Can Periodontitis Influence the Progression of Abdominal Aortic Aneurysm? A Systematic Review

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Abstract
There is some evidence that periodontitis increases the risk of atherothrombosis. Abdominal aortic aneurysm (AAA) is a cardiovascular disease with specific risk factors and physiopathological mechanisms that can lead to rupture in the absence of treatment. The aim of the present systematic review was to explore the influence of periodontitis on the progression of AAAs as a specific disease. A systematic search in PubMed/MEDLINE and Embase databases was performed. Human and animal studies exploring the influence of periodontal pathogens on the progression of AAA were considered for inclusion. After systematic screening, 5 articles were included in the review. Due to the heterogeneity of the selected studies, a meta-analysis could not be performed. The descriptive analyses of the studies emphasized that periodontal pathogens or their by-products contribute to systemic and local innate immunity likely to be associated with AAA physiopathology. Periodontitis seems to play a role in the development and progression of AAA. The present systematic review suggests that the presence of periodontal bacteria in the bloodstream or in situ in the vascular lesion is a risk associated with aneurysmal disease progression.

Keywords
periodontitis, periodontal pathogen, dental plaque, abdominal aortic aneurysm, Porphyromonas gingivalis

Introduction
Abdominal aortic aneurysms (AAAs) are responsible for 1\% to 3\% of all deaths in Western countries among men aged 65 years and older.\textsuperscript{1,2} The disease has genetic and environmental risk factors such as smoking, older age, and male gender.\textsuperscript{3-5} The estimated prevalence of AAA is between 1.3\% and 12.5\% in men and 1.0\% and 2.2\% in women. Abdominal aortic aneurysm is a chronic degenerative disorder commonly associated with an intraluminal thrombus (ILT)\textsuperscript{6} and with innate and adaptive immunities.\textsuperscript{7} The innate immunity is mainly represented by the predominant presence of neutrophils in the ILT\textsuperscript{8} and macrophages in the adventitia, and the adaptive one by the presence of lymphoid tertiary organs in the adventitia.\textsuperscript{7} The causes of the extracellular matrix (ECM) wall degradation are enzymes mainly released by the ILT components (neutrophil elastase, matrix metalloproteinase 9 [MMP-9], and plasmin).\textsuperscript{9}

On the other hand, periodontitis, a chronic bacterial aggression and inflammatory response of the periodontium,\textsuperscript{10-12} affects 50\% of the adult population.\textsuperscript{13,14} This chronic multifactorial disease is characterized by the invasion of gram-negative bacteria and their by-products in the periodontal tissues, leading to the destruction of the tooth support and subsequently to tooth loss.\textsuperscript{15-20} The presence of periodontal pathogens leads to the degradation of the ECM; the infiltration of neutrophils, macrophages, and lymphocytes; and the production of proteases (MMPs and serine proteases), resulting in progressive destruction of alveolar bone and finally tooth loss.\textsuperscript{21-27}
Similar physiopathological mechanisms are found in periodontal disease as occur in AAA: ECM destruction, innate and adaptive immunity, and the role of proteolysis in the disease progression.28-37 There is consistent and strong epidemiologic evidence that periodontitis imparts increased risk of future cardiovascular disease (CVD; eg, atherosclerosis).38-42 Preclinical and clinical studies support the interaction between these 2 diseases. Tooth brushing, mastication, debridement, or scaling can induce the passage of oral pathogens, their virulent factors, or both into the bloodstream.43 It is believed that the resulting transient or prolonged bacteremia can influence cardiovascular pathogenesis. Periodontal pathogens, and more specifically \( \text{Porphyromonas gingivalis} \) (Pg), have been found in atherosclerotic plaques.44-50 These bacteria were also present in the muscle tissue in patients with coronary heart disease or endocarditis.51,45

Three physiopathological mechanisms were suggested for the interaction between periodontal disease and systemic diseases such as CVD.52 The first mechanism is related to the secretion of in situ pro-inflammatory markers (interleukin 1 [IL-1], IL-6, and tumor necrosis factor-\( \alpha \) [TNF\( \alpha \)]) caused by the presence of periodontal pathogens such as Pg, \( \text{Tannerella forsythens} \) (Tf), \( \text{Treponema denticola} \) (Td), \( \text{Prevotella intermedia} \) (Pi), or their virulence factors inside the periodontal tissues. This can lead to an increased systemic inflammatory status that would potentiate CVD.53 The second process is associated with the passage of oral bacteria or their by-products into the bloodstream. The third physiopathological pathway is connected with the migration of periodontal bacteria through the bloodstream and their invasion into \( \text{locus minoris resistentiae} \) (LMR) of local endothelium loss and platelet aggregation.51,54 For phylogenic reasons (coagulation and immunity are common pathways in invertebrates), bacteria have more affinity for intravascular thrombus than for other tissues within a higher organism.55,56 Once bacteria have colonized the thrombus, local innate immune cascade, including neutrophil extracellular traps (NETs),57 with subsequent disease progression.58,59

