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Review

Methods and Techniques for Increasing the Safety and Efficacy of Pulmonary Vein Isolation in Patients with Atrial Fibrillation

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Abstract

The most common type of sustained arrhythmia is atrial fibrillation (AF). Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation for atrial fibrillation, which has emerged as the primary therapeutic strategy for atrial fibrillation patients. Unfortunately, about one-third of patients experience recurrent atrial arrhythmias after the procedure.

The leading cause of AF recurrence after PVI, especially during the first year, is reconnection of the pulmonary veins. There are different techniques and methods that could increase the efficacy of the procedure by making durable pulmonary vein isolation.

A literature search was conducted using the terms atrial fibrillation, ablation, pulmonary vein isolation, and durable PVI in the PubMed, Scopus, and Web of Science databases. Durable pulmonary vein isolation could be achieved by avoiding gaps in the ablation line and PV reconnections using pharmacological testing, waiting time, various indexes based on data from the electroanatomical mapping system, and special ablation catheters. Furthermore, detecting the gaps in the ablation line in the end of the procedure using different pacing and mapping techniques and application of additional energy to close those gaps could increase the success rate of the procedure.

Most commonly, AF recurrence after PVI is due to PV reconnections caused by gaps in the ablation line. To achieve safer and more effective PVI, the procedure has to be standardized and operator-independent with reproducible success rate and safety profile.

Keywords

ablation, atrial fibrillation, gap in ablation line, durable pulmonary vein isolation, durable lesion

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia. Despite the significant progress in the management of this condition, it remains the leading cause of stroke, heart failure, sudden cardiac death, and cardiac morbidity worldwide.[1] It increases the risk of all-cause mortality by twofold and the risk of stroke by fivefold.[2] Atrial fibrillation affects 2%-3% of the European population[1], and its treatment accounts for 1-3% of health care expenses[3]. In the last decades, catheter ablation has become the leading therapeutic approach to patients with symptomatic paroxysmal AF refractory to antiarrhythmic drugs and at present pulmonary vein isolation (PVI) is the cornerstone of catheter ablation for AF.[4]

AF catheter ablation efficacy is reduced by the recurrence of atrial tachyarrhythmias documented in 31.2% of patients in a two-year follow up.[5] The leading cause of recurrence, especially during the first year, is reconnection of the pulmonary veins – recovered conduction between the veins and the left atrium after successful PVI.[6] Reconnection is documented in 85%-100% of patients with redo procedures for symptomatic recurrence of AF[7,8] and it can also be proarrhythmogenic by causing re-entry atrial tachycardia.[9] Verma et al.[10] demonstrated that more than one pulmonary vein reconnection has clinical significance and leads to AF recurrence. That is why durable and sustained pulmonary vein isolation must be the operator's main goal.

Pulmonary vein reconnection mechanism

According to Rajappan et al.[11] the most common zone of reconnection in the left veins is the area between the veins or between the veins and the left atrial appendage (LAA). The most common zones of reconnection of the right veins are the area between the veins, and between them and the roof, or the floor of the left atrium.

There are several potential reconnection mechanisms. In the first place, it is possible that complete electrical isolation has not been achieved during the first procedure. The cause may be a gap in the ablation line or a non-transmural lesion.[12,13] Lack of gaps greater than 10.6 mm leads to significantly less AF recurrences in a 12-month follow-up (93.8% versus 33.3% with gaps in the ablation line).[14] Documented block in the conduction through the line does not exclude gaps.[12] This hypothesis is proved by myocardial biopsies obtained during MAZE procedures. Gaps in the ablation line and non-transmural lesions are found in the reconnected veins.[15] Cardiac magnetic resonance after PVI also shows gaps in the ablation line and these veins pose a higher risk of reconnection.[12]

Cell electrophysiological properties recover on the border of non-vital tissue for one to four weeks after PVI. Tissue heating slows down the conduction and even bigger gaps cannot conduct impulses through the line.[16] After regaining electrophysiological properties, these gaps can lead to reconnection of the pulmonary veins. Therefore, identifying, localizing, and avoiding or eliminating these gaps could lead to fewer reconnections and greater efficacy of the procedure.

