardiac echocardiography. A three-dimensional depiction of the heart was constructed by the Carto 3 system (Biosense Webster, Diamond Bar, CA, USA) or the EnSite NavX system (St. Jude Medical, Austin, TX, USA). Ablation catheters used in this procedure were open-irrigation catheters (Thermocool, SmartTuch or SmartTuch SF, Biosense Webster, and FlexiAbility, St. Jude Medical), which were introduced into the right side of the heart through the right femoral vein or into the left ventricle through a retrograde aortic approach. Pulmonary vein isolation was achieved for paroxysmal AF, and additional line blocks of the left atrial roof and mitral isthmus were achieved for persistent AF. Left atrial appendage plugging devices (Watchman [Boston Scientific, Marlborough, MA, USA] or Amplatzer [St. Jude Medical, Plymouth, MN, USA]) were implanted in patients with paroxysmal AF complicated with cerebral infarction in the one-stop operation. Systemic heparinization was implemented in all patients who underwent the left-sided heart catheterization. The initial amount was dependent on the weight of patients (unfractionated heparin, 100 U/kg) and the additional amount was adjusted according to activated clotting time of whole blood.

Severe chest pain, loss of consciousness, decrease in blood pressure and oxygen saturation, and the sound of steam pop were indications of acute cardiac tamponade during RFCA. In such cases, fluoroscopy was promptly performed to verify the suspicion through cardiac silhouette excursion in the left anterior oblique view. If cardiac silhouette excursion reduced markedly while cardiac pulsations strengthened, acute cardiac tamponade was confirmed. Moreover, transthoracic echocardiography (TTE) could accurately depict acute cardiac tamponade, and intracardiac echocardiography could be used to monitor the pericardium in real time. When cardiac tamponade was confirmed, emergency subxiphoid pericardial puncture was performed under fluoroscopic guidance to prevent hemodynamic deterioration. A six-French ventriculography pigtail catheter was introduced via the sheath

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introducer system over the wire to the pericardial cavity to drain the blood. Multiple 50-mL syringes were used alternately to drain blood from the pericardial cavity, and the salvaged blood was rapidly reinjected via the femoral venous sheath after a simple filtration. Meanwhile, protamine was recommended to be prescribed to neutralize heparin for hemostasis, and homologous blood transfusion was prepared. In most cases, cardiac tamponade could be managed conservatively. If the hemodynamics was unstable or collapsed, the patient was transferred to the operating room as soon as possible.

Statistical analysis was performed with SPSS 20.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were calculated as means ± standard deviations, and categorical variables were calculated as numbers and percentages.

Of the 1826 patients, 12 (0.66%) suffered from acute cardiac tamponade during RFCA during a 6-year period; half of those patients were male (mean age, 67 ± 5 years). RFCA was performed for AF in ten of the 12 patients (10/12 for paroxysmal AF in eight and for persistent AF in two) and for premature ventricular contraction in two patients (2/12 in the right ventricle in one patient and in the left ventricle for the other). In three patients with paroxysmal AF, left atrial appendages plugging devices were implanted after RFCA in the one-stop operation because of prior cerebral infarction.

Steam pop occurred in five cases (5/12) during firing and mechanical injury happened in seven cases (7/12) during catheter manipulation. The perforations were located in the left atrium (7/12), left ventricle (1/12), right ventricle (3/12), and coronary sinus (1/12) [Table 1]. The average volume of drainage from the pericardium was 1018 ± 742 mL (range, 250–2500 mL). Ten patients underwent autologous transfusion for continuous bleeding, and an average volume of 932 ± 774 mL (range, 230–2500 mL) was reinfused immediately.

