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Research Progress on the Factors Influencing the Recurrence of Atrial Fibrillation after Radiofrequency Ablation

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Abstract: Catheter radiofrequency ablation is an important treatment for atrial fibrillation (AF) at present. However, the recurrence rate of AF after catheter radiofrequency ablation is relatively high. Factors affecting postoperative recurrence include age, gender, type and duration of AF, ablation strategy, characteristics of the left atrium, electrocardiographic parameters, biomarkers, and coexisting diseases. Assessing the risk of postoperative recurrence in AF patients by these factors and developing a reasonable treatment strategy based on the assessment can help improve the therapeutic benefits of AF patients.

Keywords: Atrial Fibrillation; Radiofrequency Ablation; Recurrence.

1. Introduction

Atrial fibrillation (AF) is the most common persistent arrhythmia, which increases the risk of stroke, heart failure, dementia, death, and has a serious impact on patients' quality of life. With the maturity of technology, catheter radiofrequency ablation based on pulmonary vein electrical isolation (PVI) has gradually become an important treatment method for atrial fibrillation patients to control rhythm [1], but the high recurrence rate after radiofrequency ablation is still a very troubling problem. At present, a large number of studies have analyzed the influencing factors of recurrence after radiofrequency ablation, including age, duration of atrial fibrillation, size of left atrium, etc. This paper aims to analyze and summarize the researches on the influencing factors of recurrence after radiofrequency ablation of atrial fibrillation.

2. Definition of Recurrence of Atrial Fibrillation after Catheter Radiofrequency Ablation

Recurrence of atrial fibrillation after catheter radiofrequency ablation is very common, and studies [1] have shown that the recurrence rate of atrial fibrillation after surgery is as high as 40%. The recurrence of atrial fibrillation after radiofrequency ablation can be divided into early recurrence and late recurrence. Early recurrence refers to the onset of atrial fibrillation, atrial flutter and atrial tachycardia recorded by electrocardiogram for more than 30s within 3 months after surgery. Studies have shown [2] that early recurrence may be related to electrophysiological replasticity, residual conduction pathway, incomplete healing of heart tissue, inflammatory response and poor regulation of autonomic nervous system, and some early recurrence can resolve spontaneously, so early recurrence is not included in the total recurrence rate of atrial fibrillation after radiofrequency ablation. Relevant guidelines point out [3] that 3 months after ablation is a blank period, and atrial tachyarrhythmia occurring during the blank period is not considered as a recurrence after ablation of AF. Late recurrence refers to the occurrence of atrial fibrillation, atrial flutter, atrial tachycardia, etc., lasting longer than 30s after 3 months of radiofrequency catheter ablation.

3. Factors Influencing the Recurrence of Atrial Fibrillation after Catheter Radiofrequency Ablation

3.1. Age

Age is considered to be an independent predictor of recurrence after radiofrequency ablation in patients with atrial fibrillation and an unmodifiable factor for recurrence of atrial fibrillation. Studies have found that age is significantly correlated with the recurrence of atrial fibrillation after radiofrequency ablation [4]. Tris-tram et al. [5] believe that with the increase of age, the effect of RF ablation in patients with atrial fibrillation will decrease, including the recurrence and death of atrial fibrillation, which may be related to the older patients with more cardiac remodeling, more atrial myopathies and other diseases.

3.2. Gender

There are gender differences in clinical presentation, treatment and outcome of patients with atrial fibrillation. The incidence of atrial fibrillation is higher in males than in females, but the risk of recurrence of atrial fibrillation in patients who have undergone radiofrequency ablation is higher in females than in males [6]. Females are the risk factors for recurrence after radiofrequency ablation, and the risk of transient ischemic attack, heart failure, stroke and major bleeding after catheter ablation is higher in females than in males [7]. The mechanism of this gender difference is unclear, and it may be related to higher vagal tone, larger pericardial fat volume, and greater susceptibility to atrial remodeling in women [8]. Age and sex are two non-modifiable risk factors for recurrence after radiofrequency ablation, so we need to individualize the treatment of atrial fibrillation to select patients who will benefit more from ablation surgery.

