

## Editorial

# Infective Endocarditis in Cancer Patients: Incidence, Mechanisms and Approach

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## EDITORIAL

Infective endocarditis (IE) has a high mortality rate on short-term, even after appropriate medical or surgical treatment. The presence a second potentially life-threatening disease as mid-term such as cancer could pose serious therapeutic dilemmas. The association between both conditions was described in the 1950 and its findings were confirmed in the following decades [1-3]. The questions to be answered are: how often does this association occur and how can be dealt with in an appropriate way? Many case reports, and short series were published. There are also some more contemporary genomic and cell biological studies available. However, prospective case control series and nationwide surveys are rare. Between 1990 and 2010, cancer has been consistently present at a level of 11%-12% in elderly Medicare patients diagnosed with IE [4]. In patients with IE caused by *Streptococcus gallolyticus*, more than half had also colorectal cancer or polyps. This is far more compared to the general asymptomatic population [1]. Such high figures have been confirmed in other series [3,5-8]. Increase of hepatobiliary and pancreatic as well as some other cancers have also been detected [6,8,9]. This is especially true within the first three months after an episode of infective endocarditis. This cancer rate drops however in the following years [9], which is a strong indicator for its association with IE.

The digestive system is the third most common portal of entry, after the skin and the oral cavity [10]. This is corroborated by the observation that the incidence of colorectal cancer in patients with IE caused by *Streptococcus gallolyticus* is much higher compared to other types of cancer [11]. In patients with cirrhosis, an increased permeability of the gut wall also might play a role in bacteremia [12]. An oral portal of entry is important in patients with hematologic disease, especially when this condition is complicated by gingivitis and periodontitis. Inflammation and ulceration caused by chemotherapy increases the likelihood of bacterial entry into the circulation [13]. Strains of *Streptococcus viridans* are important for this type of malignancies. In patients with colorectal neoplasias, *Streptococcus gallolyticus* might just be a bystander [5,9,14], because the vicinity of tumor tissue could offer a competitive advantage. However, this is still uncertain. These microorganism also could have oncogenic capacities

because of its ability to activate cytokines, COX-2 mediated inflammation, neo-angiogenesis, and further degeneration by disabling apoptosis [8,12]. This relation is clouded by the fact that carriage of *Streptococcus gallolyticus* is unstable in time. In some patients, this microorganism has been identified in an earlier stage while it seemed absent in a later period [2,5].

The mechanism of virulence could be related to bacterial pili, with stronger binding capacity to collagen and formation of biofilms in tumors and damaged valves [1,2,14]. There is also a possible role of a polysaccharide capsule in aiding to avoid the immune system. This allows crossing of the epithelial barrier without provoking epithelial interleukin response and enhances also the ability of the microorganism to form a biofilm around collagen in diseased heart valves [6]. Similar findings were made for *Streptococcus infantarius* and *Streptococcus pasteurianus*. Furthermore, *Streptococcus infantarius* spp. coli is capable to invade tissues and to survive within macrophages. These findings stress the importance of biological typing of *Streptococci* in IE [1,2,6,15] but this is not always performed [5]. Another mechanism for IE to develop is immune suppression [10], especially in patients with hematologic disease. These mechanism include neutropenia, insufficient phagocytosis, abnormal B and T cell function, and chemotherapy-related immune suppression. An age effect or use of alcohol could be other explanations for decrease in immunity [11]. Remarkably, low platelets, as result of chemotherapy may be protective. In contrast, thrombophilia might result in formation of sterile vegetation which might serve as precursor for IE [8].

Few data are available concerning the outcome in patients with IE and cancer. Overall survival is diminished. Colorectal cancer-specific survival is not, however. Infective endocarditis leads to changes in oncologic treatment but not to worse oncologic outcome [11]. Age adjusted Charlson comorbidity index is also a predictor for all-cause hospital mortality and of long-term survival after infective endocarditis. With increasing of the index, the presence of cancer also increased [2% if 2 or less, 13% if between 3 and 5, and 21% if the index is more than 5]. The main "drivers" of age adjusted Charlson comorbidity index are cancer, diabetes and heart failure. Treatment strategy should be guided by the abovementioned findings. Colonoscopy is recommended in all patients with bacteremia or IE by *Streptococcus gallolyticus*

[3,5,7] because this is an early marker for occult colon neoplasia [8]. But this diagnostic procedure might not be necessary in enterococcus IE. In any case, the search for a portal of entry is as important as identifying the microbial organism [10]. Patients with metastatic disease have usually immune suppression, for whom cardiac surgery for IE seems futile. For patients with IE and a curable malignancy or with otherwise an acceptable mid-term survival, a serious effort should be undertaken to offer cardiac surgery if this is indicated. A scoring system to identify patients who will benefit from surgery is strongly recommended.

