Title: Adherence to ACE inhibitors and illness beliefs in older heart failure patients.

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Abstract

**Objective:** Patient beliefs about heart failure may be important determinants of adherence. This study assessed levels of adherence to angiotensin-converting enzyme inhibitors (ACEI) and examined whether beliefs about heart failure were associated with adherence to ACEI.

**Method:** Fifty-eight patients with chronic stable heart failure (80.22 years SD: ±4.62, 43% female) were recruited from outpatient clinics in Dundee Scotland. The Illness Perception Questionnaire-Revised (IPQ-R) was used to assess beliefs about heart failure. Adherence to ACEI was assessed by measuring serum levels of angiotensin-converting enzyme (sACE).

**Results:** Adherence to ACEI (defined as sACE <5 µ/l) was 72%. Beliefs about the time-line of heart failure and the consequences of heart failure accounted for 19% of the variability in adherence to ACE inhibitors in this sample. HF patients who believed that their illness had a more chronic (longer term) time frame and had beliefs about greater consequences of heart failure on their lives were less likely to adhere to ACEI.

**Conclusion:** Adherence to ACEI is sub-optimal. Beliefs about heart failure appear to be associated with objectively measured adherence to ACEI. Future studies should attempt to identify beliefs that consistently predict adherence and examine whether modifying these beliefs can increase adherence to heart failure medications.
Introduction

Adherence to medical regimens is sub-optimal in heart failure populations, particularly amongst older people (1). As the medical management of heart failure has pharmacotherapy as its mainstay, this is of considerable clinical importance (2). Estimates for non-adherence to medication in elderly heart failure patients have varied from 10% to 99%, with older patients reporting the lowest adherence rates (3).

One objective method of assessing patient adherence involves assessing levels of adherence to specific drugs in serum assays (4). The measurement of serum ACE in heart failure patients can indicate whether heart failure patients are adhering to ACE inhibitor medication (5). Serum ACE has 86% sensitivity and 95% specificity and an area under the curve (AUC) of the Receiver Operating Characteristic (ROC) curve of 0.9 at identifying nonadherence (4). Previous research has indicated that over a third of heart failure patients are less than 85% adherent to their medication (6).

There have been systematic attempts to understand the modifiable determinants of adherence (7-9). As adherence is a behavioral phenomenon, psychological theories of self-regulation have made a significant contribution to this body of work. One area has focused on individual beliefs about illness and treatment (10-14). This work has found that beliefs about illness and treatment are associated with patient self-management in a range of conditions including heart failure and coronary heart disease (15, 16). For example beliefs relating to the symptoms that individuals associate with their illness (illness identity), beliefs relating to the perceived duration of the illness (time-line) and beliefs regarding the curability or controllability of the illness (personal and treatment control) are hypothesized to predict behavioural and emotional adaptation to illness (14). This approach focusing on how these beliefs about illness influence adaptation to illness
is referred to as self-regulation i.e. how people direct their thoughts, feelings, and actions, so that strivings to obtain goals are effective.

In previous studies measures of illness perception such as the illness perception questionnaire (IPQ) (14) and the revised IPQ, the IPQ-R (17), have been found to be reliable (internally consistent and have adequate test-retest reliability) and valid (concurrent, discriminant and predictive validity) in asthma, myocardial infarction, diabetes, rheumatoid arthritis, multiple sclerosis, HIV, chronic fatigue and pain patient groups. This early work establishing the psychometric properties of the IPQ and the IPQ-R has been further advanced by meta-analytic studies that have systematically reviewed studies using these measures (18). These studies provide evidence for theoretically predictable relations between beliefs about illness and self-management behaviour in individuals with chronic illness.

In this study we aimed to measure heart failure patient beliefs about their illness using a measure systematically developed from self-regulation theory. Patient adherence to ACEI was measured using serum analysis of ACE. We aimed to answer the following question: Are patient beliefs about heart failure associated with objectively measured serum ACE in older heart failure patients?

**Methods**

*Design and setting*

This was a cross-sectional study of older patients with chronic stable heart failure that were recruited into an exercise intervention trial that has been reported elsewhere (19-21). All data presented in this paper were collected pre-randomisation at baseline.

*Participants*
Heart failure patients were recruited from the local specialist heart failure clinic and from the local Medicine for the Elderly clinics in Dundee Scotland. Patients aged \( \geq 70 \) years with a clinical diagnosis of chronic heart failure according to European Society of Cardiology guidelines, New York Heart Association class II or III symptoms, and evidence of left ventricular systolic dysfunction on echocardiography, contrast ventriculography, or radionuclide ventriculography were eligible to participate. Exclusion criteria were patients with uncontrolled atrial fibrillation, significant aortic stenosis, sustained ventricular tachycardia, recent myocardial infarction, inability to walk without human assistance, abbreviated mental test score \( >6 \) of 10, or those currently undergoing physiotherapy or rehabilitation. The study was approved by the Tayside Committee on Medical Research Ethics. Written informed consent was obtained from participants.