Protamine for anticoagulation reversal was administered in nine patients (9/12) according to the dosage of heparin in the operation. No blood could be aspirated out after the usage of protamine in five of those nine patients; meanwhile, fluoroscopy showed that the cardiac silhouette excursion disappeared during strong contraction, and then blood clots were suspected. Contrast medium was injected into the pericardium cavity via the pigtail catheter, where it spread in a patchy manner instead of rapidly throughout, especially around the pigtail. The blood pressure and oxygen saturation of the patients dropped sharply with loss of consciousness and whole-body sweating started in the next few minutes. The patients were immediately transferred to the operating room for emergency thoracotomy, and massive blood clots were found in the pericardium cavity. All the patients treated with exploratory thoracotomy ultimately survived and were discharged in 10 days.

Acute cardiac tamponade in association with RFCA is common, and the incidence has gradually increased with the number of catheter ablation operations. Our reported incidence of 0.66% during ablation of arrhythmias is consistent with that of prior published reports.[1] In addition, cardiac tamponade was reported to be the most frequent fatal complication of arrhythmias ablation.[2,3] Therefore, timely recognition of cardiac tamponade and prompt pericardiocentesis could reduce deaths.

Abrupt decrease in blood pressure and oxygen saturation, severe chest pain, loss of consciousness, and excessive sweating during the procedure were important signs of cardiac tamponade in our patients. Despite it being reported to be the golden standard to confirm cardiac tamponade,[4] not all the electrophysiology laboratories are equipped with TTE equipment. Therefore, available fluoroscopy must be used promptly to detect early signs of cardiac tamponade when cardiac silhouette excursion is reduced.[2] Intracardiac echocardiography has clear advantages over fluoroscopy

Table 1: Characteristics of the patients at baseline and managements for cardiac tamponade.

Case	Age/gender	Arrhythmias	Treatment strategy	Blood volume (mL)	Autologous transfusion volume (mL)	Mechanism of perforation	Position of perforation	Reversal agent	Blood clot	Surgery
1	68/F	PeAF	RFCA	840	800	Steam pop	RV base	Protamine/70 mg	Yes	Yes
2	67/F	PVC	RFCA	2500	2500	Steam pop	RVOT AS	No	No	No
3	70/M	PeAF	RFCA	2250	2000	Steam pop	LSPV	Protamine/30 mg	Yes	Yes
4	59/M	PaAF	RFCA	550	450	Steam pop	LSPV	Protamine/50 mg	No	No
5	67/M	PaAF	RFCA	250	230	Mechanical	RIPV	Protamine/50 mg	No	No
6	57/F	PaAF	RFCA + LAAO	1300	1300	Mechanical	RV apex	Protamine/50 mg	Yes	Yes
7	82/F	PaAF	RFCA + LAAO	280	No	Mechanical	LAA	No	No	No
8	74/M	PVC	RFCA	1500	1500	Mechanical	LV apex	Protamine/30 mg	Yes	Yes
9	69/M	PaAF	RFCA	800	800	Steam pop	Left AVG	Protamine/30 mg	Yes	Yes
10	64/M	PaAF	RFCA + LAAO	800	800	Mechanical	RSPV	Protamine/30 mg	No	No
11	72/F	PaAF	RFCA	850	800	Mechanical	LSPV	Protamine/50 mg	No	No
12	67/F	PaAF	RFCA	300	No	Mechanical	CS	No	No	No

AVG: Atrioventricular groove; CS: Coronary sinus; LAA: Left atrial appendage; LAAO: Left atrial appendage occlusion; LSPV: Left superior pulmonary vein; LV: Left ventricle; PaAF: Paroxysmal atrial fibrillation; PeAF: Persistent atrial fibrillation; PVC: Premature ventricular contraction; RFCA: Radiofrequency catheter ablation; RIPV: Right inferior pulmonary vein; RSPV: Right superior pulmonary vein; RV: Right ventricle; RVOT AS: Right ventricular outflow tract anterior septum.

and TTE in maximizing the safety and efficacy of complex interventional procedures, especially in detecting cardiac tamponade. In one of our patients (Case 11), an intracardiac echocardiography catheter was placed in the right ventricle to monitor the pericardium, and effusion was found right after the ablation catheter (SF; Biosense Webster) jumped from the ostium of the left superior pulmonary vein to the roof of the left atrium, and emergency pericardiocentesis was performed immediately.