3.3. Types and Duration of AF

AF is classified into paroxysmal, persistent, long-duration,

and permanent AF according to the duration of AF, the ease of relapse and the choice of treatment strategy for long-term sinus heart rate maintenance. Atrial fibrillation that spontaneously terminates within 7 days is called paroxysmal, atrial fibrillation that lasts for more than 7 days is called persistent, atrial fibrillation that lasts for more than 1 year is called long-term persistent, and atrial fibrillation that lasts for more than 10-20 years and is less likely to relapse and maintain a sinus heart rate is called permanent. Patients with different types of atrial fibrillation have a different risk of recurrent atrial fibrillation after radiofrequency ablation. Studies have shown [9] that patients with non-paroxysmal AF have about 60% higher risk of recurrence than those with paroxysmal AF. Non-paroxysmal AF usually means that the atrial fibrillation has persisted for some time, which can lead to deeper remodeling of the atrial structure and electrophysiological properties. This remodeling may include atrial fibrosis and atrial enlargement, which increases the risk of recurrent atrial fibrillation [10]. Studies have found [11] that the time between first diagnosis of atrial fibrillation and radiofrequency ablation is an important factor affecting the recurrence of atrial fibrillation. Shorter time from diagnosis to ablation is associated with lower recurrence rate of atrial fibrillation, while longer time from diagnosis to ablation is associated with higher recurrence rate, suggesting that early catheter ablation may help reduce the risk of recurrence of atrial fibrillation. Early catheter ablation may help to reduce the risk of recurrence and improve the therapeutic effect.

3.4. Ablation Strategies

Radiofrequency catheter ablation has become an effective method for the treatment of atrial fibrillation, but the impact of different ablation strategies on the recurrence rate is different. PVI is the cornerstone of radiofrequency catheter ablation. However, isolation of pulmonary vein alone is not suitable for all patients with atrial fibrillation.

Because of the heterogeneity of the atrial fibrillation population. A network meta-analysis comparing different ablation strategies found [12] that PVI strategies were superior to non-PVI strategies, and that combining PVI with other ablation strategies, such as autonomic modulation and additional ablation lines, appeared to increase treatment effectiveness and reduce the risk of AF recurrence. Moo-Nyun et al. [13] found that in addition to peripheral pulmonary vein isolation, additional linear ablation of superior vena cava to the right atrial septa (SVC-L) during catheter ablation for atrial fibrillation can significantly reduce the recurrence rate of postoperative atrial fibrillation without increasing the incidence of surgical complications. The underlying mechanism seems to be related to the effect of SVC-L on the cardiac autonomic nervous system and the wave dynamics of atrial fibrillation. Ablation with additional SVC-L significantly reduces the biatrial dominant frequency and increases the rate of atrial fibrillation termination and fragmentation compared with isolation of the pulmonary static vein alone. In the course of ablation in patients with paroxysmal atrial fibrillation, the use of a novel multi-electrode radiofrequency balloon catheter for PVI can reduce the recurrence rate[14] of atrial fibrillation compared with the traditional method for PVI. In the ablation treatment of patients with persistent atrial fibrillation, Joanne et al. [15] suggested that adding left posterior atrial wall isolation on top of pulmonary vein isolation would increase the recurrence rate of postoperative atrial fibrillation, possibly because the isolation of a larger atrial region creates a substrate for macro reentrant arrhythmias (such as atrial fibrillation). The selection of ablation strategies may need to be individualized to adapt to the specific needs of different patients, so as to improve the success rate of surgery and improve the quality of life of patients.

3.5. Left Atrial Characteristics

Left atrial size (LAD) is considered to be an important risk factor for atrial fibrillation recurrence after radiofrequency ablation. Studies have shown [16] that the risk of atrial fibrillation recurrence increases linearly with the increase in left atrial size, which is related to atrial remodeling caused by left atrial enlargement. A recent study [17] showed that left atrial size had a U-shaped relationship with the risk of recurrence of atrial fibrillation, and LAD was significantly higher. The 3.0-4.6 cm range was associated with a lower risk of AF recurrence, and patients with too small or too large left atrium size had a higher risk of AF recurrence. Khashayar et al. [18] quantified the left atrial characteristics through cardiac magnetic resonance imaging and found that every 10% increase in left atrial fibrosis was associated with a 1.54-fold increase in the risk of postoperative atrial fibrillation recurrence, and every 10ml increase in left atrial volume was associated with a 1.07-fold increase in the risk of postoperative atrial fibrillation recurrence. Left atrial fibrosis can be used as a predictor of atrial fibrillation recurrence, and the increase in the degree of fibrosis is proportional to the risk of postoperative atrial fibrillation recurrence, which may be because fibrosis changes the electrophysiological characteristics of the atrium and increases the heterogeneity of electrical signal propagation, thus promoting the maintenance and recurrence of atrial fibrillation. Increased left atrial volume is also associated with the risk of atrial fibrillation recurrence, although the strength of the association is not as strong as that of fibrosis, and the increased volume may reflect atrial remodeling, including atrial wall thickening and atrial lumen enlargement, which may lead to changes in cardiac electrical activity and increase the likelihood of atrial fibrillation recurrence.