There are several serious limitations in our understanding of the association between cancer and IE. Many series are underpowered due to small size, while larger surveys have less detailed data. In many patients, important comorbid conditions are also present, which cannot always be accounted for. Bias due to patient recruitment, to increased surveillance as well as to a referral policy to a tertiary cardiac center may be important. There is also considerable heterogeneity between the included manuscripts with different study design, different age groups and difference in comorbidity. Infective endocarditis and bacteremia are sometimes investigated together; the latter is a precondition to the former but is distinctively different. The same remark applies to colorectal polyps and colorectal cancer. Last but not least, microbial description is not always uniform. The term “*Streptococcus bovis*” should be avoided and the more recently introduced biotypes *Streptococcus gallolyticus* with its subspecies should be used.

## REFERENCES

1. Boleij A, van Gelder MMHJ, Swinkels DW, Tjalsma H. Clinical Importance of *Streptococcus gallolyticus* Infection Among Colorectal Cancer Patients: Systematic Review and Meta-analysis. *Clin Infect Dis*. 2011; 53: 870-878.
2. Chirouze C, Patry I, Duval X, Baty V, Tattevin P, Aparicio T et al. *Streptococcus bovis*/*Streptococcus equinus* complex fecal carriage, colorectal carcinoma, and infective endocarditis: a new appraisal of a complex connection. *Eur J Clin Microbiol Infect Dis*. 2013; 32: 1171-1176.
3. Corredoira-Sánchez J, García-Garrote F, Rabuñal R, López-Roses L, García-Pais MJ, Castro E, et al. Association Between Bacteremia Due to *Streptococcus gallolyticus* subsp. *Gallolyticus* (*Streptococcus bovis* I) and Colorectal Neoplasia: A Case-Control Study. *Clin Infect Dis*. 2012; 55: 491-496.
4. Bikdeli B, Wang Y, Kim N, Desai MM, Qiagliarello V, Krumholz HM. Trends in Hospitalization Rates and Outcomes of Endocarditis Among Medicare Beneficiaries. *J Am Coll Cardiol*. 2013; 62: 2217-2226.
5. Boltin D, Goldberg E, Bugaevsky O, Kelner E, Bireknfeld S, Gingold-Belfer R, et al. Colonic carriage of *Streptococcus bovis* and colorectal neoplasia: a prospective 17-year longitudinal case-control study. *Eur J Gastroenterol & Hepatol*. 2015; 27: 1449-1453.
6. Marmolin AS, Hartmeyer G, Christensen JJ, Nielsen XC, Dargis R, Skov MN, et al. Bacteremia with the bovis group streptococci: species identification and association with infective endocarditis and with gastrointestinal disease. *Diagn Microbiol Infect Dis*. 2016; 85: 239-242.
7. Sharara AI, AbouHamdan T, Malli A, El-Halabi MM, Hashash JG, Gaith OA, et al. Association of *Streptococcus bovis* endocarditis and advanced colorectal neoplasia: A case-control study. *J Dig Dis*. 2013; 4: 382-387.
8. Sun LM, Wu JN, Lin CL, Day JD, Liang JA, Liou LR, et al. Infective Endocarditis and Cancer Risk A Population-Based Cohort Study. *Medicine*. 2016; 95; e3198.
9. Thomsen RW, Farkas DK, Friis S, Svaerke C, Ording AG, Norgaard M, et al. Endocarditis and Risk of Cancer: A Danish Nationwide Cohort Study. *Am J Med*. 2013; 126: 58-67.
10. Delahaye F, M'Hammedi M, Guerpillon B, de Givigny G, Bobieux A, Dauwalder O, et al. Systematic Search for Present and Potential Portals of Entry for Infective Endocarditis. *J Am Coll Cardiol*. 2016; 67: 151-158.
11. García-Albéniz X, Hsu J, Lipsitch M, Logan RW, Hernandez-Diaz S, Hernan NA. Infective endocarditis and cancer in the elderly. *Eur J Epidemiol*. 2016; 31: 41-49.
12. Zammit SC, Azzopardi N, Ellul P. *Streptococcus gallolyticus* bacteraemia in hepatobiliary-pancreatic and colonic pathologies. *Q JM*. 2014; 107: 355-361.
13. Raber-Durlacher JE, Laheij AMGA, Epstein JKB, Epstein M, Geerligs GM, Wolffe GN, et al. Periodontal status and bacteremia with oral viridans streptococci and coagulase negative staphylococci in allogeneic hematopoietic stem cell transplantation recipients: a prospective observational study. *Support Care Cancer*. 2013; 21: 1621-1627.
14. Martins M, Aymeric L, du Merle L, Dann C, Robbe-Masselot C, Trieu-Cuot P, et al. *Streptococcus gallolyticus* Pil3 Pilus Is Required for Adhesion to Colonic Mucus and for Colonization of Mouse Distal Colon. *J Infect Dis*. 2015; 212: 1646-1655.
15. Lin IH, Liu TT, Teng YT, Wu HL, Liu YM, Wu KM, et al. Sequencing and Comparative Genome Analysis of Two Pathogenic *Streptococcus gallolyticus* Subspecies: Genome Plasticity, Adaptation and Virulence. *PLoS ONE*. 6: e20519.

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