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Commentary: “Käytännöllistelemälläkin”: Antiaggregants, anticoagulants, and endocarditis

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The clumsy first word in the title of this Commentary is in Finnish and signifies approximately “doing something practical too.” Although grammatically correct, the word is relatively uncommon also in Finland, if concerns of oversimplifying a matter exists. “Keep it simple” and “stay on the main subject” are examples of compensating expressions, but there is a limit in dealing with complex matters in condensed fashion.

An ingenious preclinical theory may add to clinical research and future practice. Although cardiac endothelium is naturally resistant to transient bacteremia, it may become vulnerable upon injury or inflammation, eg, during sepsis.¹ Preclinical research suggests that endothelial injury and subsequent inflammation are associated with the accumulation of circulating bacteria.^{2,3} Some antiaggregants may impact coagulation, fibrinolysis, inflammation, and endothelial function, thus interacting with the development and magnitude of infection.⁴

This study by Theys and colleagues⁵ investigated in an unprejudiced manner the association of antiaggregants or anticoagulants with the risk of endocarditis in 2 retrospective cohorts that included 333 patients with aortic valve bioprosthesis between 2009 and 2019 and 137 patients with infected native aortic valves between 2007 and 2015. Multi-variable Fine–Gray and logistic regression models were used. There was no association between antiaggregants

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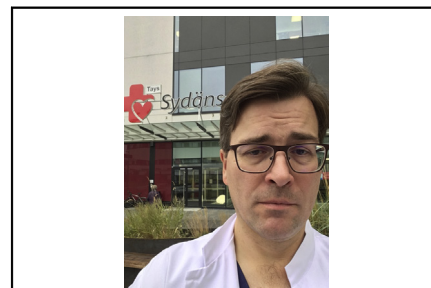
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CENTRAL MESSAGE

Antiaggregants and anticoagulation may add to the complex clinical scenario of infection during endocarditis.

and bioprosthesis valve endocarditis, whereas vitamin K antagonists, double antiplatelet therapy, novel oral anticoagulants, and fondaparinux or low-molecular-weight heparins, but not acetylsalicylic acid, were associated with native-valve endocarditis. The authors rightfully concluded that investigating the possible protective effect of antiaggregants or anticoagulants requires well-controlled studies.

Indeed, the antithrombotic therapies included many options: vitamin K antagonists, such as acenocoumarin, fenprocoumon, and warfarin; acetyl salicylic acid and its derivatives; novel oral anticoagulants including rivaroxaban, apixaban, edoxaban, and dabigatran; P2Y₁₂-receptor antagonists, including clopidogrel, ticagrelor, prasugrel, ticlopidine, and cangrelor; fondaparinux and low-molecular-weight heparins such as enoxaparin, dalteparin, and nadroparin; and dual antiplatelet medication consisting of P2Y₁₂-receptor antagonist and acetyl salicylic acid. Some patients received several antithrombotic therapies. The complex molecular mechanisms of these drugs cannot be overestimated.

Causative pathogens were also divergent and numerous. Pathogens such as *Streptococcus* species, *Staphylococcus aureus*, and *Enterococcus faecalis* react very differently and necessitate different antibiotic combinations. Combined with the different patient characteristics and surgical techniques, excluding patients with stenotic or mechanical valves and those with endocarditis within some other anatomical location besides the aortic valve position may not suffice to obtain homogeneous research cohorts. In contrast, the confidence intervals of several outcome results

appeared wide, suggesting the relatively small number of patients. The authors speculate that large numbers of patients could be included in future studies through collaboration with other centers, since only limited patient databases of infective endocarditis are available.

There may be another important message for discussion. Lumping different patients and information together in hope of obtaining large registry data sets without strict selection criteria may mask important and individual details beyond meaningful analysis of the results. Maybe some diseases and related therapies are too complex to address in a generalized way. The study by Theys and colleagues⁵ confirms that patients with endocarditis are a very heterogeneous and complex group of individuals.

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