Although these pathways have been well documented for the development of atherothrombosis (ATH), the role of periodontal disease as an additional risk of the progression of AAA specifically remains poorly explored.45,60-65 Even though ATH and AAA have similarities in their pathogenesis, additional synergetic or independent factors such as increased hemodynamic force, hypercholesterolemia, or genetics promotes the AAA. Moreover, it has also been proposed that specific infection by \( \text{Chlamydia pneumoniae} \) plays a significant role in the AAA progression.66-68

Therefore, it is of interest to independently assess the influence of periodontitis and periodontal-specific bacteria on AAA development. The aim of the present systematic review was to investigate the current knowledge about the influence of periodontitis on AAA to answer the key question, “Does periodontal disease influence the progression of AAA?”

### Materials and Methods

#### Study Design

The present study was designed as a systematic review focusing on the relationship between AAA and periodontitis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-analyses checklist and guidelines for systematic review were followed.69 All studies involving AAA and periodontitis were assessed. Due to a limitation of data in humans, animal studies were also included.

#### Focused Question and Search strategy

The controlled vocabulary (MeSH terms) and free keywords in the search strategy were defined based on the following focus question and PECO framework (P: population, E: exposure, C: control, O: outcome):70 “Does periodontitis influence the progression of abdominal aortic aneurysms”? This question is addressed according to the following criteria:

- **Population**: Animals or humans or both presenting AAA
- **Exposure**: Exposed to periodontitis or periodontal pathogens
- **Control**: Not exposed to periodontitis or periodontal pathogens
- **Outcome**: AAA growth, expansion, rupture, or progression

The search algorithm is shown in Table 1. An electronic search of the literature was performed using PubMed/MEDLINE and Embase. Selected publications were collected in Reference Manager software (Endnote X7, Thomson Reuters, New York, New York) until June 2017; duplicates were discarded electronically. In addition, a manual search was carried out on the reference lists of all potentially eligible studies obtained as full text.

#### Study Selection and Statistical Analysis

Two independent reviewers (L.S. and D.V.) screened titles, then abstracts, and finally full texts of all articles identified by the electronic and manual searches. The level of agreement

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**Table 1. Algorithm for Electronic Search.**

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(((((("periodontitis") OR "periodontal pathogen") OR "dental plaque") OR "porphyromonas gingivalis" [MeSH Terms]) OR "aggregatibacter actinomycetemcomitans" [MeSH Terms]) OR "prevotella intermedia" [MeSH Terms]) OR "treponema denticola" [MeSH Terms]) OR "tannerella forsythia" [MeSH Terms]) AND "aortic aneurysm, abdominal" [MeSH Terms]) OR (("abdominal aortic aneurysm expansion" OR "abdominal aortic aneurysm growth" OR "abdominal aortic aneurysm progression" OR "abdominal aortic aneurysm thrombosis" OR "abdominal aortic aneurysm rupture") OR "abdominal aortic aneurysm thrombus")
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between the reviewers was calculated using the Cohen \( \kappa \) coefficient at each level of selection.

To enhance sensitivity, records were removed only if both reviewers excluded them based on the titles. In case of disagreements, a discussion with a third reviewer (F.L.) resolved the issue. The selection was done according the inclusion and exclusion criteria (see below). No statistical meta-analysis was performed, but in studies, a \( P < .05 \) was considered significant.

**Assessment of Study Quality**

Quality assessments were performed according to the AMSTAR methodological quality assessment of systematic reviews\(^7^1\) (Supplementary Appendix II). Each animal or human study was rated independently based on its quality by 2 reviewers, using the criteria outlined in the Systematic Review Centre for Laboratory Animal Experimentation Office of Health Assessment\(^7^2\) and Translation (risk of bias) tool.\(^7^3\) The tool contains 10 entries that are related to selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases (Supplementary Appendix III and IV).\(^7^2\)

**Inclusion and Exclusion Criteria**

The inclusion criteria were (1) animal or human studies, (2) studies focusing on the relationship between periodontitis and AAA growth or progression or expansion or rupture or thrombosis, (3) in vivo studies, and (4) randomized controlled clinical trials, case-control studies, prospective clinical series, and retrospective studies.

