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Iron deficiency in patients with chronic heart failure: A systematic literature review

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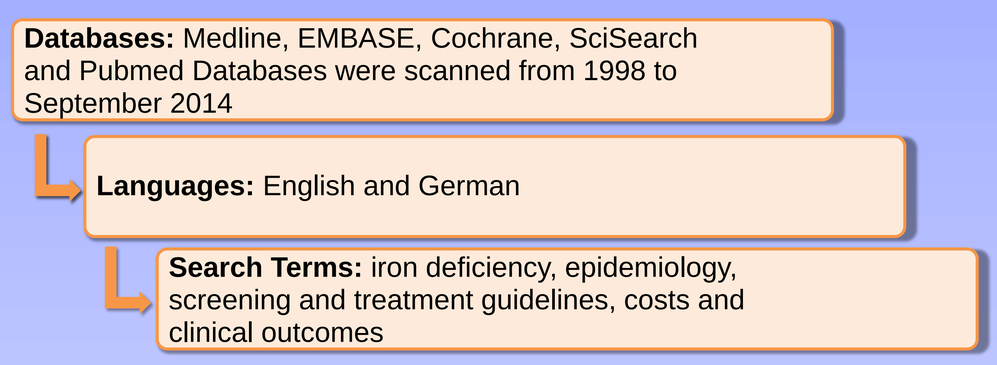
Objectives

Iron deficiency (ID), a non-cardiovascular comorbidity, is highly prevalent in chronic heart failure (CHF) patients and imposes a significant disease burden for CHF patients with enormous impact on their outcome and health care costs. Thus, this study was designed to identify epidemiological data, screening and treatment guidelines, costs as well as outcome of intravenous iron treatment in patients with CHF and iron deficiency.

Methods

A comprehensive literature review was undertaken for all publications from 1998 to September 2014 using Medline, EMBASE, Cochrane, Science Direct and Pubmed databases, comprising English and German articles. The review focused on studies based on patients with chronic heart failure and iron deficiency, with or without anemia. Articles were systematically selected if they included data for iron deficiency on at least one of the following criteria: epidemiology, screening and treatment guidelines, costs and clinical outcomes. Additional articles were found via hand search using references from eligible articles.

Fig. 1: Literature search strategy



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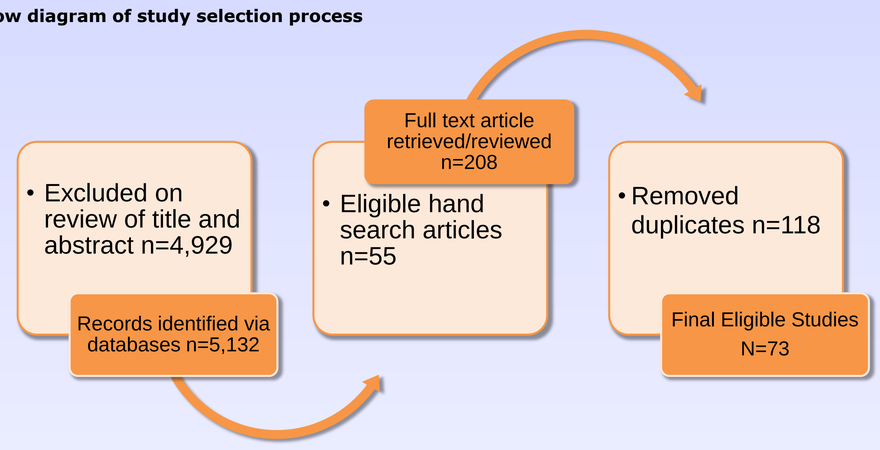
Results

Database search yielded 5,132 articles and 55 additional articles were identified via secondary hand search. Of the 73 eligible articles; 30 provided information on epidemiological data, 14 on screening and treatment guidelines, 15 on costs and 14 on clinical outcomes.