Methods for avoiding gaps in ablation line and PV reconnections

Pharmacological testing for latent conduction

Some authors suggest using adenosine for unmasking latent conduction and identifying veins with a high risk for reconnection.[17] Applying additional amount of energy in these zones of latent conduction could reduce recurrence rate by 27%.[18]

Adenosine causes cell hyperpolarization by increasing K^+ inflow.[19] This counteracts the depolarization caused by radiofrequency (RF) application and if functional but hibernating myocardium is present, it regains conduction properties. If the myocardial damage is irreversible, adenosine administration cannot restore conduction.[19]

The meta-analysis of McLellan et al.[20] showed that adenosine testing reveals the zones with latent conduction, and their elimination with additional RF applications leads to a significant decrease in AF recurrences after the procedure. Surprisingly, patients with documented latent conduction after an adenosine test are at higher risk of AF recurrence despite additional RF applications in that zone.[20]

Moreover, a randomized controlled trial with 2113 patients has shown that there is no significant difference in the AF recurrence rate between the two groups – with and without the adenosine test. After a one-year follow-up (with a 3-month blind period), 68.7% of the adenosine group and 67.1% of the group without adenosine had no atrial tachyarrhythmia recurrence (p=0.25).[21]

Impedance monitoring

Ablation lesion size correlates with impedance drop during RF application.[22] At the same time, lower impedance during the same energy RF application leads to the formation of a bigger lesion.[23]

When RF energy is applied, tissue heating leads to a decrease in myocardial resistance and an impedance drop.[24] Animal models show that impedance drop correlates with the amount of pressure applied (R=0.73)[25], the depth (R^2=0.68)[26], the diameter (R^2=0.66)[26] and the volume of the lesion (R=0.72)[24-26].

Early trials point out that good catheter-tissue contact leads to a higher impedance drop.[25,26] The former is confirmed in trials with contact force ablation catheters: the greater the contact force, the higher the impedance drop.[27] Therefore, impedance monitoring can be used as a marker of catheter-tissue contact.

Based on these theories, Reichlin et al.[28] test a PVI protocol in which the impedance drop is used as a marker of tissue heating and good catheter-tissue contact. The ablation line consists of RF applications in which there is an impedance drop of at least 5 Ω (mean 7.6 Ω). Atrial arrhythmia recurrence rate was 16% during the 431±87 days of follow-up, and redo procedures were performed in 8% during the first year. In 94% of the patients, PVI was achieved at the first pass of the catheter, and adenosine testing found latent conduction in only 4% of PVs. The frequency of complications such as esophageal ulceration and late pericardial effusion proves deep transmural lesions.[28] Therefore, a better method for titrating energy must be discovered, especially when applying RF energy on the LA posterior wall.

On the other hand, Kumar et al.[29] showed weaker correlation between the impedance drop and real-time measured contact force. Stronger correlation with lesion formation and contact force is found when impedance is measured with specially designed ablation catheter with 3 miniature electrodes on its tip.

This contradicting data makes impedance measurement alone an unreliable marker for durable RF lesion formation.

Utilization of catheters measuring contact force

Ablation catheters measuring contact force (CF) have an advantage because they add another variable that affects lesion formation. Some data shows that when the position of the catheter is stable and the energy delivered is constant, then depth, width, and volume of the lesion increase proportionally to the increase in the CF.[22,30]

Several studies with CF catheters have demonstrated the better durability of PVI and lower recurrence rate during a one-year follow-up.[31,32] The frequency of latent conduction is significantly lower when CF-controlled RF ablation is performed (8% vs. 35%). This leads to better arrhythmia-free survival rate (88% vs. 66%).[32] During a one-year follow-up, a meta-analysis of nine non-randomized clinical trials found a 37% reduction of the risk of AF recurrence (p=0.01).[33] However, this was not proven by randomized clinical trials, in which there is no difference between groups with and without CF technology in long-term follow-up.[34,35]

In a multicenter randomized trial including 117 patients with paroxysmal AF, Ullah et al. failed to demonstrate any benefits of CF use in long-term follow-up arrhythmia free survival.[36] Other randomized trials have shown similar results.[37] Only in the subgroup with CF greater than 10 grams in more than 90% of RF applications is there a lower recurrence rate compared to the one with suboptimal CF (24% vs. 42% during the first year).[37]

It becomes clear from the above-mentioned that a redo procedure is needed in 20% of patients despite the use of CF. Therefore, besides a transmural lesion, the continuity of the ablation line could also affect the reconnection frequency.

