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Risk & Danger

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Atrial fibrillation

Latest treatments

New techniques in ablation and imaging are broadening the options for treating patients with symptomatic and asymptomatic atrial fibrillation.

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Atrial fibrillation (AF) is the most common clinical arrhythmia seen in the daily clinic. It has an important impact on the economic health burden, as many patients are affected by this symptomatic heart rhythm disturbance.

AF increases the risk of stroke, which has the highest impact on AF-associated mortality. The most common preventive treatment is oral anticoagulation. The introduction of novel oral anticoagulants (NOACs) in 2009 increased appropriate therapy for patients for whom oral anticoagulation was withheld because of risk of bleeding (Connolly et al. 2009; Camm et al. 2017).

Another treatment for prevention of stroke in AF patients is left atrial appendage occlusion (LAA). This treatment is for AF patients who are at risk of stroke, but who cannot undergo oral anticoagulation, for example due to recurrent gastrointestinal bleeding. For this small group of patients, interventional therapy by occlusion of the left atrial appendage by the device hook is an option. After patients have successfully undergone this intervention without complications and the device is placed within the left atrial appendage of the left atrium they undergo endothelialisation and can stop the oral anti-coagulation (Holmes et al., 2014, Holmes et al. 2009; Reddy et al. 2011). If after 3-6 months everything is fine, the patients can stop taking oral anti-coagulants. They are protected both by the device and by the cessation of oral anti-coagulation. The combination of NOACs and LAA occlusion has improved stroke prevention in AF patients and is applicable to more patients. Before we had these treatments only 60% of AF patients at risk of stroke underwent adequate therapy (Camm et al. 2017).

Symptomatic atrial fibrillation: pulmonary vein isolation

Approximately 25 to 40% of AF patients are symptomatic: symptoms include palpitations, shortness of breath, dizziness, reduced exercise capability and cardiac decompensation. These patients need specific symptomatic treatment, which is interventional therapy by ablation, known as pulmonary vein isolation. The rationale is that in the pulmonary veins connected to the left atrium, in the affected muscles originate the electric impulses which initiate atrial fibrillation. Electrically isolating the pulmonary veins positively affects the initiation or maintenance of the arrhythmia. PVI is performed with a puncture in the groin, then going up the femoral vein to the right atrium to perform the trans-septal puncture to access the left atrium. The technique was introduced 20 years ago by the French cardiologist Michel Haïssaguerre, and has been evaluated in controlled trials (Morillo et al. 2014; Haissaguerre et al. 1998; Cosedis Nielsen et al. 2012). Around 70% et al. 2016a; of patients are free from any arrhythmia after one year if they undergo PVI. However, this leaves 30% of symptomatic AF patients who are non-responders (Kuck et al. 2016, Haissaguerre et al., 1998; Cosedis Nielsen et al. 2012). For patients with persistent AF this interventional therapy has a success rate of 50% (Tilz et al. 2012). Therefore there are new treatments being developed and trialled.

Mapping systems

A new development is mapping systems, which aim to get an electrical anatomical map of the atrium in respect to AF. These aim to characterise the atrial muscle, the atrial cardiomyocytes and the atrial electrical activity, in order to understand which electrical misfunction is present in the patient and is causing the atrial fibrillation, beside the role of the pulmonary vein which is already established. Rotor mapping looks for rotational activity in the atrial electrical activity similar to nature when a tornado makes a typical movement in the centre and in the core. If we ablate in the atrium building up electrical borders eliminating the rotational activity we may stop AF (Narayan et al. 2012).

High-density mapping systems provide the basis for high-resolution electrical anatomical mapping. While moving the catheter through the atrial chamber, touching the tissue, the system is able to provide the reconstruction of this atrium, including the information from 30-40,000 3D points and coding electrical information of the electrical signal of this channel. High amplitudes represent a healthy myocardium. Low electrical amplitudes may display many cardiomyocytes

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with an impaired function or represent areas of fibrotic tissue. With this system we can create a map of diseased tissue and healthy tissue and can see how the electrical impulse information is moving around within the atrium. In addition, if we have a structured electrical activity like a circle, the re-entry tachycardia, we are able to build up this tachycardia in the 3D map and the operator is able to much better understand what pathway the arrhythmia goes along and intervene at the critical region of the pathway to stop arrhythmia and prevent recurrence. This is a huge step forward as it gives a much better resolution and a much better picture of what is really going on in the myocardium (Schaeffer et al. 2016).

> “IN THE FUTURE WE ARE LOOKING FORWARD TO BETTER UNDERSTAND THE PATHOPHYSIOLOGY OF PATIENTS THAT DON’T BENEFIT FROM CURRENT TREATMENTS”

Contact force ablation catheters

Contact force ablation catheters enable the operator performing the intervention to use the ablation catheter as the energy source to burn the critical region of tissue for arrhythmia. We have investigated the role of real-time compact force measurement. This technology gives an estimate of the compact catheter tissue, based on the rationale that we cannot just work with the critical region of the myocardium to get rid of the critical or cardiac cells which are important for the arrhythmia. Before we had this technique it was just an estimate, by looking at x-rays and reading at the hand when putting in the catheter. Now we have the information of real-time catheter force. This makes the procedure much more efficient in respect to procedural parameters, but it has not shown a significant effect on patient outcome yet either in my clinic or in ongoing clinical trials (Reddy et al. 2015). However, in the future we hope to better identify the patient benefiting the most from this procedure. The technique is beneficial for operators learning the technique as it’s not a steep learning curve and brings them faster to the status of an experienced operator.