Fig. 2: Flow diagram of study selection process



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Prevalence

Despite new therapeutic advances, CHF remains a severe disease with a poor outcome. CHF patients have also decrease functional capacity and low quality of life. The recent ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 recognize ID as a common co-morbidity in heart failure. The highest published prevalence rates of CHF, up to 11.5%, are documented for Europe. In Europe nearly 50% of patients with chronic heart failure are iron deficient. The prevalence of anemia in patients with CHF is around 22% (4-73%). In addition there is a correlation between the prevalence of ID and the NYHA stages. Disease severity assessed by NYHA class proved to be powerful and an independent predictor of a disordered iron status.

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Table 1: Prevalence rates

	Europe	America	Study design	No. of studies
Prevalence chronic heart failure	0,2%-11,5%	1%	Cohort studies, Reviews, Registries	7
Prevalence iron deficiency	25%-75,3%	5%-21%	Cohort studies, Reviews, Registries	7
Prevalence anemia	4%-73%	4%-70%	Cohort studies, Reviews, Registries	18
Prevalence iron deficiency in patients with anemia	5%-74,1%	21%-30%	Cohort studies, Reviews, Registries	8
Prevalence iron deficiency in patients without anemia	22%-78,7%	-	Cohort studies, Reviews, Registries	4

Source: own depiction

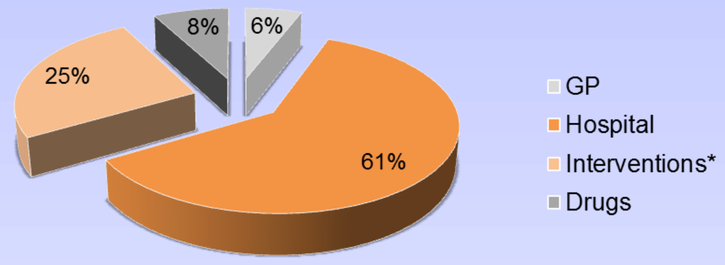
Screening and treatment

Current guidelines recommend that assessment of all patients with suspected heart failure should include an evaluation of iron status to detect ID. Iron therapy should be considered in all patients with CHF who have ID regardless of whether anemia is present or not. A correction of ID with oral iron will often take longer due to non-adherence or interruption due to side effects (e.g. gastrointestinal). Moreover the intolerance of oral iron preparations is very common as well as the impaired intestinal absorption due to hepcidin upregulation, presence of GI mucosal edema and reduced blood. Therefore, replenishment of iron stores with intravenous iron can achieve rapid improvement, less side effects and better compliance to treatment.

Costs

Considering the included studies of this review, healthcare expenditure on CHF consumes 1-2% of the total healthcare budget. The highest proportion of costs is related to hospital care (61%) followed by rehabilitation and nursing homes (25%). Moreover there is a significant correlation between healthcare costs and NYHA stages. Compared with the NYHA class I, there is a cost increase in NYHA II of 14%, in NYHA III of 48% and in NYHA IV of 71%.

Fig. 3: Percentage of healthcare expenditure



*Rehabilitation and nursing
Source: own depiction

All included studies reported higher costs in patients with CHF and anemia ranging between 2-133%. Thus, the prevention of anemia by treating ID from the economic perspective is cost effective. Compared to non-iron deficient patients the cost-effectiveness of iron repletion using intravenous iron in patients with CHF with ID with or without anemia results in significantly reduced healthcare costs (-24%).

Health related Outcome

The results of CONFIRM-HF and FAIR-HF study (based on 456 patients) have shown significant improvements in functional capacity, symptoms and QoI in patients with systolic CHF with intravenous ferric carboxymaltose (FCM). Moreover a meta-analysis (n=631) has shown that patients treated with FCM had significant reductions in hospitalizations (OR 0.26, 95% CI 0.08-0.80), adverse events (OR 0.35, 95% CI 0.21-0.60), NYHA class (mean improvement 1.2 classes, 95% CI 0.69-1.78, and LVEF (mean improvement 5.0%, 95% CI 0.13-9.80).

Conclusion

CHF represents a major and growing public health problem and is often associated with ID as co-morbidity. Intravenous iron can be an option to improve outcome (patient status), and reduce health care costs.

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Additional Literature with the author.
Literature not cited in the text, due to the high number of references, please contact the author.

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