Smoking and Arrhythmias

Introduction

Management of patients with Arrhythmias can range from medical therapies such as rate control medications to advanced interventions such as ablation and ICDs. However, are we paying enough attention to simple risk factor modification, such as stopping smoking that may make a huge difference to our arrhythmia patients. This review will outline the links between smoking and heart rhythm disorders.

General Cardiovascular Effects of Smoking

Tobacco smoking has a wide range of effects on the cardiovascular system ranging from endothelial dysfunction, increased thrombosis, increased atherosclerosis, damage to coronary artery vessels, arrhythmias, coronary artery spasm and heart failure. (1)(2)(3)(4)(5)

Smoking causes endothelial dysfunction through reduction in nitric oxide level and damage to the endothelium. Oxygen radicals are released by cigarette smoking and cause increased atherosclerosis through a number of pathways. Smoking causes increased levels of prothrombotic factors such as tissue factor (TF) and von Willebrand factor vWF.

There are significantly increased rates of atherosclerosis in patients who smoke due to a number of mechanisms such as smoking’s effect on inflammatory factors and macrophages. Smoking also increases angiogenesis, red cell mass and levels of leucocytes.

Smoking causes increased arterial stiffness and subsequent hypertension. The main risk factor for coronary artery spasm is also smoking. Smoking also predisposes to increased left ventricular dysfunction and increased rates of ventricular tachycardia in patients with left ventricular dysfunction. Also, smoking increases mortality in impaired left ventricular function, to which increased arrhythmias caused by smoking in these patients are a contributor.

Other forms of tobacco exposure such as smokeless or tobacco chewing have been found to have varying levels of cardiovascular risk. Also, passive smoking is considered to be a significant risk factor for coronary artery disease which in turn eventually leads to arrhythmias.

Smoking and Arrhythmias

Through multiple mechanisms described above (atherogenesis, hypoxia, increased catecholamine release, thrombotic and inflammatory effects), smoking causes arrhythmias. Patients with chronic obstructive pulmonary disease have high level of carbon monoxide which causes hypoxia and such patients have an increased propensity to ventricular arrhythmia and left ventricular dysfunction in exercise(39). Most COPD patients are smokers or these patients have similar carbon monoxide levels to smokers. Carbon monoxide inhalation increases ventricular fibrillation (VF) in animal models(40). Patients with left ventricular (LV) dysfunction and implantable cardioverter defibrillators were found to have much higher rates of ventricular tachycardia if they smoked rather than if they did not, despite the fact that patients who smoked were much younger (41). Nicotine causes increased catecholamine release that in turn leads to increased rates of arrhythmias. The carbon monoxide and oxygen radicals released from cigarette smoking cause hypoxia induced arrhythmias.

The CAST trial involved 2,752 patients and looked at the antiarrhythmic drugs and their efficacy in reducing ectopic ventricular activity. A sub-group analysis of patients who continued smoking as compared to those who stopped showed that those who stopped smoking had reduced arrhythmia induced mortality at one year however this finding was not statistically significant. The sub-group of patients who had untreated coronary artery disease
or LV dysfunction had the greatest statistical significant reduction in arrhythmias on the cessation of smoking(42). Smoking is a risk factor for nocturnal ventricular tachycardia in patients who have poor LV function(43).

Tsai et al., found in a large study group of 375,000 patients that areca nut (which is chewed with smokeless tobacco) was independently associated with higher levels of atrial fibrillation (AF), with adjusted odd ratio for 1.02 (95% confidence interval (Cl)=1.00-1.04) in risk of AF prevalence(43). The ARIC study of 15,000 patients showed that smoking was a strong risk factor for AF with hazard ratios of 1.32 (95% Cl = 1.10-1.57) in former smokers, 2.05 (95% Cl 1.71-2.47) in current smokers, and 1.58 (95% Cl 1.35-1.85) in non-smokers(44). The CHARGE-AF consortium looked at individual data for three large studies which had 26,000 participants and found an increased risk of AF in smokers which was adjusted into their model to predict AF over five years(45). Patients with AF who smoke were also found to have higher mortality rates over time in the AFFIRM dataset of 4060 patients with 21% of smokers as compared to non-smokers dying over five years (46). Among 7115 patients undergoing coronary bypass grafting (CABG) a higher risk for postoperative atrial fibrillation was found if they were smokers prior to surgery(47).

**Smoking and Sudden Cardiac Death**

As discussed above, smoking accelerates many cardiovascular insults including fatal arrhythmias. Sudden cardiac death is a major cause of cardiovascular mortality which has been found to be associated with cigarette smoking(48). Smoking was also found to be a risk factor (p=0.06) for sudden cardiac death (albeit not as strong as high cholesterol or pre-existing heart disease) in a British study of 7735 patients(49). A similar prospective study in Paris of 7746 men also found that smoking was an independent risk factor for sudden cardiac death(50)

**Evidence for Aggressive Risk Factor Modification**

Abed et al carried out a landmark trial in 150 obese patients which involved controlling their cardiovascular risk. They found a significant reduction in atrial fibrillation burden due to aggressive control of cardiovascular risk factors. The website Heart.org called this paper one of the top ten stories in cardiology last year and it was the top oral abstract at Heart Rhythm Society in San Francisco this year.

This partially blinded, single centre trial randomised 150 patients to two groups of 75 each. These patients were followed up for eighteen months. The intervention was aggressive control of cardiometabolic risk factors such as low calorie replacement meal sachets (later transitioned to low glycemic index meals), an intense exercise program, blood pressure control, smoking cessation and reduction in alcohol intake. This intervention program was intense, targeted and successful in controlling cardiometabolic risk factors. The intervention group showed a significantly greater reduction in weight (14.3 and 3.6 kg, respectively; P<0.001)

Both sets of these patients had the AFSS (Atrial Fibrillation Severity Score) questionnaire administered at baseline and at 3 monthly intervals until fifteen months. The atrial fibrillation symptom burden scores (11.8 and 2.6 points, P<0.001), symptom severity scores (8.4 and 1.7 points, P<0.001) were significantly improved in the intervention group. They also had Holter monitoring which was done at baseline and at 12 months. The non-intervention versus the intervention group showed significant improvement with the number of episodes (2.5 and no change, P=0.01), and cumulative duration (692-minute decline and 419-minute increase, P=0.002). This study showed a significant reduction in both atrial fibrillation severity and burden. (51)

**Conclusions**
Smoking has a wide range of cardiovascular effects which include endothelial dysfunction, coronary artery disease and left ventricular dysfunction and pre-dispose patients to arrhythmias. Patients with poor left ventricular function and implanted ICDs tend to have much higher rates of ventricular tachycardia if they smoked as compared to patients who abstain from smoking. Similarly patients who smoke have much higher rates of atrial fibrillation, a result which has been shown in multiple trials. Smoking is also a risk factor for sudden cardiac death. Finally risk factor modification has been shown to be strongly associated with reduction of atrial fibrillation in a landmark trial carried out by Abed et al. A smoking cessation referral for those patients who need them as well as controlling other cardio-metabolic risk factors would go a long way in providing a more complete approach to treating our arrhythmia patients.

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