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Prevention of relapse in patients with congestive heart failure: the role of precipitating factors

J Feenstra, D E Grobbee, F A M Jonkman, A W Hoes, B H Ch Stricker

Abstract
Relapse of congestive heart failure (CHF) frequently occurs and has serious consequences in terms of morbidity, mortality, and health care expenditure. Many studies have investigated the aetiological and prognostic factors of CHF, but there are only limited data on the role of precipitating factors that trigger relapse of CHF. Knowledge of potential precipitating factors may help to optimise treatment and provide guidance for patients with CHF. The literature was reviewed to identify factors that may influence haemodynamic homeostasis in CHF. Precipitating factors that may offer opportunities for preventing relapse of CHF were selected. Potential precipitating factors are discussed in relation to the pathophysiology of CHF: alcohol, smoking, psychological stress, uncontrolled hypertension, cardiac arrhythmias, myocardial ischaemia, poor treatment compliance, and inappropriate medical treatment. Poor treatment compliance in particular is frequently encountered in patients with CHF. Furthermore, studies of medical treatment under everyday circumstances indicate that some aspects of the management of CHF can be improved. In conclusion, the identification of precipitating factors for relapse of CHF may strongly contribute to optimal treatment. Improvement of treatment compliance and optimisation of medical treatment may offer important possibilities to clinicians to reduce the number of relapses in patients with CHF.

Keywords: congestive heart failure; precipitating factors; prevention

There is increasing interest in congestive heart failure (CHF) from both clinicians and researchers. The prevalence of CHF continues to increase despite advances in the treatment of various risk factors for this disease, such as hypertension and coronary artery disease. This increase is the result of several medical and demographic developments: an aging population, decreasing mortality of patients with acute myocardial infarction, and improved treatment of patients with angina pectoris and hypertension. In addition, survival in patients with CHF has improved since the introduction of angiotensin converting enzyme (ACE) inhibitors.

CHF is clinically characterised by periods of remission and exacerbation. Readmission rates of up to 25% within six months after a previous hospital discharge for CHF have been reported in patients older than 65 years. Relapse of CHF in patients with previously stable compensated heart failure may be caused by deteriorating ventricular function, but several precipitating factors have been suggested.

Some precipitating factors can be regarded as potentially preventable. Research on precipitating factors leading to relapses of CHF, however, is scarce. Nevertheless, timely identification of potential precipitating factors may offer an important advantage in efforts to reduce morbidity and the number of hospital admissions attributed to the syndrome of CHF.

We conducted a search of the MEDLINE database from 1966 to December 1997 and used lateral references to review the literature on potential precipitating factors. In this article we focus on the role of precipitating factors that are relatively common in clinical practice and potentially modifiable: the effects of alcohol, smoking, psychological stress, uncontrolled hypertension, cardiac arrhythmias, myocardial ischaemia, lack of compliance, and inappropriate medical treatment.

Precipitating factors for relapse of congestive heart failure
Knowledge of potential precipitating factors for relapse of CHF is crucial to prevent or postpone such relapses. In a descriptive study, Ghali et al examined potential precipitating factors in 101 hospital readmissions for CHF. Precipitating factors were identified in 93% of patients. The most common factor was lack of adherence to the prescribed medical regimen (64% of patients). Other frequently identified precipitating factors were uncontrolled hypertension (44%), cardiac arrhythmias (29%), iatrogenic factors (21%), and pulmonary infection (17%) (table 1). In a more recent study, Opasich et al identified precipitating factors in 91% of 328 instances of non-fatal decompensation in 304 patients. All patients had a history of at least one previous episode of severe decompensation.
Prevention of relapse in patients with CHF

**Table 1 Factors that may precipitate relapses in patients with pre-existing CHF**

<table>
<thead>
<tr>
<th>Factor</th>
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<tbody>
<tr>
<td>Lack of treatment compliance</td>
</tr>
<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Angina pectoris or painless myocardial ischaemia</td>
</tr>
<tr>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
</tr>
<tr>
<td>Inappropriate medical treatment</td>
</tr>
<tr>
<td>Infections</td>
</tr>
<tr>
<td>Anaemia</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Thyroid disease</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Physical, dietary, fluid, and environmental excesses</td>
</tr>
<tr>
<td>Emotional stress</td>
</tr>
<tr>
<td>Systemic hypertension</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
</tbody>
</table>

Common precipitating factors were cardiac arrhythmias (24% of patients), poor compliance (15%), infection (23%), angina pectoris (14%), and iatrogenic factors (10%). Frequency differences in specific precipitating factors reflect the different populations and designs of the two studies. In addition, the absence of a control group excludes assessment of the relative risk of these potential precipitating factors.

