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# Intestinal Blood Flow in Patients With Chronic Heart Failure

## A Link With Bacterial Growth, Gastrointestinal Symptoms, and Cachexia

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## ABSTRACT

**BACKGROUND** Blood flow in the intestinal arteries is reduced in patients with stable heart failure (HF) and relates to gastrointestinal (GI) symptoms and cardiac cachexia.

**OBJECTIVES** The aims of this study were to measure arterial intestinal blood flow and assess its role in juxtamucosal bacterial growth, GI symptoms, and cachexia in patients with HF.

**METHODS** A total of 65 patients and 25 controls were investigated. Twelve patients were cachectic. Intestinal blood flow and bowel wall thickness were measured using ultrasound. GI symptoms were documented. Bacteria in stool and juxtamucosal bacteria on biopsies taken during sigmoidoscopy were studied in a subgroup by fluorescence in situ hybridization. Serum lipopolysaccharide antibodies were measured.

**RESULTS** Patients showed 30% to 43% reduced mean systolic blood flow in the superior and inferior mesenteric arteries and celiac trunk (CT) compared with controls ($p < 0.007$ for all). Cachectic patients had the lowest blood flow ($p < 0.002$). Lower blood flow in the superior mesenteric artery and CT was correlated with HF severity ($p < 0.04$ for all). Patients had more feelings of repletion, flatulence, intestinal murmurs, and burping ($p < 0.04$). Burping and nausea or vomiting were most severe in patients with cachexia ($p < 0.05$). Patients with lower CT blood flow had more abdominal discomfort and immunoglobulin A-antilipopolysaccharide ($r = 0.76$, $p < 0.02$). Antilipopolysaccharide response was correlated with increased growth of juxtamucosal but not stool bacteria. Patients with intestinal murmurs had greater bowel wall thickness of the sigmoid and descending colon, suggestive of edema contributing to GI symptoms ($p < 0.05$). In multivariate regression analysis, lower blood flow in the superior mesenteric artery, CT ($p < 0.04$), and inferior mesenteric artery ($p = 0.056$) was correlated with the presence of cardiac cachexia.

**CONCLUSIONS** Intestinal blood flow is reduced in patients with HF. This may contribute to juxtamucosal bacterial growth and GI symptoms in patients with advanced HF complicated by cachexia. (J Am Coll Cardiol 2014;64:1092–102)


Chronic heart failure (HF) is a multisystem disease. Along with increased sympathetic tone and chronic low-grade systemic inflammation, there is an anabolic-catabolic imbalance, with cardiac cachexia as a terminal stage of the disease. The occurrence of this unintentional weight loss is a serious complication and predicts poor survival (1). The prevalence of cachexia

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in patients with chronic HF ranges from 16% to 42% (2).

The role of the gut in the pathophysiology of chronic HF has only recently undergone detailed investigations. There is increasing evidence that the gut plays an important pathophysiological role in malnutrition and cachexia in chronic HF. Significant morphological and functional alterations of the intestine in patients with chronic HF have been previously shown (3). Patients display a thickened bowel wall, suggestive of bowel wall edema; intestinal barrier dysfunction; and diminished transcellular transport activity (4). There are increased numbers of bacteria in the mucus layer adjacent to the apical surface of the colonic mucosa, and increased permeability of both the small and large intestines has been demonstrated. Restricted arterial blood flow to the intestine is a major candidate explaining these functional alterations and may create an abnormal environment in the juxtamucosal mucus layer that encourages the increased growth of bacteria. However, arterial blood flow to the intestine and gastrointestinal (GI) symptoms in cachectic and noncachectic patients with HF has not yet been analyzed.

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We hypothesized that arterial blood flow in the main intestinal arteries is reduced in patients with stable compensated HF and relates to possible GI symptoms and to the prevalence of cardiac cachexia.

## METHODS

We prospectively studied intestinal blood flow in 65 patients with chronic HF and 25 control subjects. Demographic and clinical details are shown in **Table 1**. The diagnosis of chronic HF was based on symptoms arising during exercise, clinical signs, and documented left ventricular impairment (left ventricular ejection fraction [LVEF] ≤ 40%) according to guidelines (5). Patients were classified as cachectic independent of their absolute body mass indexes if they had experienced nonedematous unintentional weight loss of ≥5% within the previous 6 to 12 months (6). All patients were clinically stable (mean New York Heart Association [NYHA] functional class 2.5 ± 0.5) and received unchanged medications for at least 4 weeks before assessments. Patients were allowed to take aspirin 100 mg once daily but no other nonsteroidal anti-inflammatory drugs, steroid hormones, or antibiotics within at least 4 weeks before study participation. In patients with HF, medications consisted of angiotensin-converting enzyme inhibitors (71%), angiotensin receptor blockers (32%), beta-blockers (88%), aldosterone receptor antagonists (52%), other diuretic agents (72%), glycoside agents (20%), and statins (80%) in varying combinations. None of the control subjects were taking any cardiovascular medications, except for a calcium channel blocker in 1 subject and angiotensin-converting enzyme inhibitors in 2 subjects for mild arterial hypertension without evidence of left ventricular dysfunction. Subjects with clinical signs of infection, rheumatoid arthritis, renal failure, intestinal diseases, severe chronic obstructive pulmonary disease, significant valvular heart disease, cancer, or histories of autoimmune disorders were excluded. None of the subjects had known immune system disorders, and no subject received immune modulation therapy. The local ethics committee approved the study, and all subjects gave written informed consent.

**ABBREVIATIONS AND ACRONYMS**

**ANP** = atrial natriuretic peptide
**CT** = celiac trunk
**GI** = gastrointestinal
**HF** = heart failure
**IgA** = immunoglobulin A
**IMA** = inferior mesenteric artery
**LVEF** = left ventricular ejection fraction
**LPS** = Lipopolysaccharide
**NYHA** = New York Heart Association
**SMA** = superior mesenteric artery
**TAMV** = time-averaged mean velocity

**CLINICAL ASSESSMENTS.** Echocardiography was performed according to standard procedures. LVEF was measured using the biplane Simpson's technique. All subjects underwent symptom-limited treadmill exercise testing (instantaneous breath-by-breath method) using the modified Naughton protocol (Innocor system [Innovision, Odense, Denmark]; HP Cosmos treadmill [HP Cosmos Sports & Medical GmbH, Nussdorf-Traunstein, Germany]). The following variables were measured: peak oxygen consumption, total exercise time, ventilatory response to exercise, anaerobic threshold, peak heart rate, and peak systolic and diastolic blood pressures.

Blood flow velocities in the celiac trunk (CT), superior mesenteric artery (SMA), and inferior mesenteric

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