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ATORVASTATIN ATTENUATES ATRIAL STRUCTURAL, AUTONOMIC AND ELECTROPHYSIOLOGIC REMODELLING BY ITS ANTI-OXIDANT AND ANTI-INFLAMMATORY ACTION IN ATRIAL FIBRILLATION DOGS

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Purpose The protective effects of statins against atrial fibrillation (AF) have been observed in many clinical trials but the underlying mechanisms remain unclear. Therefore we investigated the role of atorvastatin on atrial remodelling in AF dogs and explored the potential mechanism.

Methods Three groups of dogs were used: sham-operated, AF and atorvastatin. Dogs in the AF and atorvastatin groups underwent 6-week atrial pacing. Atorvastatin was administered 1 week before and during the pacing. Then atrial electrophysiological parameters were measured. Oxidative stress markers and serum C-reactive protein (CRP) concentration were estimated. Atrial structural and functional alterations were assessed by echocardiography, histopathological changes by microscopy, cardiomyocyte apoptosis by TUNEL and apoptosis-related proteins by immunohistochemistry and Western blotting. The degree of nerve sprouting and sympathetic innervation were quantified by immunohistochemistry. Nerve Growth Factor (NGF) was detected by Western blotting and RT-PCR.

Results Atorvastatin prevented pacing-induced increases in inducibility and duration of AF, alterations of oxidative stress markers and up-regulations of CRP. AF dogs showed impaired atrial structure and function manifested by lower left atrial (LA) ejection fraction, higher LA volume and ultrastructural changes of myocytes, which were mitigated by atorvastatin treatment. Atorvastatin partly inhibited the increased apoptotic cell number and the changes of apoptosis-related proteins. Additionally, atorvastatin also dramatically reversed nerve sprouting, sympathetic hyperinnervation and increased mRNA and protein levels of NGF.

Conclusion Atorvastatin attenuates atrial structural, autonomic and electrophysiologic remodelling possibly by its anti-oxidant and anti-inflammatory action, which contributes to its beneficial effect in preventing AF promotion.