It is even possible that a continuous ablation line is more important than contact force and the energy applied on one spot. Objective lesion assessment using the electroanatomical mapping system could lead to more reproducible and durable PVI. The use of the AutoMark function and CF catheters have achieved arrhythmia free survival in 92.3% of the patients in a 12-month follow-up.[38]

Improving catheters stability

Catheter stability is hard to achieve, especially when one depends on the subjective markers of the electroanatomical mapping system which usually do not correspond to the objective electrogram analysis. Moreover, the respiratory excursions and heart movement during the cardiac cycle can lead to an intermittent catheter-tissue contact, interrupted lesions, and PV reconnections.

Some studies with steerable sheaths and mechanical jet ventilation proved better catheter stability and less acute and chronic reconnections.[39]

Reddy et al.[14] showed that contact consistency is more important than contact force, which is a catheter stability marker. Better results are obtained by maintaining constant contact force throughout the procedure (at least 73% of the time).[14] Therefore, achieving catheter stability with sufficient minimum of contact force leads to better results than achieving greater amount of contact force only.

Using very high power RF applications (90 W) for a short duration (4 sec), solves the problem with catheter stability because they achieve transmural lesion before catheter displacement, and there is no longer a need to maintain a stable position for a long time.[40] This method has the potential to minimize collateral tissue and organ damage, such as esophageal injury, because it diminishes conduction heating.[41,42]

Avoiding gaps in the ablation line during RF ablation

The best way to achieve durable PVI at the end of the procedure is to avoid gaps in the ablation line. It is necessary to use an ablation protocol that avoids gaps in the ablation line and is based on objective criteria for lesion formation and line continuity.

There are different combinations of biophysical parameters during RF application that could be combined as indices. The force-time integral (FTI) is such an index. It is calculated automatically, and, in some studies, lower FTI leads to a higher frequency of latent conduction and acute reconnections. Durable PVI can be achieved when FTI is above 400 gram-seconds.[43]

Das et al.[44] suggest using the ablation index (AI) which includes contact force, time, and RF application power all combined in a complicated equation. In their study, AI correlates with impedance drop, and segments with lower AI are at higher risk of reconnection during redo procedures. On the other hand, AI cannot predict complications such as steam pops which can lead to atrial rupture and tamponade. Low energy RF application with longer duration can achieve high AI avoiding the risk of steam pops. High energy RF application can have low AI due to interruption because of steam pop occurrence.[45]

The lesion index (LSI) is similar to the ablation index. LSI consists of contact force, RF application duration, and power and predicts lesion size in an in-vitro model. Mean LSI above 5 predicts durable PVI.[46] More prospective randomized trials are needed to prove LSI efficacy for PVI.

These findings led to the establishment of the CLOSE protocol[38] in which AI is used with an algorithm for non-interruption of the ablation line chosen by the scientists. In that manner, two aspects of durable PVI are combined: lesion depth and ablation line non-interruption. When using the protocol, PVI becomes standard procedure and there is first pass PV isolation in 98% (100% for the right veins and 97% for the left).[38]

Discovering gaps in the ablation line

Gaps visualized by the electroanatomical mapping system

PVI can be achieved without completing the circumferential line, but there is evidence that in this case it is not durable. Miller et al.[47] showed that visual gaps in the ablation line registered by the electroanatomical mapping system are zones with dormant conduction between the vein and LA. Successful PVI in that case can be caused by tissue edema or other non-permanent damage to the tissue. In time, conduction recovers and leads to reconnection.

A sub-analysis of SMART-AF[14] proves that the procedure success correlates with lesion distance. Park et al. confirmed that theory.[48] In their study, acute reconnection could occur when there is a distance greater than 5 mm between the lesions. In another study with redo procedures for symptomatic AF recurrence in the zone of reconnection, there was a visual gap in the line during the first procedure (66.6% vs. 17.6% in the segments with no reconnection, $p<0.001$).[49] This once again confirms the importance of avoiding visual gaps in the ablation line to achieve durable PVI.

Waiting period after PVI

There is contradicting evidence about the benefit of a waiting period and its duration before checking the conduction. According to some studies, PVI reconnections occur in 30% and most of them are within 30 minutes of the isolation.[50] Wang et al.[50] showed that applying RF energy in the zones of reconnection after a 30-minute waiting period and obtaining complete PVI leads to less reconnections in a follow-up of 7 months.

