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Pathogenic Gut Flora in Patients With Chronic Heart Failure

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CME Objective for This Article: After reading this article, the reader should be able to discuss: 1) the finding of abnormal gut flora in patients with heart failure; 2) the increased intestinal permeability seen in patients with heart failure; and 3) the clinical implications of these findings.

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ABSTRACT

OBJECTIVES The goal of this study was to measure the presence of pathogenic gut flora and intestinal permeability (IP) and their correlations with disease severity, venous blood congestion, and inflammation in patients with chronic heart failure (CHF).

BACKGROUND Evidence suggests that translocation of gut flora and/or their toxins from the intestine to the bloodstream is a possible trigger of systemic CHF inflammation. However, the relation between pathogenic gut flora and CHF severity, as well as IP, venous blood congestion as right atrial pressure (RAP), and/or systemic inflammation (C-reactive protein [CRP]), is still unknown.

METHODS This study analyzed 60 well-nourished patients in stable condition with mild CHF (New York Heart Association [NYHA] functional class I to II; n = 30) and moderate to severe CHF (NYHA functional class III to IV; n = 30) and matched healthy control subjects (n = 20). In all subjects, the presence and development in the feces of bacteria and fungi (*Candida* species) were measured; IP according to cellobiose sugar test results was documented. The study data were then correlated with RAP (echocardiography) and systemic inflammation.

RESULTS Compared with normal control subjects, the entire CHF population had massive quantities of pathogenic bacteria and *Candida* such as *Campylobacter* (85.3 ± 3.7 CFU/ml vs. 1.0 ± 0.3 CFU/ml; $p < 0.001$), *Shigella* (38.9 ± 12.3 CFU/ml vs. 1.6 ± 0.2 CFU/ml; $p < 0.001$), *Salmonella* (31.3 ± 9.1 CFU/ml vs 0 CFU/ml; $p < 0.001$), *Yersinia enterocolitica* (22.9 ± 6.3 CFU/ml vs. 0 CFU/ml; $p < 0.0001$), and *Candida* species (21.3 ± 1.6 CFU/ml vs. 0.8 ± 0.4 CFU/ml; $p < 0.001$); altered IP (10.2 ± 1.2 mg vs. 1.5 ± 0.8 mg; $p < 0.001$); and increased RAP (12.6 ± 0.6 mm Hg) and inflammation (12.5 ± 0.6 mg/dl). These variables were more pronounced in patients with moderate to severe NYHA functional classes than in patients with the mild NYHA functional class. Notably, IP, RAP, and CRP were mutually interrelated (IP vs. RAP, $r = 0.55$; $p < 0.0001$; IP vs. CRP, $r = 0.78$; $p < 0.0001$; and RAP vs. CRP, $r = 0.78$; $p < 0.0001$).

CONCLUSIONS This study showed that patients with CHF may have intestinal overgrowth of pathogenic bacteria and *Candida* species and increased IP associated with clinical disease severity, venous blood congestion, and inflammation.
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It is well established that chronic heart failure (CHF) is also a systemic chronic inflammatory disease (1). Morphological, functional, and bacterial flora alterations in the intestine have all been reported as causes of inflammation (2). Indeed, increased wall thickness and permeability of both the small and large intestine, as well as increased bacterial populations (e.g., *Bacteroides, Prevotella, Eubacterium, Fusobacterium*) adherent to the intestinal mucosa, have been found (3). Bacteria and/or translocation of their toxins, from the intestine to the bloodstream, directly correlate with systemic inflammation (4).

The present study considered 2 hypotheses: 1) that the CHF intestine may be colonized by more pathogenic bacteria than have so far been reported; and 2) that this state may be associated with the severity of the CHF deterioration and venous blood congestion. These hypotheses are based on the following suppositions. First, the high prevalence of infection in patients with CHF (12%) (5) affects heart failure (despite optimal treatment) and increases the mortality rate (6). Second, the antibiotics used to treat infection may select the development of gut pathogenic bacteria over saprophytes. Third, the plasma levels of toxin lipopolysaccharide, a component of pathogenic bacteria walls, are higher during edematous heart decompensation (4). This finding would suggest that severe venous blood congestion may be an important factor for both intestinal pathogen overgrowth and increased intestinal permeability (IP) (7).

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The present study was conducted in patients with moderate and severe CHF to determine the intestinal pathogenic bacterial and fungal (*Candida* species) profiles in addition to IP. We also related IP to venous blood congestion as indicated by right atrial pressure (RAP).