American Journal of Infectious Diseases

Editorials

Association between Infective Endocarditis and Premalignant Colorectal Lesions

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The association between Infective Endocarditis (IE) and Colorectal Cancer (CRC) has been known for more than 50 years. The microorganisms in which this association has been described are *Streptococcus gallolyticus* (formerly *Streptococcus bovis*) (Corredoira-Sánchez *et al*., 2012; Boleij *et al*., 2011), in different subspecies and, more recently, *Enterococcus faecalis* (Pericàs *et al*., 2016; 2017; Escolà-Vergé *et al*., 2020; Pericàs *et al*., 2021).

Colonoscopy is the gold standard for the screening and diagnosis of colorectal cancer. American and European IE guidelines recommend the systematic performance of colonoscopy in patients with *S. gallolyticus* bacteremia and high suspicion of IE (Baddour *et al*., 2015; Habib *et al*., 2015). Previous studies have shown that colorectal neoplasms in patients with IE due to *S. gallolyticus* are much more frequent than in the general population, so colonoscopy is mandatory (Corredoira-Sánchez *et al*., 2012). Boleij *et al*. (2011) systematic review and meta-analysis reported an association between infection from *S. gallolyticus* and CRC in 65% of cases. Although the association between *S. gallolyticus* IE and CRC is robust, the association with Colorectal Adenomas (CRA) is less conclusive, because CRA are also very frequent in the general population. Recent studies have shown that, like *S. gallolyticus* IE, *E. faecalis* IE is associated with Colorectal Neoplasms (CRN) and thus colonoscopy should also be mandatory in these patients (Pericàs *et al*., 2016; 2017; Escolà-Vergé *et al*., 2020; Pericàs *et al*., 2021).

The association between IE (*S. gallolyticus* or *E. faecalis*) and CRA is highly relevant in clinical practice. In these patients, the diagnosis of severe infectious disease may allow the early diagnosis and treatment of a premalignant colorectal neoplasm.

In the present issue, Vilardell *et al*. analyze the relationship between streptococcal infective endocarditis and pre-neoplastic colorectal lesions in a retrospective single-center study of a Mediterranean population. In this study, 71 patients with IE due to any microorganism underwent colonoscopy as part of the extension analysis during hospitalization: 49 patients (69%) had IE without colorectal lesions, 14 patients (20%) had IE with dysplastic adenomas and eight (11%) had IE with CRC. *S. gallolyticus* was the microorganism most frequently associated with colorectal disease, especially with pre-neoplastic lesions (50%). Not only high-degree but also low-degree dysplastic adenomas presented this association. The authors conclude that *S. gallolyticus* IE is associated with pre-cancerous colorectal lesions, including low-degree dysplastic adenomas. The results support the current recommendation to perform colonoscopy for the screening of colorectal cancer and pre-neoplastic lesions in patients with *S. gallolyticus* IE.

The relationship between *S. gallolyticus* and colorectal cancer is not well clarified. Colorectal lesions may simply be the gateway for the microorganism, but it may be that it is both a passenger and a cancer-promoting bacterium. For *S. gallolyticus* to facilitate the development of cancer it needs premalignant conditions, like CRA. Therefore, *S. gallolyticus* is not the main cause of CRC, but an auxiliary factor that accelerates its development (Pasquereau-Kotula *et al*., 2018).

S. gallolyticus is not the only microorganism associated with CRN. Several studies have found that *E. faecalis* might bear carcinogenetic properties contributing to CRN development. Pericàs *et al*. (2016; 2017) reported a 17-fold higher prevalence of CRN in patients with *E. faecalis* IE with an unknown source of the infection undergoing colonoscopy than in the general population. Escolà-Vergé *et al*. (2020) also found similar rates of CRN in patients with a known source. More recently, a study from the GAMES cohort added to previous evidence suggesting a much higher rate of CRN among patients with *E. faecalis* IE than in the general population of the same age and sex (Pericàs *et al*., 2021).

Conclusion

The association between *S. gallolyticus* IE and CRN (cancer and pre-malignant lesions) is well established. The indication for colonoscopy in these patients should be mandatory. In light of current data, colonoscopy

should also be recommended in patients with *E. faecalis* IE until further studies are available.

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