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Atrial Translocation of *Porphyromonas gingivalis* Exacerbates Atrial Fibrosis and Atrial Fibrillation

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Abstract

Background: Recent studies have indicated an association between periodontitis and atrial fibrillation (AF), although the underlying mechanisms remain unclear. *Porphyromonas gingivalis* (*P gingivalis*) is a causative agent of periodontal disease and is highly pathogenic. This study focused on *P gingivalis* and aimed to investigate the relationship among periodontitis, atrial translocation of *P gingivalis*, and atrial fibrosis and AF.

Methods: An experiment was conducted using *P gingivalis*-infected C57BL/6J mice, in which *P gingivalis* was inoculated into the pulp of the molars. Immunohistochemistry was used to visualize the localization of *P gingivalis*, and loop-mediated isothermal amplification was employed to detect *P gingivalis* DNA in the left atrium. AF inducibility was examined by intracardiac stimulation. Moreover, left atrial appendage specimens were obtained from 68 patients with AF. A periodontal examination was conducted before the surgery, and the periodontal epithelial surface area and periodontal inflamed surface area, which are quantitative indices used to determine the clinical severity of periodontitis, were measured. The bacterial number of *P gingivalis* in human atrial tissue was analyzed via quantitative polymerase chain reaction. Atrial fibrosis was assessed using Azan-Mallory staining.

Results: The translocation path of *P gingivalis* from the dental granuloma to the left atrium via the circulatory system was demonstrated by immunohistochemistry and loop-mediated isothermal amplification in *P gingivalis*-infected mice, which showed a higher degree of atrial fibrosis (21.9% versus 16.3%; $P=0.0003$) and a higher AF inducibility (30.0% versus 5.0%; $P=0.04$) than the control mice. Upregulation of galectin-3 and transforming growth factor-beta 1 in the left atrium was observed in *P gingivalis*-infected mice. Moreover, immunohistochemistry revealed that *P gingivalis* was also present in human atrial tissue. The number of *P gingivalis* in the human atrial tissue was positively correlated with periodontal epithelial surface area ($\rho=0.35$; $P=0.004$), periodontal inflamed surface area ($\rho=0.52$, $P<0.0001$), and the degree of atrial fibrosis ($\rho=0.38$; $P=0.002$).

Conclusions: *P gingivalis* translocation to the left atrium correlates with the clinical severity of periodontitis, which may exacerbate atrial fibrosis and AF. Atrial translocation of *P gingivalis* is a potential pathway explaining the causal relationship between periodontitis and AF.

Keywords: Porphyromonas gingivalis; atrial fibrillation; bacterial translocation; periodontitis.

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Conflict of interest statement

None.

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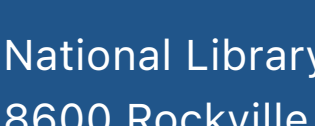
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