The exclusion criteria were (1) literature reviews, (2) editorials, (3) studies involving AAA not related to periodontitis, (4) studies involving the relationship between periodontitis and CVDs but not specifically AAA, and (5) studies involving AAA treatment.

**Data Extraction**

All selected studies were read carefully to identify the following data.

For human studies:
- Author(s) and year of publication
- Study design
- Objectives of the study
- Number and origin of the AAA biopsy in the test and control groups
- Methods for periodontitis identification and characterization
- Periodontitis prevalence and type and proportion of the pathogens
- Size of the aortic diameter or size of the thrombus
- Detection of local inflammation in the vascular wall or in the thrombus
- Retrieved periodontal DNA in the vascular wall
- Conclusion of the authors

For animal studies:
- Author(s) and year of publication
- Animals species and variety
- Experimental model/aneurysm induction method
- Objectives of the study
- Type of periodontal pathogens
- Study design and groups distribution
- Size of the AAA diameter
- Plasmatic inflammatory biomarkers
- Detection of local inflammation in the vascular wall or in the thrombus
- Retrieved periodontal DNA in the vascular wall
- Conclusion of the authors

In cases of missing data, the authors were contacted by e-mail to collect the information.

**Results**

**Search and Selection**

The search strategy and selected publications are shown in Figure 1 and Tables 2 and 3. The Embase and PubMed search strategy resulted in 297 articles. After screening the titles, 289 (97.3\%) and 288 (97.0\%) were excluded, respectively, by the first and second reviewers, resulting in a Cohen \( \kappa \) coefficient of .94 (95\% confidence interval, 0.82-1.0). Nine titles were selected for abstract reading, of which 3 were excluded (\( \kappa = 1.0 \)). After full-text assessments, 1 article was additionally excluded. Finally, both reviewers agreed to include 5 articles in the systematic review. The studies excluded and the reasons for exclusion are reported in Supplementary Appendix I. Five articles were found eligible for a systematic review, but a meta-analysis could not be performed due to the heterogeneity of the studies.

**Study Characteristics**

There was substantial heterogeneity between studies in terms of study design. One study was a human observational study,\(^6^5\) 1 ex vivo human study,\(^6^2\) 2 were ex vivo animal studies,\(^6^0,7^4\) and 1 study involved ex vivo samples from both animals and humans.\(^7^5\) The relationship between AAA and periodontitis was explored in several ways: correlating clinical periodontal measurements with the presence of AAA,\(^6^5\) bacterial detection by polymerase chain reaction (PCR) in different fluids (saliva, subgingival plaque, blood) or in the aneurysm,\(^6^2,7^5,6^4\) immunohistochemical analyses,\(^7^4\) and analysis of the AAA volume.\(^7^4,6^0,7^5\) An attempt was made to present a qualitative report for both clinical and preclinical studies. Details are presented in Tables 2 and 3.

In a clinical study,\(^6^6\) investigating the incidence and the severity of periodontitis in patients with AAA versus patients with non-AAA CVD (myocardial ischemia, arrhythmia, heart failure, and valvular disease), the authors observed that patients affected by AAA presented a more severe periodontitis (deeper mean pocket depth) than those without AAA. However, they
found similar periodontal bacteria in saliva and subgingival plaque samples for the 2 groups. The authors concluded that periodontitis may have a stronger influence on the progression of AAA than on other CVDs. In another clinical study, all patients with AAA presented with periodontitis. Clinical evaluations revealed that the periodontitis was moderate in 22% of patients (7/32), severe in 63% of patients (20/32), and 16% of the patients (5/32) were edentulous. Periodontal bacteria were found in 88% of their oral samples (saliva or subgingival plaque or both), and most of the detected pathogens were Pg (81%), followed by Tf (72%), Td (59%), Pi (41%), *Campylobacter rectus* (34%), *Prevotella nigrescens* (19%), and *Actinobacillus actinomycetemcomitans* (3%). The authors concluded that all patients with AAA had poor periodontal conditions from clinical and microbiological points of view.