Several diseases may induce the syndrome of CHF. Patients in whom CHF is diagnosed should be given optimal medical care to prevent clinical worsening while maintaining quality of life. An accurate evaluation of potential precipitating factors should also be routinely performed in patients with relapse of CHF.

The haemodynamic effects of these precipitating factors are discussed within the framework of current views on the pathophysiology of CHF. Apart from the precipitating factors discussed here, CHF may also be precipitated by infection, anaemia, pulmonary embolism, thyroid disease, pregnancy, and physical, dietary, fluid, and environmental excesses. As most of these factors have either known causes, such as excessive salt intake and excessive intravenous fluid administration, or relatively uncommon causes, they are not discussed in further detail.

**ALCOHOL**

CHF resulting from alcoholic cardiomyopathy is a relatively common cause of non-ischaemic cardiomyopathy. The amount and duration of alcohol consumption required to induce alcoholic cardiomyopathy is not well defined, but has been estimated at five to six ounces (1 oz = 28 ml) of ethanol daily for at least 10 years. Abstention from alcohol is crucial in patients with alcohol induced cardiomyopathy.

Echocardiographic studies show that major clinical improvement and normalisation of left ventricular function can be achieved after abstention from alcohol. Resumed alcohol intake may be a precipitating factor for relapse of CHF.

There is no convincing evidence for absolute abstention from alcohol in patients with CHF not induced by alcohol. In a study in which the acute effects of moderate alcohol consumption (0.9 g/kg) in patients with New York Heart Association (NYHA) class III–IV heart failure were assessed, small but significant reductions in arterial pressure, pulmonary artery pressure, pulmonary artery wedge pressure, and systemic vascular resistance were seen after a single dose of alcohol, but CHF did not deteriorate. Chronic heavy alcohol consumption should be strongly discouraged in all patients with CHF, but there are no convincing reasons to warn against incidental moderate consumption of alcohol. Clinical practice shows, however, that some patients with apparently non-alcoholic induced CHF may have significant improvement after complete abstention from even incidental moderate alcohol consumption. Therefore, evaluation of a period of complete alcohol abstention in patients with severe CHF may be worthwhile.

**SMOKING**

Several studies have been performed on the acute haemodynamic effects of smoking. Cigarette smoking increases heart rate and blood pressure, both principal determinants of myocardial oxygen consumption. Goldbarg et al showed in healthy individuals that the left ventricular stroke index decreased significantly at several levels of exercise after smoking, although there was no significant change at rest. Aronow et al investigated the effects of cigarette smoking and breathing carbon monoxide on cardiovascular haemodynamics in patients with angina. This study showed that an increased level of carboxyhaemoglobin had a negative inotropic effect and increased left ventricular end diastolic pressure. There was a significant decrease in the stroke index after smoking. Pentecost et al indicated that cigarette smoking tends to decrease cardiac output especially in older patients with a history of myocardial infarction. Nicolozakes et al investigated the effects of smoking in patients with NYHA class III CHF. Cardiac output remained unchanged after smoking, but other haemodynamic changes were observed. Heart rate and systemic blood pressure (double product) increased substantially after smoking. In addition, there were mild increases in pulmonary artery pressure, ventricular filling pressures, and total systemic and pulmonary vascular resistance. The increased ventricular afterload probably accounts for the observed mild decrease in stroke volume. Thus smoking increases oxygen demand but decreases myocardial oxygen supply because of reduced diastolic filling time and increased carboxyhaemoglobin level. This finding has important negative consequences for myocardial oxygen supply. Patients with CHF should be strongly advised to stop smoking and informed that continued smoking can unfavourably affect CHF. It remains unclear to what extent smoking may act as a precipitating factor for relapse of CHF.

**PSYCHOLOGICAL STRESS**

Mental stress in patients with ischaemic heart disease can induce transient myocardial ischaemia and transient wall motion abnormalities. Rozanski et al reported that wall motion abnormalities occurred in 59% of patients with coronary artery disease during mental stress. A drop in ejection fraction of more than 5% was seen in...
36% of patients. Wall motion abnormalities were seen in only 8% of normal controls during mental stress. There was no clear effect on ejection fraction in the controls. Mental stress may also induce transient changes of the electrophysiological properties of the myocardium, which may sensitise the heart to life threatening ventricular arrhythmias.\textsuperscript{21} Emotional factors preceding hospitalisation for CHF have been reported in 49% of patients.\textsuperscript{7} Stress induced heart failure has been described.\textsuperscript{2,25} Giannuzzi et al reported that psychological stress induced changes in left ventricular diastolic function in patients with idiopathic cardiomyopathy.\textsuperscript{11} The effects of mental arithmetic on these patients were compared with those on controls. The ratio of transmural peak flow velocity in early versus late diastole significantly increased during mental arithmetic, while transmitral deceleration time greatly decreased. These findings suggest that left ventricular function is impaired during psychological stress. Neuroendocrine activation and a significant increase in arterial blood pressure may also contribute to the haemodynamic consequences of psychological stress.

