The Left Atrial Appendage in Health and Disease

Abstract

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia and results in significant morbidity and mortality. The left atrial appendage (LAA), a small embryonic remnant of the left atrium (LA), has been shown to play a key role in the pathophysiology of AF-related stroke and thromboembolism. As a consequence the LAA, in spite of its meagre size, has been described as 'our most lethal human attachment'. Despite being a recognised harbinger of disease, the LAA has also been shown to play an important role in health. This review seeks to address our current understanding of this vital structure in both health and disease states.

Keywords: Left atrial appendage; Thrombus; Atrial fibrillation; Stroke; Thromboembolism

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Abbreviations: AF: Atrial Fibrillation; LAA: Left Atrial Appendage; LA: Left Atrium; ANP: Atrial Natriuretic Peptide; TOE: Trans Oesophageal Echocardiography

Introduction

Atrial fibrillation (AF) affects 2% of the general population rising with age to affect over 10% of octogenarians [1]. Importantly AF has been predicted to increase in prevalence by three-fold by 2050 [2]. This arrhythmia is by no means benign since it confers a five-fold risk of stroke and thromboembolism and independently results in a two-fold risk of excess mortality [3]. Although formerly a somewhat neglected structure, the left atrial appendage (LAA) has been found to be a key player in stroke secondary to AF. Accordingly the LAA has in recent times been proposed as a potential therapeutic target.

LAA anatomy

The LAA is a remnant of the embryonic left atrium (LA), which is formed during the third week of gestation. The LA itself develops later from the pulmonary veins [4]. The LAA, an outpunching of the LA, is a long, tubular structure lying in the left atrioventricular groove between the left upper pulmonary vein and the left ventricle. It comprises a single layer of endothelium and is trabeculated with underlying pectinate muscles lining the cavity. The LAA varies considerably in size from 16-51mm in length, 10-40mm in diameter and 0.77-19.27cm^3 in volume [5,6]. The LAA also appears to differ in morphology with distinct variants including the 'chicken wing', 'cactus', 'windsock' and 'cauliflower' being described in 48%, 30%, 19% and 3% of cases respectively [7].

LAA Physiology

It has become increasingly apparent that the LAA has not only specific anatomical, but also, physiological properties. Like the LA, the LAA is a dynamic structure and plays a number of mechanical roles throughout the cardiac cycle. It serves as a reservoir during left ventricular systole, a conduit during early diastole, provides an active pump function in late diastole and its elasticity enforces backward flow to refill in early systole [8]. The LAA also been shown to maintain intravascular volume status through activation of stretch receptors located within its body. These afferent signals play a role in fluid haemostasis and control of heart rate in response to changes in LA pressure. In support of this, one study demonstrated that 30% of all cardiac atrial natriuretic peptide (ANP) was found within the LAA [9]. Furthermore in the healthy human heart, ANP concentration in the LAA is present in 40-times the concentration of the rest of the LA [10]. The significance of the LAA in fluid balance has been reinforced in humans after clamping of the LAA during cardiac surgery yielded increased LA and left ventricular filling pressures [8]. Animal studies have also shown that by removing the LAA, reduction of both LA compliance and LA function occurs [11]. Notably, a dramatic reduction in cardiac output, of nearly 50%, was witnessed in guinea pigs following ligation of the LAA. This finding was attributed to the contractile function of the LAA [12]. Conversely, distension of the LAA in a dog model was found to increase diuresis as well as sodium excretion and heart rate [13].

The LAA in disease

The most notable association between the LAA and disease is in the context of AF. In this setting, reduced contractility and stasis of the LAA occur, resulting in thrombus formation and thereafter the potentially catastrophic consequences of embolisation. In individuals with non-valvular AF, 90% of thrombi have been identified within the LAA; (Figure 1) [14]. Additionally it has been observed that up to 14% of patients have thrombus identifiable in the LAA within 3 days of AF onset [15]. It is these observations which have led to the LAA being termed 'our most lethal human attachment [16]. Remodelling of the LAA in subjects with AF has been observed with chamber enlargement and decreased pectinate muscle volume [17]. Typical histological appearances include endocardial thickening, fibrosis and myocyte hypertrophy [18]. A reduced LAA peak flow velocity studied during transoesophageal echocardiography (TOE) is established to be an independent and powerful predictor of thromboembolic risk [19]. Likewise LAA morphology has been proposed as another marker of thromboembolism with the 'cauliflower' LAA conferring the highest risk of thrombus. In contrast patients with a 'chicken-wing' appearance LAA have lowest risk of embolism [7].

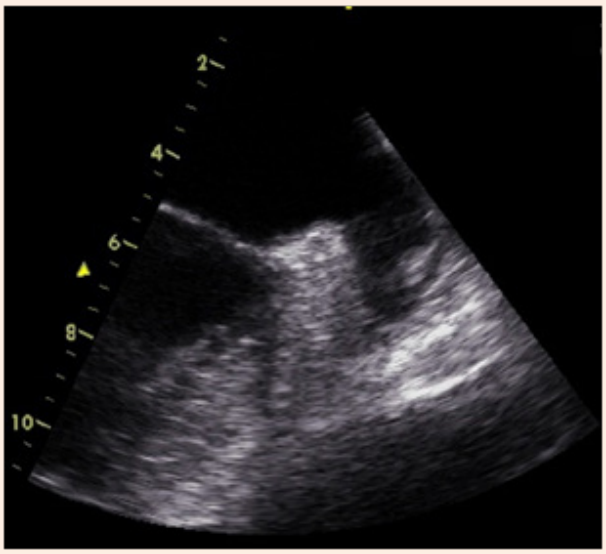

Figure 1: Thrombus identified with in the left atrial appendage during TOE.

Similar to the LA, the LAA has been shown to increase in size in patients with a history of hypertension when compared with controls. This was also associated with a reduction in emptying velocities as demonstrated during TOE [20].

Likewise it appears that the LAA also plays a dynamic role in the setting of left ventricular dysfunction. Firstly left ventricular impairment results in a 10-fold increase in LAA ANP concentration [10]. Furthermore, another study indicated that after successful heart failure therapy, LAA function improved significantly. It was also noted that, after treatment, LAA size reduced markedly more than LA size, demonstrating relatively increased compliance [21].

The LAA as a therapeutic target

Since the LAA has been documented to be a major culprit of thromboembolism in AF it has also been proposed as a potential therapeutic target through LAA occlusion or ligation. This treatment option is of considerable interest given the well-documented bleeding risk of anticoagulants and the significant proportion of patients who are intolerant of anticoagulation therapy [22]. To date both surgical and transcatheter LAA exclusion have been investigated with encouraging results, although trials have been criticised both for their small sample size and lack of randomisation in the majority. Recently published long-term data from the PROTECT-AF trial, randomising patients to transcatheter LAA ligation or warfarin, suggests in fact that LAA ligation may be superior to warfarin for prevention of stroke, systemic embolisation and all-cause mortality [23].

Conclusion

In summary the LAA plays a vital role in the pathogenesis of stroke secondary to AF. Furthermore from the available evidence it is clear that the LAA is not a redundant structure in the absence of disease. Despite outcomes suggesting that surgical and transcatheter LAA exclusion may be an alternative to conventional stroke prevention therapy, interference with the mechanical and neurohumoral functions of the LAA may result in, as yet unaccounted for, clinical sequelae. These potential consequences merit further evaluation in future trials.

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