

# Major Predictors of Incidence of Congestive Heart Failure and the Responsive Character of Enteral Nutrition: Meta-Analysis

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## Abstract

**Background:** Statistical data from the USA estimate that 5.7 million Americans over 20 years of age have congestive heart failure (CHF) and this number is expected to increase approximately 46.0% between 2012 and 2030. In Brazil, there are no epidemiological studies involving the incidence of heart failure; however, according to other countries, it can be estimated that up to 6.4 million Brazilians suffer from this syndrome. Randomized and controlled clinical studies on the efficacy of enteral nutrition (EN) in patients with CHF are lacking. The aim of the present study was to perform a systematic review of the main predictors of CHF that promote EN, as well as to find if the literary findings were conclusive in the efficacy of EN for treatment and prophylaxis of CHF.

**Methods:** A total of 105 papers were submitted to the eligibility analysis, after which 28 studies were selected, following the rules of the systematic review - PRISMA. The search strategy was followed in MEDLINE/Pubmed, Web of Science, ScienceDirect Journals (Elsevier), Scopus (Elsevier) and ONEFile (Gale), with the following steps: search for *mesh terms* and use of bouleanos “and” between terms and “or” between historical findings.

**Results:** The present study listed the major predictors of CHF with indication for EN. After testing the normality of each group of variables of causes of decompensation in CHF, it was analyzed that all the variables did not present normal distribution, with  $P < 0.10$ . Thus, a non-parametric Kruskal-Wallis analysis was performed, obtaining  $P > 0.05$  in all analyses, that is, in all groups of causes of decompensation in CHF, there was no statistical difference in each group studied.

**Conclusion:** There is still no known influence of the efficacy of EN

on increasing survival and reducing the morbidity of patients with CHF because there are few clinical trials that have evaluated this question; however, EN is very indicated in the attempt to mitigate the weight loss in these patients.

**Keywords:** Enteral therapy; Enteral nutrition; Cardiac insufficiency; Congestive heart failure; Clinical trials

## Introduction

Congestive heart failure (CHF) is a serious and growing public health problem worldwide, being the final common pathway of most heart diseases [1, 2]. Although the scientific and technological advances and the better socioeconomic conditions have allowed the increase of the longevity of the general population and of the cardiac patients, there has been an increase in the incidence of CHF in the world [2-4]. Approximately 23 million people are carriers of this disease and two million new cases are diagnosed each year. CHF is an important public health issue due to its high prevalence, severity of clinical manifestations and reserved prognosis [3, 4].

Statistical data from the USA estimate that 5.7 million Americans over 20 years of age have CHF; an increase of approximately 46.0% is expected between 2012 and 2030, resulting in more than eight million adults [4]. In Brazil, there are no epidemiological studies involving the incidence of heart failure. However, according to other countries, up to 6.4 million Brazilians can be estimated to suffer from this syndrome [5].

CHF is caused by structural and functional abnormalities of the heart, leading to ventricular ejection defects and/or ventricular filling capacity [5-7]. In Brazil, the main causes of CHF are myocardial ischemia, systemic arterial hypertension, dilated cardiomyopathy and Chagas disease, as well as valvular disease [5]. After cardiac injury, the consequent molecular, structural and functional ventricular changes are known as cardiac remodeling. This process is accompanied by cardiac and systemic inflammatory and neuro-hormonal activation, which adversely affects the heart in a vicious cycle and compromises different organs and systems [5].

In recent decades, it has become clear that pathological changes involve not only the cardiovascular system, but also

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the renal, neuro-endocrinological, immunological, hematological, gastrointestinal and musculoskeletal systems, as well as nutritional status [1-3, 6, 7]. Currently, experimental and clinical studies have focused on the pathophysiology of systemic complications related to CHF in order to establish treatments to improve quality of life and increase survival [7, 8].

The clinical evolution of patients with CHF, as a rule, goes to varying degrees of malnutrition [5-8], necessitating the adhesion of enteral nutrition (EN). This may occur due to inadequate intake, altered metabolism, proinflammatory status, increased oxidative stress and increased nutrient loss, even through drug interactions. Anorexia is a consequence of reduced nutrient intake or the association of metabolic and absorptive changes (hypermetabolism, hypoxia, increased energy expenditure, inflammation) [8, 9].

Bowel edema in heart failure may be responsible for the presence of nausea, lipid malabsorption, gastric fullness sensation and protein losses [10].