The full effects of psychological stress on cardiovascular function in patients with CHF are not known, but many of the discussed effects may be considered unfavourable.

**UNCONTROLLED HYPERTENSION**

Recent data from the Framingham study underscore the importance of hypertension as a major risk factor for CHF.\textsuperscript{21} Hypertension may impair ventricular function by increasing afterload and impairing systolic contraction and diastolic relaxation.\textsuperscript{23} Approximately 50% of patients with hypertension and a normal coronary angiogram have transient ST segment depression during 24 hour Holter monitoring, usually without angina pectoris.\textsuperscript{25} As there is no relation with left ventricular hypertrophy, these findings reflect a disturbed coronary microvasculature. Intervention trials have provided convincing evidence of the efficacy of hypertension treatment in reducing the incidence of CHF.\textsuperscript{26} Obviously, persistent hypertension in patients with CHF will have a detrimental effect on ventricular performance. Blood pressure in patients with end stage CHF usually decreases because of low cardiac output. Uncontrolled hypertension despite antihypertensive treatment, defined as diastolic blood pressure of 105 mm Hg or more, was identified in 44% of patients readmitted to hospital for CHF.\textsuperscript{3} Adequate blood pressure control in patients with CHF is crucial because of the numerous haemodynamic effects of hypertension, although there are few data on the extent to which uncontrolled hypertension may account for relapse of CHF.

**ARRHYTHMIAS**

Cardiac arrhythmias are frequently present in patients with CHF and are regarded as a sign of impaired left ventricular function. Atrial fibrillation is the most prevalent cardiac arrhythmia in patients with CHF. Nevertheless, its prognostic significance is controversial. There have been studies in which atrial fibrillation did not increase morbidity and mortality as well as studies in which atrial fibrillation was a marker for an increased mortality risk.\textsuperscript{27,28} Ghali et al reported that cardiac arrhythmias, particularly atrial fibrillation, were present in 29% of patients studied and were considered to be directly responsible for relapse of CHF in 78% of patients.\textsuperscript{3} Cardioversion of chronic atrial fibrillation to sinus rhythm in patients with NYHA functional class I or II significantly increased cardiac output during exercise, maximum oxygen uptake, and maximal tolerated workload.\textsuperscript{29} Successful cardioversion in patients with chronic atrial fibrillation and idiopathic dilated cardiomyopathy significantly improved left ventricular ejection fraction from 32% to 53%.\textsuperscript{30} Several studies have reported on patients with severe left ventricular dysfunction and atrial fibrillation with rapid ventricular response.\textsuperscript{31,32} Left ventricular dysfunction in these patients may be completely reversed by controlling ventricular rate or restoring sinus rhythm. The unfavourable haemodynamic consequences of atrial fibrillation compared with those of sinus rhythm suggest that development of this arrhythmia may be a trigger for relapse of CHF.

**MYOCARDIAL ISCHAEMIA**

The detrimental effects of myocardial ischaemia on ventricular function have been well documented.\textsuperscript{33} The main cause of progressive myocardial failure is postulated as subendocardial ischaemia, even in patients with non-ischaemic CHF.\textsuperscript{34} Silent or symptomatic myocardial ischaemia can also be identified as part of the pathway relating other potential precipitating factors, such as psychological stress, smoking, cardiac arrhythmias, and hypertension, to relapses of CHF.\textsuperscript{35,36} Impairment of systolic and diastolic ventricular function persists from hours to days after transient myocardial ischaemia.\textsuperscript{37} Hibernating myocardium is a widely accepted concept in modern cardiology, defined as a state of persistently impaired myocardial and left ventricular function at rest because of reduced coronary blood flow.\textsuperscript{38} Hibernating myocardium can be considered as a myocardial adaptation to reduced coronary blood flow, to prevent irreversible myocardial damage. The significant improvement of left ventricular function after coronary revascularisation is mainly based on this principle.\textsuperscript{39} Although the exact frequency of hibernating myocardium is not known, Carlson et al reported hibernating myocardium in 75% of patients with unstable angina pectoris and in 25% of patients with stable angina pectoris.\textsuperscript{40} Abolition of myocardial hibernation can improve left ventricular function.\textsuperscript{39} Therefore, prevention of myocardial ischaemia may contribute to the maintenance of haemodynamic homeostasis in patients with CHF.