On the other hand, Bänsch et al.[51] showed no effect of the 1-hour waiting period on AF recurrence. But in this study recurrences during the 3-month blind period are also counted as an end point.[4,51]

Pacing from the ablation line

Some older studies showed efficacy of stimulation from the ablation line and application of RF energy in the zones of capture until loss of capture.[52] This method is confirmed by a randomized trial, and it leads to lower recurrence rate compared to standard PVI.[53] However, using very high pacing output can cause atrial capture and mislead the operator that there is a gap in the line.[52]

Miller et al.[47] showed that pacing from intentionally left large gap in the ablation line does not lead to myocardial capture. This could be explained by pacing threshold augmentation caused by tissue edema.[54,55] These gaps can lead to PV reconnections after conduction recovery.[12,47]

Therefore, this method is not reliable for proving durable PVI.

Mapping

There are different methods for discovering gaps in the ablation line with mapping. In one of them, a local activation map of PV antrum behind the ablation line during sinus rhythm or atrial stimulation is created. Signals of the mapping catheter are recorded, annotated, and projected on the 3D model of the LA and PVs.[56] One must look for the zone where the impulse enters the PV and propagates. If the sequence changes after additional RF application, there are other gaps in the line and the mapping must be repeated.[56] The same map can be made for the LA around the ablation line during stimulation from the PV. One must look for the zone where the impulse enters the LA (the zone of earliest activation).[57] Mapping of the LA is more accurate because PV conduction is complex and has fractionated electrograms, but it cannot be used when there is a one-way conduction block.[57]

In addition, mapping could be done during stimulation around the ablation line. Activation slowing and activation sequence are measured with the PV catheter. One must look for the shortest activation slowing and the number of the gaps and their location (by the activation sequence on the PV catheter).[58]

Using high density mapping catheters to create a voltage or activation map is more accurate and less RF applications are needed for gap closure.[59]

Future directions

Novel catheters that allow direct endoscopic visualization of the endocardium, ablation line, and its gaps are being tested. This technique allows elimination of the gaps with direct real-time visual control.[60] More studies are needed before this technique can be used in clinical practice.

CONCLUSIONS

Most commonly, AF recurrence after PVI is due to PV reconnections caused by gaps in the ablation line. To achieve safer and more effective PVI, lesions have to be measured in real-time or there must be reliable software to predict their dimensions. Using this type of technology could lead to a standard and operator-independent AF ablation procedure with reproducible success rate and safety profile.

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Методы и технологии повышения безопасности и эффективности изоляции лёгочных вен у больных фибрилляцией предсердий

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Резюме

Наиболее распространённым типом устойчивой аритмии является фибрилляция предсердий (ФП). Изоляция лёгочных вен (PVI) является краеугольным камнем катетерной абляции при фибрилляции предсердий, которая стала основной терапевтической стратегией для пациентов с фибрилляцией предсердий. К сожалению, около трети пациентов после процедуры испытывают рецидивирующие предсердные аритмии. Ведущей причиной рецидива ФП после PVI, особенно в течение первого года, является повторное соединение лёгочных вен. Существуют различные приёмы и методы, которые могут повысить эффективность процедуры за счёт прочной изоляции лёгочных вен. Был проведён поиск литературы с использованием терминов „мерцательная аритмия", „абляция", „изоляция лёгочных вен" и „стойкий PVI" в базах данных PubMed, Scopus и Web of Science. Надёжная изоляция лёгочных вен может быть достигнута за счёт исключения разрывов в линии абляции и повторных соединений ЛВ с использованием некоторых фармакологических тестов, времени ожидания, данных системы электроанатомического картирования, объединённых в различные индексы, и специальных абляционных катетеров. Кроме того, обнаружение разрывов в линии абляции в конце процедуры с использованием различных методов стимуляции и картирования, а также применение дополнительной энергии для закрытия этих разрывов может повысить вероятность успеха процедуры. Чаще всего рецидивы ФП после PVI возникают из-за повторных соединений ЛВ, вызванных разрывами в линии абляции. Для достижения более безопасного и эффективного PVI, процедура должна быть стандартизирована и независима от оператора, с воспроизводимым уровнем успеха и профилем безопасности.

Ключевые слова

абляция, фибрилляция предсердий, разрыв в линии абляции, прочная изоляция лёгочной вены, прочное поражение