The presence of malnutrition is an important predictor of survival reduction in patients with CHF regardless of important variables such as age, functional class and ejection fraction [2, 10, 11]. Thus, it becomes imperative to EN in an attempt to treat or mitigate the comorbidities of CHF.

The aim of the present study was to perform a systematic review of the main predictors of CHF that lead to EN, as well as to find if the literary findings were conclusive in the efficacy of enteral nutrition for treatment and prophylaxis of CHF.

## Patients and Methods

### Study design

A total of 105 papers that were submitted to the eligibility analysis were collected and, after that, 27 studies were selected, following the rules of the systematic review - PRISMA (Transparent Report of Systematic Reviews and Meta-Analyses - <http://www.prisma-statement.org/>), according to Fig. 1.

### Information source

The review protocol was based on the literary search criteria with the use of Mesh Terms in the main databases such as Pubmed, Medline, Bireme, EBSCO, Scielo, etc. All references are registered in EndNote by the site:

<http://www.myendnoteweb.com/EndNoteWeb.html?cat=myrefs&>.

### Search strategy

The search strategy was followed in MEDLINE/Pubmed, Web of Science, ScienceDirect Journals (Elsevier), Scopus (Elsevier) and ONEFile (Gale), with the following steps: search mesh terms (enteral therapy; enteral nutrition; heart failure; congestive heart failure; clinical trials), and use of bouleanos “and” between terms and “or” between historical findings.

## Statistical treatment of literary findings

A descriptive analysis was performed with standard parameters of mean, standard deviation and amplitude. Anderson-Darling normality test ( $\alpha$ -level  $> 0.10$  considered as “normal”) was also performed for continuous and categorical data, with consequent application of Kruskal-Wallis analysis of variance to the internal data of each study alone, accepting  $P < 0.05$  for statistical significance.

## Results

The present study listed the major predictors of CHF with indication for enteral nutrition, according to Table 1. After testing the normality of each group of variables of causes of decompensation in CHF, it was analyzed that all the variables did not present normal distribution, with  $P < 0.10$ . Thus, a non-parametric Kruskal-Wallis analysis was performed, obtaining  $P > 0.05$  in all analyses ( $\alpha$ -level  $< 0.05$  as a statistical difference reference), that is, in all groups of causes of decompensation in CHF, there was no statistical difference in each group studied. Therefore, the literary works evaluated in the present study presented the same response regarding the causes of decompensation in CHF.