In 3 preclinical studies in rats or mice, the intravenous (IV) or subcutaneous (SC) injection of Pg led to a significant increase in the abdominal aortic diameter or to an expansion of the ILT (*P* < .03 for mice and *P* < .05 for rat studies). In the clinical part of their study, Delbosc et al. highlighted a significant correlation between Pg antibodies and the AAA diameter and its thrombus volume (*r* = 0.731, *P* < .0001). The 4 studies concluded that Pg infection was linked to the growth of the AAA.

The physiopathological pathways of how periodontitis may influence AAA pathogenesis were explored in 3 preclinical and 2 clinical studies. The possible relationship between the 2 diseases involves the presence of systemic periodontal pathogens leading to (1) an increase in plasmatic inflammatory and immunologic biomarkers, (2) a local innate and adaptive process in the AAA thrombus and wall, and (3) retrieval of periodontal bacterial DNA in AAA lesions.

**Increase in plasma-free DNA and proteases and immunologic biomarkers.** In 2 preclinical studies, repeated SC or IV injections of Pg in mice and rats induced an elevated level of nonspecific periodontal biomarkers such as MMP-2, MMP-9, and cell-free DNA (cf-DNA). In the ILT of rats that received IV Pg injections, an increase in plasma cf-DNA (*P* < .0001) indicating the presence of the NETs was observed. From these results, the authors concluded that systemic neutrophil diapedesis within the ILT, a recognized risk factor for the development of AAA, can be induced by periodontal bacteria and may promote AAA progression. In addition, in a clinical study, Pg antibodies and cf-DNA were found in the plasma of patients with AAA. The authors noted the consistent correlation between these biomarkers and AAA diameter and thrombus volume. The 3 studies concluded that Pg induces local accumulation of neutrophils and may initiate or accelerate the growth of the AAA.

**Local inflammatory process in the AAA wall or thrombus.** In 3 preclinical studies in mice or rats, the inoculation of Pg induced the destruction of the abdominal aortic ECM due to local response to Pg trapping inside the ILT and AAA wall consequences, involving the fragmentation of the elastic fibers (*P* < .05) by metalloproteases MMP-2 and MMP-9 and serine proteases (leukocyte elastase, u-PA, cathepsin G, ...
In 2 of these preclinical studies\textsuperscript{75,78} and 1 clinical study,\textsuperscript{76} an increased number of inflammatory cells, namely, CD-8, neutrophil (NET), and cf-DNA as well as Pg antibodies, were found in the aneurysmal wall and in the ILT. The 4 studies concluded that Pg seems to promote the progression of the AAA through increasing inflammation in the wall or in the thrombus of the AAA.

**Retrieval of periodontal bacteria DNA in AAA lesions.** In the ex vivo analyses of human AAA, 2 authors\textsuperscript{62,75} found genetic material...
Table 3. Results Clinical Studies.