3.6. P Wave Duration

P Wave duration (PWD) is an important marker of atrial electrical conduction and represents the process of atrial depolarization. Studies have shown that PWD is related to atrial remodeling and atrial fibrosis, and can predict the recurrence of atrial fibrillation after radiofrequency ablation [19]. For patients with persistent AF undergoing early radiofrequency ablation, Miao et al. [20] demonstrated that there is a linear positive correlation between PWD measured within 72h after surgery and the risk of recurrence. With the increase of PWD, the risk of recurrence gradually increases, and patients with PWD ≥125 ms have the highest risk of AF recurrence. A meta-analysis showed [21] that preoperative PWD was an independent predictor of AF recurrence after RF ablation, with PWD>120ms before surgery doubling the risk of AF recurrence during follow-up, and when PWD was further extended to > 150ms before surgery, it resulted in a 10-fold increase in the risk of AF recurrence.

3.7. Biomarkers

3.7.1. BNP

B-type natriuretic peptide (BNP) can be used as a biomarker to predict recurrence after radiofrequency ablation.

A recent study reported that BNP concentrations in patients who relapsed after radiofrequency ablation were significantly higher than those who did not [22]. Hui et al. [23] found that increased BNP levels before ablation were associated with an increased risk of AF recurrence after RFCA. A large multicenter retrospective study of 1750 patients [24] showed that preoperative BNP concentration and BNP concentration at 3 months post-operative follow-up were independent risk factors for recurrence of AF. The beneficial effect of low preoperative BNP concentration on recurrence of AF was significant in patients with paroxysmal AF, but in patients with non-paroxysmal AF, Especially in patients with long-term atrial fibrillation, the beneficial effect was weakened, while BNP concentration at 3 months post-operative follow-up was significantly improved compared with before, and low BNP concentration at follow-up was significantly associated with a lower risk of recurrence of atrial fibrillation [25].

3.7.2. Serum Albumin

Serum albumin is the main protein in plasma, accounting for 50% of the plasma protein content. High levels of serum albumin are considered to be a risk factor for the occurrence of atrial fibrillation and the postoperative radiofrequency ablation of atrial fibrillation. Studies have shown [26] that the higher the level of serum albumin, the lower the risk of atrial fibrillation, which may be related to the anti-inflammatory and antioxidant properties of albumin, and inflammation and oxidative stress are important factors in the occurrence of atrial fibrillation. One study [27] found that the negative association of serum albumin levels in the development of AF may be mediated by the influence of specific serum metabolites (such as docosatrienoate and oleate/vaccenate) in the serum. Albumin levels reduce the risk of atrial fibrillation by increasing the levels of these metabolites, and this mediating effect may be a new idea for the prevention and treatment of atrial fibrillation, which needs more research to prove. Serum albumin concentration can be used as an independent predictor of atrial fibrillation recurrence after radiofrequency catheter ablation. Zhang et al. [28] found that higher serum albumin concentration is associated with a higher risk of recurrent atrial fibrillation. Patients with persistent atrial fibrillation with left atrial diameter (LAD) ≥ 43.5mm and serum albumin concentration ≥ 42.2g /L are at higher risk of recurrent atrial fibrillation.