## Discussion

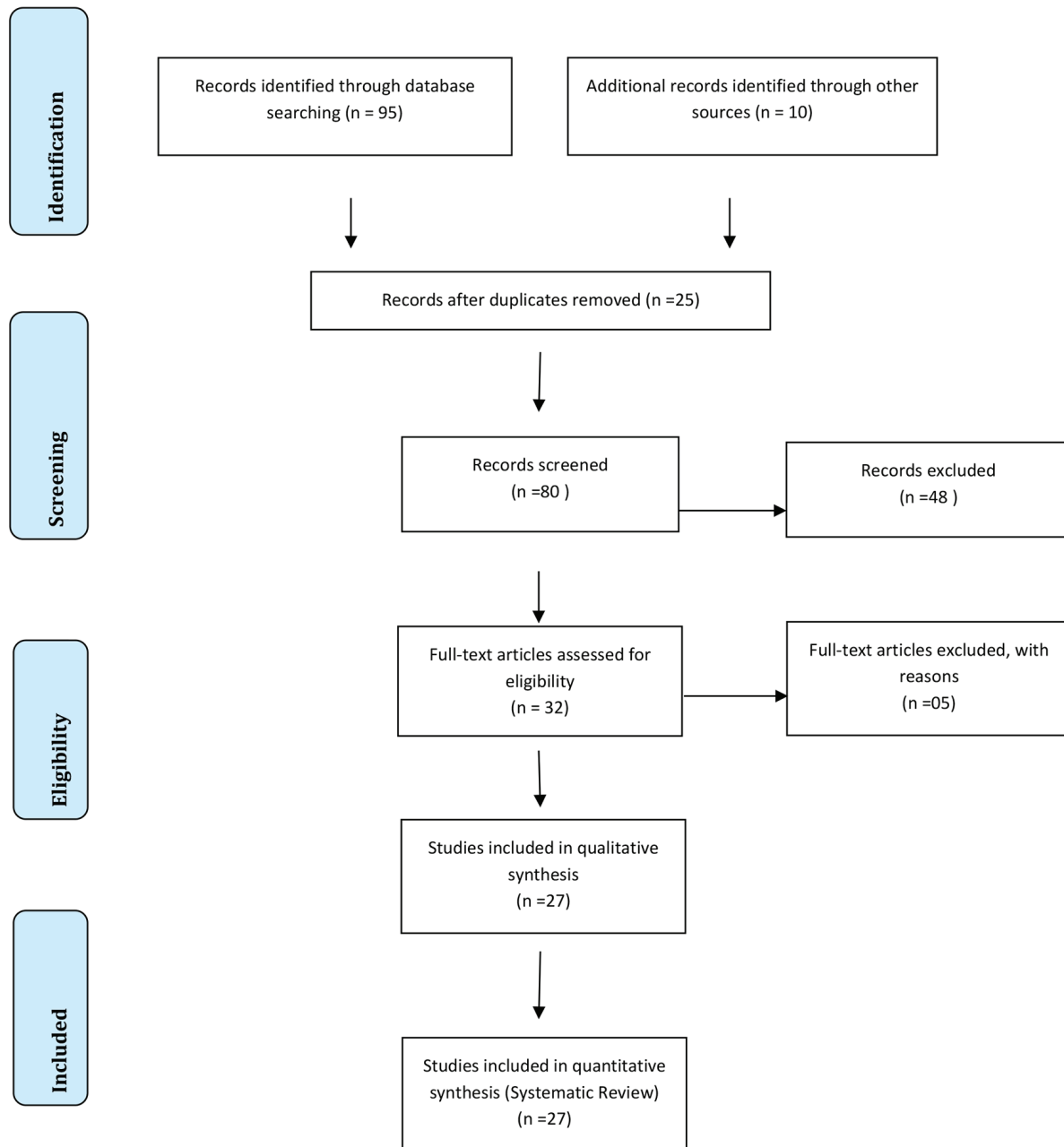
Thus, CHF is a pathology in which circulatory, neuro-hormonal and metabolic factors interact causing cardiac muscle dysfunction, ventricular hypertrophy and hemodynamic changes [1-3]. The symptoms cause the individual great cardiac repercussions, with repeated hospitalizations and even death [3]. Mortality in CHF is related to age, with an increase of 27.0% per decade of life for men and 61.0% for women [4].

In CHF, there are multiple causal factors of malnutrition, called cardiac cachexia [1-5], as shown in Table 1. It is necessary to distinguish in CHF the eutrophic individual from those who present with insufficient nutrition or with severe malnutrition or cachexia, according to the classification of the New York Heart Association class III and IV [5].

Thus, the innumerable hospitalizations make the patients depressive and not receptive to feeding at restricted salt feeding and unattractive [5, 6]. Dyspnoea, muscular fatigue and edema, even in the gastrointestinal tract, makes a set for the reduction of oral intake, and EN is necessary [7-11].

Patients with CHF need to be evaluated by a multidisciplinary team to determine the patient's state of depletion and thus, measures need to be taken to reduce the high catabolism caused by CHF, preserving the tissues and reducing the use of endogenous nutrients in order to recover organic functions to mitigate morbidity and mortality [12-15].

Severe malnutrition of the myocardiopathy is multifactorial [1-3, 16-18]. Metabolic imbalance occurs due to high basal energy expenditure, around 20.0%, and not always adequate caloric replacement [19]. Recent articles report the action of cytokines in the pathogenesis of cardiac cachexia [1-4].



**Figure 1.** Flow chart.

Furthermore, tumor necrosis factor (TNF) has also been correlated with its elevation in class IV functional patients, especially those with cardiac cachexia, many believed to be caused by the accelerated effect of skeletal muscle catabolism [20]. Only patients with EN, associated or not with oral diet therapy can recover the catabolism generated by CHF [20, 21]. Other studies corroborate the early onset in stable myocardio-pathic patients, around 24 - 48 h after cardiac decompensation [2, 3, 22].

EN is indicated for patients who do not meet the protein-calorie needs of oral diet [3, 23]. The use of the enteral route is

well tolerated in patients, from 80.0% to 90.0% [1-3, 5, 24]. In patients malnourished by cardiac decompensation, by means of enteral infusion, one can achieve adequate nutritional intake, allied or not with oral diet [5, 25].