<table>
<thead>
<tr>
<th>Study design</th>
<th>Kurihara et al&lt;sup&gt;62&lt;/sup&gt;</th>
<th>Delbosc et al&lt;sup&gt;75&lt;/sup&gt;</th>
<th>Suzuki et al&lt;sup&gt;65&lt;/sup&gt;</th>
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<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>- Look for the occurrence of periodontitis in patients with AAA.</td>
<td>Human-controlled trial - Look, in the plasma and in AAA biopsies, at the influence of periodontitis on:</td>
<td>Human-controlled trial - Look for presence of periodontitis in patients with AAA - Identify and characterize for the presence of periodontal bacteria DNA (Pg, Pi, and Aa) on oral samples of patients with AAA and non-AAA.</td>
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<td></td>
<td>- Identify and characterize the presence of periodontal bacteria DNA (Pg, Td, Pi, Cr, Tf, Pn, and Aa) both on oral and AAA samples of all patients</td>
<td>- The neutrophil activation - The NET formation (in the intraluminal thrombus) - The presence of periodontal bacteria - The cell-free DNA</td>
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<td>- Correlate the 2 outcomes</td>
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<td><strong>Biopsies samples (AAA)</strong></td>
<td>Test 32 AAA: wall and thrombus Control - 1 popliteal artery - 2 visceral arteries</td>
<td>Test 16 AAA: wall and thrombus Control</td>
<td>Test 12 AAA Control 24 non-AAA lesions: - 8 myocardial ischemia - 7 arrhythmia - 5 heart failures - 4 valvular diseases</td>
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<tr>
<td><strong>Results</strong></td>
<td>Detection of periodontitis or intraoral periodontal pathogens - 28 of 32 patients (88%) were positive for periodontopathic bacteria in the oral samples (saliva and/or subgingival plaque) - Types of bacteria in oral samples were: Pg 81%, Tf 72%, Td 59%, Pi 41%, Cr 34%, Pn 19%, and Aa 3%</td>
<td>NA</td>
<td>- Patients with AAA presented significantly deeper PD compared to patients with non-AAA (P &lt; .05) - BOP and bacterial characteristics were not significantly different between the 2 groups</td>
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<td></td>
<td>Size of the aortic diameter/thrombus NA</td>
<td>AAA diameter and the thrombus volume were positively correlated with Pg antibodies and cell-free DNA in the plasma (P &lt; .0001)</td>
<td>NA</td>
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<td></td>
<td>Plasmatic levels of inflammatory and immunologic biomarkers NA</td>
<td>- Higher plasmatic level anti-Pg immunoglobulins were found in patients with AAA compared to control (P &lt; .001)</td>
<td>NA</td>
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<td></td>
<td>Local inflammatory process in the AAA wall or thrombus NA</td>
<td>- Higher plasmatic level of cell-free DNA was found in patients with AAA compared to control (P &lt; .05)</td>
<td>NA</td>
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<td>- Higher level of Pg antibodies and cell-free DNA were found in the aortic wall of patients with AAA compared to control (P &lt; .05)</td>
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<td>- In patients with AAA, a positive correlation was found between Pg antibodies in the plasma and in the aortic wall (P &lt; .039)</td>
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Table 3. (continued)

<table>
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<tr>
<th>Retrieval of periodontal bacteria DNA in AAA lesions (wall or thrombus)</th>
<th>Kurihara et al\textsuperscript{62}</th>
<th>Delbosc et al\textsuperscript{75}</th>
<th>Suzuki et al\textsuperscript{65}</th>
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<tr>
<td>- Bacterial DNA were found in 86% of aneurysmal walls (24/28), mainly Pg 85% and Td 63 %</td>
<td>- Test group: all bacteria DNA detection 10 of 16 thrombi 11 of 16 aneurysmal wall Pg DNA detection 6 of 16 thrombi 7 of 16 aneurysmal wall - Control group: Bacteria DNA detection in control group was negative for all bacteria</td>
<td>- Bacterial DNA were found in 88% of the thrombi (14/16), mainly Pg 80% and Td 30 % - Bacterial DNA was not detected in any control specimens</td>
<td>NA</td>
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**Conclusion**
- The periodontal bacteria may play a role in the development of AAA and/or contribute to the weakening the aneurysmal wall
- The ILT in the human samples is enriched with NETs
- The most prevalent bacteria found in AAA samples was Pg
- Pg promotes NET formation, by recruitment and activation of neutrophils
- Deeper PD may have an influence on the AAA progression

Abbreviations: Aa, Actinobacillus actinomycetemcomitans; AAA, abdominal aortic aneurysm; BOP, bleeding on probing; CPI, community periodontal index; Cr, Campylobacter rectus; ILT, intraluminal thrombus; NA, not applicable; NET, neutrophil extracellular trap; PCR, polymerase chain reaction; PD, pocket depth; Pg, Porphyromonas gingivalis; Pi, Prevotella intermedia; Pn, Prevotella nigrescens; Td, Treponema denticola; Tf, Tannerella forsythensis.
of periopathogens and antibodies specific to periodontal bacteria or Pg-lipopolysaccharide (Pg-LPS) in AAA thrombi or in the aneurysmal wall. The authors concluded that periodontal bacteria contribute directly to weakening the aneurysmal wall and that the prevention or the treatment of periodontitis may limit AAA progression.

Discussion

Periodontitis is a chronic inflammatory disease caused by dental plaque, more specifically by gram-negative anaerobic bacteria accumulation in periodontal pockets. The bacterial species forms a bacterial complex described by Socransky among them, the orange and the red clusters are specific for periodontitis. The red one involves Td, Pg, and Tf, and the orange bacterial association is characterized by Fusobacterium nucleatum and Pi. Inside this complex, bacteria exchange nutrients, virulence factors and/or factors of resistance such as cytotoxins, proteases, hemagglutinin, and LPS were able to neutralize local host defenses. Therefore, the imbalance between host–parasite interactions participates in disease progression. Moreover, due to mastication and tooth brushing, these specific pathogens or their endotoxins can reach the systemic blood circulation, where they are destroyed by the reticuloendothelial system, or they colonize different intravascular sites such as the LMR. The consequences of these metastatic infections are an augmentation of host inflammation and influence the development of systemic diseases such as CVDs, diabetes, and preterm birth.