The volume of spontaneous bleeding was dependent on the size, site, and geometric configuration of the perforation, on intra-cavity pressure, and on level of anticoagulation. The greatest degree of blood leak (Case 2) occurred because of steam pop at the anterior septum of the right ventricular outflow tract [Table 1]. Direct autologous blood transfusion, whereby filtered blood was reinfused via a femoral vein with a simple syringe, is an alternative method of maintaining stable hemodynamic status in spite of possible complications, such as microembolisms, sepsis, and thrombosis. This technique was characterized by availability, flexibility, and safety and was strongly promoted by Fiocca *et al*[5] An average volume of 932 ± 774 mL of autologous blood was transfused to replace the large volume of acute pericardial bleeding.

In general, protamine was administered to neutralize the anticoagulation action of heparin while the blood was aspirated from the pericardium, with the expectation that a locally formed thrombus could plug the perforation, further stop bleeding, and finally eliminate cardiac tamponade. However, we observed a more drastic event: hypercoagulable blood accumulated in the cavity of pericardium, gradually formed massive blood clots, and consequently aggravated cardiac tamponade, which necessitated emergency thoracotomy. Five patients were transferred to the operating room for emergency thoracotomy as a result of massive blood clots after the administration of protamine, as the clots could not be drained out.

We consequently debated whether protamine was necessary in dealing with acute cardiac tamponade during RFCA. Without protamine, constant drainage, and reinfusion of drained blood, might have been the only option for conservative treatment, which might have worked, but would run the risk of systemic inflammatory response syndrome. Therefore, the timing of protamine administration and the prevention of blood clots are important. In our patients, protamine was administered when a large amount of blood remained in the cavity of the pericardium and blood clots might then have formed easily, which would have blocked the six-French pigtail catheter and exacerbated cardiac tamponade. The following methods may prevent blood clot formation: (1) administering protamine when the blood is almost completely drained, in which case continuous observation is recommended for recurrent or persistent bleeding; (2) injecting heparin saline into the cavity of the pericardium to neutralize protamine for preventing blood clot formation and then aspirating the effusion; and (3) replacing the six-French pigtail catheter with a much thicker sheath (ten-French–12-French), which could drain the massive blood clots. With these measures, acute cardiac tamponade might be managed conservatively in most cases.

Our study had some limitations. It was an observative study, and the sample size was small. Additionally, the proposed methods of preventing blood clot formation should be verified in clinical practices.

In conclusion, protamine might exacerbate cardiac tamponade by resulting in blood clot formation, which in turn might necessitate further thoracotomy.

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Conflicts of interest

None.

References

1. Scheinman MM, Huang S. The 1998 NASPE prospective catheter ablation registry. Pacing Clin Electrophysiol 2000;23:1020–1028. doi: 10.1111/j.1540-8159.2000.tb00891.x.
2. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, *et al*. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol 2009;53:1798–1803. doi: 10.1016/j.jacc.2009.02.022.
3. Chen M, Wang ZQ, Wang QS, Sun J, Zhang PP, Feng XF, *et al*. One-stop strategy for treatment of atrial fibrillation: feasibility and safety of combining catheter ablation and left atrial appendage closure in a single procedure. Chin Med J 2020;133:1422–1428. doi: 10.1097/CM9.0000000000000855.
4. Tsang TS, Freeman WK, Barnes ME, Reeder GS, Packer DL, Seward JB. Rescue echocardiographically guided pericardiocentesis for cardiac perforation complicating catheter-based procedures. The Mayo Clinic experience. J Am Coll Cardiol 1998;32:1345–1350. doi: 10.1016/s0735-1097(98)00390-8.
5. Fiocca L, Cereda AF, Bernelli C, Canova PA, Serino F, Niglio T, *et al*. Autologous blood reinfusion during iatrogenic acute hemorrhagic cardiac tamponade: safety and feasibility in a cohort of 30 patients. Catheter Cardiovasc Interv 2019;93:E56–E62. doi: 10.1002/ccd.27784.

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