The elemental diet is indicated for patients with malabsorption, have pre-digested proteins and free amino acids [26]. The polymeric diet contains 30.0-40.0% of lipids, proteins and polysaccharides. If there is decreased gastric motility, the best choice is the elemental diet [26, 27].

Enteral diet may be infused continuously or intermittently. Studies have shown that patients who are more debilitated and

**Table 1.** Major Predictors of CHF with Indication for Enteral Nutrition, with  $\alpha$ -Level < 0.05 as a Statistical Difference Reference

Causes of decompensation in CHF	Data (%); results with P > 0.05 for each group (no statistical difference)
Lack of adherence	74.0; P > 0.05
The diet	24.0; P > 0.05
To medicines	8.0; P > 0.05
Both previous	41.0; P > 0.05
The uncontrolled SAH	46.0; P > 0.05
Cardiac arrhythmias	31.0; P > 0.05
Environmental factors	22.0; P > 0.05
Inadequate therapy	19.0; P > 0.05
Pulmonary infection	14.0; P > 0.05
Emotional stress	8.0; P > 0.05
Administration of inappropriate medications or excess fluids	5.5; P > 0.05
Acute myocardial infarction	6.5; P > 0.05
Thyrotoxicosis	1.5; P > 0.05

less active accept diet better via a continuous probe, slowly and for a longer period, even in patients with heart disease [2, 6, 7]. According to the authors, continuous infusion should be decreased if the probability of gastric distension, diarrhea, pulmonary aspiration and metabolic abnormalities exists.

In case of diarrhea or intolerance, the fibers and ammonia in the diet formulation should be altered to protect the gastrointestinal tract [27]. In this sense, a higher rate of diarrhea was observed in the elderly when administered to the enteral diet intermittently [27]. Normally, diarrhea does not present a higher frequency in CHF patients, but constipation due to the lower amount of endogenous water and less physical movement [6, 7].

In addition, the pre-pyloric positioning is performed by nasogastric tube or gastrostomy, and the post-pyloric by naso-jejunal or jejunostomy probe [8, 9]. In the literature, a higher probability of aspiration of the diet was not confirmed by intra-gastric or pyloric probe. However, the clinical body has a preference for post-pyloric placement [9].

The enteral infusion access is the percutaneous endoscopic gastrostomy, with low morbidity rates [3]. Due to the characteristics of the duodenal mucosa in the cardiopathic patient, the diet should be chosen by evaluating its osmolarity, caloric density and infusion rate [3, 4].

### Complications of EN

Despite the support provided by EN, there may be gastrointestinal, metabolic and mechanical complications [8]. In addition, infectious, respiratory and psychological complications may also occur [9-12]. Gastrointestinal complications are the most common, including nausea and vomiting of 2.5-10% [12]. Gastric stasis greatly impairs diabetic patients. Diarrhea is the most frequent, reaching up to 10.0-68.0% of cases [5].

In this context, according to the reports of complications observed by the Enteral and Parenteral Nutritional Support

Group (GAENP) in Brazil, which analyzed 80 patients who used vasoactive drugs, 45.0% of them presented some digestive complications, in 21.0%, the complication was associated with probe discharge and, in 10.0%, diarrhea [5]. In another multicenter study conducted in the USA, it was verified in 360 patients that aspiration as a pulmonary complication was present in 88.0% of the cases [6].

### Is there scientific evidence of EN in the treatment and prophylaxis of CHF?

Although few studies or case reports show the efficacy of EN to treat the comorbidities of patients with CHF, there is an urgent need for randomized and controlled trials of nutritional treatment in this condition, with the aim of improving cardiac function through a higher supply nutrients and energy.

The other goal of such treatment is also the complementation with other therapies to provide extra protein during treatment. In addition, other forms of nutritional support were tested in a small number of patients with cachexia, particularly those undergoing cardiac surgery, in whom preoperative feeding reduced the number of complications, mortality and duration of the postoperative hospital [5].

However, a major disadvantage of these favorable nutritional studies in CHF is the fact that they were all performed in the era before modern standard treatment with angiotensin-converting enzyme inhibitors and beta-blockers [2]. There is evidence that angiotensin-converting enzyme inhibitors prevent weight loss [5].

### Conclusions

There is still no known influence of the efficacy of EN on increasing survival and reducing the morbidity of CHF patients because there are few clinical trials that have evaluated this

question; however, EN is very indicated in the attempt to mitigate weight loss in these patients.

### Conflict of Interest

None.

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