As demonstrated, Pg participates in the CVD progression due to its fixation on the atheroma as LMR. These particular anaerobic, gram-negative bacteria can aggregate in red blood cells due to its capacity of hemagglutination, they also affect blood cholesterol levels and therefore participate in thrombosis. Already in 2009, Paraskevas et al. in a literature review considered the possible mechanisms involved between AAA and periodontitis, namely, the role of the inflammatory response and the effect on periodontal pathogens in the tissues of the host.

The present systematic review highlighted AAA as LMR for periodontal pathogens and how periodontal bacteria could participate in this particular CVD progression. To interpret the association between the 2 diseases, it is prudent to emphasize certain aspects of AAA pathogenesis. The disease involves a thinner arterial wall with (1) the production of circulating cytokines (IL-1, IL-6, and TNFα), MMPs, and serine proteases with high proteolytic activity; (2) the destruction of the structural matrix proteins, the loosening of elastic fibers, and the depletion of smooth-muscle cells; and (3) the increased amount of neutrophil in the ILT.

The selected articles highlighted the implication of periodontitis on the ATH progression with ILT and the aortic wall as key places. The Pg DNA was detected by PCR on human aneurysmal samples, mainly in the thrombus and in the wall of the aneurysm. This corroborates the fact that the anaerobic bacteria can be transported by blood circulation and then can reach the ILT due to its direct connection with the lumen of the vessel and also the wall of AAA. It was also suggested that Toll-like receptors (TLR-2 and TLR-4) may play a role in the AAA inflammatory process by their specific recognition of gram-negative bacteria LPS, such as Pg. These TLRs, found on endothelial cells, participate to increase the activation of kinases such as nuclear factor-kB and therefore induce the cytokines activation, such as TNFα and IL-6, resulting in the high inflammatory activity inside the AAA wall. The mechanism of bacterial invasion on the endothelial ILT seems to involve fimbriae, specific of Pg, and therefore would explain the Pg DNA detection on the aneurysm samples. The consequences of Pg fimbriae anchorage would induce the expression of IL-8 and chemotaxic monocytes and therefore would participate in the increased amount of neutrophil found in the ILT as LMR (Figure 2). As demonstrated, Pg promotes the formation of NETs on the interface between the thrombus and the blood circulation with, as a consequence, the increase in the volume of the ILT, which stimulates the AAA growth and size. It can be assumed that the severity of periodontitis characterized by bacterial burden (quantity of periopathogens) may influence the AAA expansion. Therefore, it would be expected that patient with AAA with severe periodontitis would be more exposed to bacterial penetration in the bloodstream and more susceptible for the AAA progression compared with patients presenting mild periodontitis.

As mentioned, the disease progression also involves the destruction of elastic fibers and a high protease activity. The selected preclinical studies highlighted more elastolysis, the colonization of the abdominal aortic wall, and the ILT by inflammatory cells (CD-8, neutrophils) and a higher proteolytic activity in cases of Pg infection compared with the non-Pg-infected controls. In these studies, the aortic wall of Pg-infected animals presented higher level activity of MMP-9, suggesting more proteolytic activities and neutrophil attraction in the luminal layer of the ILT. Moreover, Pg infection
involved a significant increase in myeloperoxidase-DNA complexes in both plasma and aneurysm samples, inducing oxidative stress, which participates in AAA pathogenesis, namely, by contribution to the dysregulation of MMPs and the apoptosis of smooth-muscle cells.  

Despite the limited number of available studies dealing with the relationship between AAA and periodontitis, the present systematic review suggests that the presence of periodontal bacteria in the bloodstream or in situ in the vascular lesion is a risk associated with aneurysmal disease progression.

In order to establish the relationship between these 2 chronic inflammatory diseases, further evidence is needed. Cross-sectional studies correlating the AAA size with the severity of periodontitis would be of interest. Moreover, prospective multicenter study on large cohort and further exploration of surgically retrieved aneurysms should be considered.

Authors’ Note
All authors substantial contributed to (1) conception and design, or acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published.

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