**LACK OF TREATMENT COMPLIANCE**

Non-compliance to medication and diet has repeatedly been identified as a frequent precipitating factor for admission to hospital for decompensated heart failure.\textsuperscript{41,42} Moreover, several studies have reported approximately 50%
Prevention of relapse in patients with CHF
non-compliance with long term medication
regimens. This may represent an important
impediment to effective treatment of CHF.
Interestingly, physicians’ personal characteris-
tics and characteristics of their practices also
influence patients’ adherence to medical
treatments. Therefore, physicians’ personal characteris-
tics may contribute to the prevention of relapse in patients with CHF.
Non-compliance deserves major attention
from health professionals, as it may offer an
opportunity to make a significant contribution
to preventing relapse in patients with CHF.

INAPPROPRIATE MEDICAL TREATMENT
Iatrogenic factors responsible for relapses of CHF were identified by Ghali et al in 21% of
relapses and by Opaschi et al in 10% of
relapses. The most important causes of
iatrogenic CHF are usually inappropriate
medication and excessive intravenous fluid
administration. Although not discussed in
detail here, several categories of drugs, such as
non-steroidal anti-inflammatory drugs, β
blockers, and antiarrhythmics, may affect
cardiovascular homeostasis, especially in
patients with pre-existing left ventricular impair-
ment. Rich et al prospectively studied the
occurrence of iatrogenic CHF in 401 patients
hospitalised for CHF. CHF was considered
iatrogenic in 28 (7%) patients. As a result of the
inability of the researchers to reliably assess
causality between suspected inadequate medi-
cation and the onset of CHF, most instances of
iatrogenic CHF were attributed to excessive
intravenous fluid administration. Therefore,
the importance of inappropriate medication,
such as withdrawal of ACE inhibitors, seems to
have been underestimated in this study.

Patients with CHF deserve optimal treat-
ment and investigation. However, some studies
have reported flaws in the management of
CHF. Clarke et al carried out a retrospective
study in six general practices of 505 patients
given loop diuretics. Seventy four per cent of
281 patients who fulfilled diagnostic criteria
for CHF were referred to hospital, but only one
third had echocardiography. Furthermore, 234
of 281 patients who fulfilled diagnostic criteria
for CHF were not treated with ACE inhibitors.
Among them were 26 patients with docu-
mented evidence of left ventricular impair-
ment. These findings strongly suggest short-
comings in the diagnosis and treatment of
CHF, but lack of information on the severity of
CHF in this study makes it difficult to draw
definite conclusions. Hillis et al reported in
a review of the case notes of 343 patients discharged from hospital with a diagnosis of
CHF that only 40% of patients received ACE
inhibitors. Of patients with NYHA class III
and IV CHF, only 50% were treated with ACE
inhibitors at the time of discharge from hospit-
al. Although retrospective studies may have
methodological limitations, they clearly high-
light some aspects of the management of CHF
that need to be improved.

Prevention of iatrogenic CHF should be a
major issue in optimising medical treatment
in these patients.

Conclusions
Relapse in patients with CHF is the result of
deteriorating underlying cardiac disease. Clin-
ical practice and observational studies have
however, shown that precipitating factors can
be identified in many patients with increased
symptoms of CHF. These precipitating factors
may have contributed to or even induced
symptoms of CHF. Few studies have investi-
gated these precipitating factors despite their
presence in relapse of CHF. Suboptimal medi-
tical treatment and poor patient compliance in
particular deserve more attention, as these fac-
tors can be considered as potentially prevent-
able determinants of relapse of CHF.

Most of the discussed factors are common in
daily practice, but little is known about their
influence on cardiac performance in patients
with CHF under everyday circumstances.
Most studies on the haemodynamic effects of
smoking, alcohol, or psychological stress have
been laboratory experiments. Such findings do
not always reflect the effects in clinical practice.
Despite these limitations the negative haemo-
dynamic effects of most precipitating factors
discussed here are sufficient for them to be
considered as unfavourable. Therefore, the
presence of potential precipitating factors as
listed in the table 1 should be routinely evalu-
ated in patients presenting with CHF. Elimina-
tion of these precipitating factors, if possible,
may contribute to the prevention of relapse in
patients with CHF.

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