3.8. Concomitant Disease

3.8.1. Periodontitis

Periodontitis can be considered as a risk factor for the recurrence of atrial fibrillation. Periodontal treatment after radiofrequency ablation can reduce the recurrence rate of atrial fibrillation. Studies have shown [29] that patients with periodontitis have a higher risk of developing atrial fibrillation, which may be related to the systemic inflammatory response caused by periodontitis. Relevant studies have reported that periodontitis can activate the NLRP3 inflammatory body [30], which is related to the occurrence of atrial fibrillation [31]. Shunsuke et al. [32] used the periodontal inflammatory surface area to measure the degree of periodontitis and found that the greater the periodontal inflammatory surface area, the higher the recurrence rate of atrial fibrillation. The periodontal inflammatory surface area can be used as a marker to predict the recurrence of atrial fibrillation, and periodontal treatment during the gap period after radiofofency ablation can reduce the periodontal inflammatory surface area. However, the recurrence rate of atrial fibrillation was significantly reduced in patients receiving periodontal therapy.

3.8.2. Diabetes Mellitus

Mellitus is an important risk factor for AF, which may be related to the expansion and inflammation of epicardial adipose tissue, resulting in microvascular dysfunction and cardiac fibrosis [33]. A multicenter observational study of 2,504 AF patients undergoing catheter ablation showed that diabetes mellitus is associated with an increased recurrence rate of AF after radiofrequency ablation, especially in patients with persistent AF [34]. Sodium-glucose cotransporter 2 inhibitor (SGLT2i) is a new type of oral antidiabetic drug. Zixu et al. [35] confirmed that patients with diabetes treated with SGLT2i had a lower risk of AF recurrence after RF ablation, suggesting that diabetes itself may increase the risk of AF recurrence. This also provides a therapeutic option to reduce the recurrence rate of atrial fibrillation in patients with diabetes coexisting with atrial fibrillation.

3.8.3. Obstructive Sleep Apnea Syndrome (OSAS)

Obstructive sleep apnea syndrome is a risk factor for recurrence of atrial fibrillation after radiofrequency ablation. A meta-analysis [36] showed that atrial fibrillation patients with OSAS had a 25% higher risk of recurrent atrial fibrillation after RF ablation than non-OSAS patients, which may be related to the structural changes in the heart, autonomic dysfunction, vascular endothelial dysfunction, inflammation, and oxidative stress response caused by OSAS. Treatment with continuous positive pressure ventilation (CPAP) was found [37] to reduce the rate of recurrence of atrial fibrillation in patients with OSAS. However, a prospective study showed [38] that patients treated with CPAP did not have a significant reduction in the recurrence rate of atrial fibrillation compared with untreated patients. Whether CPAP therapy can increase the success rate of radiofrequency ablation in patients with OSAS combined with atrial fibrillation is controversial, which may be related to factors such as reduced patient compliance and high selectivity in the study population, and more studies are needed to verify it. Related studies reported [39] that autonomic nerve activation plays a role in the pathogenesis of AF in OSAS patients. Acute apnea events lead to co-activation of sympathy-vagus nerve, shortening the atrial refractory period and promoting the occurrence of AF. Sympathetic nerve activation caused by chronic sleep apnea plays a key role in atrial autonomic, structural and electrical remodeling. Providing a basis for the maintenance and recurrence of AF, autonomic nerve modulation therapy targeting this mechanism may become a new treatment method for OSAS-related atrial fibrillation.

4. Conclusion

With the development of technology, radiofrequency catheter ablation plays an increasingly important role in controlling the rhythm of patients with atrial fibrillation. Relevant studies have shown that radiofrequency ablation is superior to drug therapy in terms of efficacy, but the high recurrence rate of atrial fibrillation after ablation is still troubling us. There are many factors affecting the recurrence of postoperative atrial fibrillation, such as age, gender, size of left atrium, BNP, accompanying diabetes, etc. Some factors are immutable, but some factors can be changed. We hope to understand the clinical status of patients by summarizing their clinical characteristics before surgery, and then individually

assess the risk of postoperative recurrence of patients after radiofrequency ablation, and on this basis, formulate a reasonable treatment strategy: Patients with a high probability of success in preoperative evaluation should be actively encouraged to undergo surgery instead of waiting for antiarrhythmic drugs to fail. For patients with a very low success rate, the accompanying risk factors should be actively controlled while ablation should be considered to reduce the symptoms of patients. This has important implications for reducing unnecessary procedures, reducing complications, and reducing medical costs.

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