Imaging

Another recent innovation is gadolinium delayed enhancement magnetic resonance imaging (MRI). Prof. Marrouche’s group from Utah investigated the role of late enhancement MRI of the atrial wall with the goal to visualise zones of scarring and fibrosis. The DECAAF trial showed that with intervention by ablation, you characterise late enhancement atrium and find out that the higher burden of fibrosis is associated with less good outcome after one year of ablation therapy (Marrouche et al. 2014). This information can help us stratify therapy and identify the patients in which therapy could be successful—those with low fibrosis burden, and also stratify patients who have so much fibrosis in the atrium that therapy by ablation is not likely to be successful. Therefore we would not put these patients forward for this procedure, but prescribe drugs instead. Prof. Marrouche’s group is now undertaking the DECAAF-II trial (**https://clinicaltrials.gov/ct2/show/NCT02529319**) to evaluate the role of ablating or burning these disease regions, which is especially important in patients with persistent AF. To improve treatment one hypothesis is that if you could target a specific region of fibrotic tissue, which might represent diseased arrhythmogenic myocardium and thereby positively affecting the outcome of the procedure. This fibrotic area ablation is performed in addition to regular pulmonary vein isolation. So this might be one approach—imaging characterisation, identifying areas of diseased myocardium, which is probably fibrosis and then perform a pulmonary vein ablation and try to target these key areas to improve outcome. The DECAAF-II trial is ongoing and aims to enroll around 900 to 1000 patients investigating the therapeutic role of this late-enhancement MRI. This information about the atrium may give a better understanding of the underlying pathophysiology of the disease of the patient. The hypothesis is that AF is just one stage of atrial cardiomyopathy so you have a cardiomyopathy and one manifestation of this cardiomyopathy might be this rhythm disturbance. More and more we think in the order of a cardiomyopathy—if you are able to image the atrium and determine the nature of the disease assessed by fibrosis you can also identify patients at risk for AF and initiate upstream therapy such as blood pressure control and coronary heart disease checks (Goette et al. 2016). We can then look for hypercholesterolaemia and sleep apnoea syndrome in these patients.

Autonomic nerve system

The autonomic nerve system by sympathetic and parasympathetic activation plays an important role in the initiation of ventricular arrhythmias and are thought to play an important role in initiation of atrial arrhythmias as well (Chen et al. 2014). For example, in endurance sports such as marathon this is a risk factor for AF; the parasympathetic system and normal high activity could be one underlying contributor to initiation of the arrhythimia (Guasch et al. 2013). There are nuclear medicine imaging technologies using specific

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sympathetic tracers like ^{123}Iod-Metaiodbenzylguanidine (^{123}I-MIBG), which enables us to visualise sympathetic innervation in the myocardium. At the moment it is reliably feasible on the ventricular level and there are studies ongoing evaluating this technique on the atrial level. In future imaging technologies using nuclear medicine tracers for the autonomic nerve system will help us to further understand what could be the critical variables for the arrhythmia in the individual patient.

> “IN FUTURE IMAGING TECHNOLOGIES USING NUCLEAR MEDICINE TRACERS FOR THE AUTONOMIC NERVE SYSTEM WILL HELP US TO FURTHER UNDERSTAND WHAT COULD BE THE CRITICAL VARIABLES FOR THE ARRHYTHMIA IN THE INDIVIDUAL PATIENT”

Cryoballoon ablation

Cryoballoon ablation is an alternative to radiofrequency-guided ablation. A recently published study that compared the two found that cryoballoon ablation was non-inferior compared to the radiofrequency-guided approach in pulmonary vein ablation in AF (Kuck et al. 2016a). Cryoballoon ablation has a lot of potential benefits; it is easier to handle and easier to use for less experienced operators. It is a single shot device. The operator does not have to go around the veins with a catheter; they put a balloon in the vein, freeze and the procedure is completed. It is also less time consuming and less invasive. The second generation cryoballoon ablation device might also have the potential be superior in respect to recurrence and avoiding unnecessary repeat procedures (Kuck et al. 2016b). Trials are ongoing into the role in persistent AF, and it may turn out to be actually superior to RF ablation.

Conclusion

There are several developments in the treatment of AF to prevent stroke—therapies for symptomatic patients with rhythm disturbance and further developments for pulmonary ablation. In the future we are looking forward to better understand the pathophysiology of patients that don’t benefit from current treatments, by using mapping systems, rotor mapping signal analysis and also imaging technologies to get better insight into the condition and guide therapy. Nuclear medicine will enable better analysis of the autonomic nerve system. Cryoballoon ablation is now well-established for a broad group of patients and broad group of operators. ■

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