Is the Current Periodontitis Classification Supported by Pathophysiological Evidence?

Periodontitis is one of the most prevalent diseases in humans.[1] In the past few decades, the disease has been repeatedly subdivided into groups with different rates of progression and/or age of onset, with the 1999 World Workshop designating the entity of 'aggressive periodontitis' as characterised by rapid attachment loss in systemically healthy subjects with possible familial aggregation.[2] Importantly, the 1999 classification relies on symptoms, rather than causes, of disease to reach the diagnosis.[3] This means that rapidly progressing aggressive periodontitis can only be diagnosed after irreversible attachment loss has occurred.[4]

A decade after the 1999 workshop, evidence was summarised in an entire Periodontology 2000 volume which pointed out the shortcoming that no distinctive differences between the two major entities of periodontitis, aggressive and chronic periodontitis, had been identified thus far on the pathophysiological level.[5-9]

Our group was the first to perform a comprehensive assessment of the differences between chronic and aggressive periodontitis lesions on the transcriptomic level. In 120 systemically health non-smoking subjects with previously untreated moderate to severe aggressive or chronic periodontitis who were diagnosed strictly according to the 1999 workshop criteria, a total of 240 full-thickness gingival tissue biopsies were obtained during resective periodontal surgery, and subjected to a genome-wide transcriptomic analysis.[10,11] We found only limited differences in gene expression between the two entities, with genes related to immune functions, programmed cell death and signal transduction significantly enriched in aggressive periodontis lesions, and genes related to cellular metabolism and epithelial integrity significantly enriched in chronic periodontitis lesions.[12]

Based on these data, we subsequently identified specific differences in the activation patterns and mechanisms of natural killer[13] and invariant natural killer T-cell populations[14] in aggressive vs chronic periodontitis that could in part explain the higher progression rates of aggressive periodontitis.

Nevertheless, our analyses showed that, while both entities, aggressive and chronic periodontitis, could be differentiated by diagnostic algorithms, there was evidence for a substantial diagnostic imprecision.[12] This indicates that the symptom-based 1999 classification, albeit showing some detectable differences, is not characterised by substantial distinctive features on the pathophysiological level.

Therefore, we subsequently assessed whether there was evidence for the presence of alternative subgroups of periodontitis with stronger distinctive features. To do so, we used the same genomic database of 240 gingival tissue biopsies from periodontitis sites that we had employed for the comparison of aggressive and chronic periodontitis.[12] The 120 subjects who had contributed the samples were clustered into subgroups using a mixture model-based clustering approach that allowed the correction for clinical variables[15] based on their genomic profiles. The best model fit was obtained for a solution with two subgroups that did not show any substantial overlap with the 1999 classification. Importantly, we found these two novel classes of periodontitis subjects to markedly differ in clinical variables, microbiological profiles, and serological parameters.[16]

Although these data strongly point to the presence of alternative classes of periodontitis, and an aetiology-based classification is a standard procedure in many fields of medicine today, it must still be realised that this cross-sectional work only constitutes a first step towards a new classification based on pathophysiological features. More studies need to be performed in different cohorts, and in a longitudinal setting, to confirm the presence and the clinical attributes of new subclasses. In addition, it would be advantageous to not base this clustering merely on transcriptomic profiles, but also to incorporate additional aetiological information, e.g. epigenetic data.[17] Indeed, most recently, a similar work based on microbiological data and radiological information was published, confirming that not all types of periodontitis are equal.[18]

In addition, using the machine learning methodology employed in the studies mentioned above, it seems timely to address the question of the pathophysiological basis of peri-implant diseases – it is still unclear whether peri-implantitis is pathophysiologically distinct from periodontitis, or an entirely different disease.[19]

By the time this volume has been published, a revision of the 1999 classification will have been performed by a new World Workshop in Periodontology, jointly organised by the AAP and EFP in Chicago, IL in November, 2017. While I am enthusiastic about the possibilities of this workshop, given the limitations outlined above, a classification based on aetiology would be premature at this point.

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