**Measures**

Background socio-demographic and clinical data was collected from medical notes and interview at outpatient clinics. Blood was drawn by a research nurse or clinical research fellow. Serum ACE activity was assayed using serum from clotted blood. The change in absorbance at 340nm due to hydrolysis of furylacrylolyphenylalanylglucylglycine was measured using a Roche MIRA analyzer (Roche Diagnostic systems, Welwyn Garden City, Herts UK). Serum ACE activity of \(<5\)U/L was taken as denoting adherence to ACE inhibitor therapy; a level previously validated by the authors (22).

The illness perception questionnaire-revised (IPQ-R) (17) was used to assess patient beliefs about their illness. This measure has been systematically developed and refined in a range of clinical conditions and is based on a psychological theory of self-regulation (14, 17). Beliefs regarding the symptoms associated with the illness (identity),
the perceived temporality (timeline), the perceived consequences of the illness (consequences), the perceived personal control over the illness (personal control), the perceived efficacy or outcome of medical treatment (treatment control), the perceived coherence of the condition (illness coherence) and emotional beliefs relating to the illness were assessed using the IPQ-R (emotional reps).

Statistical Analysis

Logistic regression was used to assess the % variability in adherence to ACEI accounted for by the sub-scales of the IPQ-R.

Results

Patient characteristics

Two hundred and twenty nine patients were approached at the two outpatient clinics. Patients that chose not to participate (n= 147) had a mean age was 79.9 years (SD: 6.0) and 70/147 (48%) were male. Eighty-one patients were enrolled in an exercise study (20). Fifty-eight (72%) of these patients were prescribed ACEI and these comprised the sample for the present study. Table 1 shows the demographic and clinical characteristics of the sample.

| Insert table 1 |

Adherence to ACEI:

Analysis of serum levels of ACE showed that 42 out of the 58 patients in the study had serum ACE levels that were < 5 µ/l suggesting that adherence to ACEI in this sample was 72%. Comparing adherent and non-adherent groups, they were of a similar mean age
(t(56) = -.60, p = .55) and there were no significant differences in gender ($\chi^2(1) = 1.56, p = .21$) or NYHA functional classification ($\chi^2(1) = .67, p = .41$).

**Illness perceptions as predictors of adherence to ACEI**

Figure 1 shows the comparisons of the mean scores in illness beliefs between the ACEI adherent and non-adherent groups. Higher scores relate to stronger beliefs that the illness will last a long time as opposed to a short time, that the illness will be cyclical, that the illness will have greater consequences, that you have greater personal control over the illness, that treatments will be effective in managing illness, that the illness makes sense, that the illness makes you emotionally distressed and that the illness has more symptoms. Logistic regression analysis showed that Timeline-acute/chronic ($\beta = -.92, SE = .48$, Wald = 3.65, Odds Ratio = 0.40, p = .06) marginally and Consequences ($\beta = -1.02, SE = .51$, Wald = 3.92, Odds Ratio = 0.36, p = .05) significantly predicted medication-adherence separately, explaining 11% and 10% of the variance, respectively. Further details are provided in table 2 which provides the univariate and multivariate logistic regression analysis predicting adherence to ACEI.

> Insert table 2

When both variables were entered into multivariate analysis, both Timeline-acute/chronic ($\beta = -.92, SE = .51$, Wald = 3.26, Odds Ratio = 0.40, p = .07) and Consequences ($\beta = -.97, SE = .52$, Wald = 3.47, Odds Ratio = 0.38, p = .06) were found to be marginal predictors of medication-adherence, and explained 19% of the variance. The results indicate that with every increase of 1 in Timeline-acute/chronic or Consequences score, participants were 2.5 times or 2.6 times less likely to be adherent to ACEI medication.
respectively. That is, participants who believed that they had a more chronic timeline of illness or perceived more Consequences of illness were less likely to adhere to ACEI.

**Discussion**

Certain patient beliefs about heart failure were associated with objectively measured serum ACE in older heart failure patients. Heart failure patients who believed that their illness would last a long time (i.e. a chronic timeline, example questionnaire items: *My illness is likely to be permanent rather than temporary, I expect to have this illness for the rest of my life*) and had more consequences (example questionnaire items: *My illness has major consequences on my life, My illness causes difficulties for those who are close to me*) were less likely to adhere to ACEI. Adherence to ACEI was 72% in this sample of older heart failure patients. Patient beliefs about the duration of heart failure as an illness and the consequences of this condition may be important determinants of medication adherence that warrant attention in health-care provider and patient interactions concerning medication regimens. It is possible that patients may intentionally decide to stop or intermittently adhere to ACEI if they view ACEI as unnecessary in managing an illness that is permanent and has serious consequences (12).

A larger previous study in older heart failure patients found that overall adherence to physicians recommendations was 72% (23). The similarity of this estimate with the present study is striking, however the previous study found that medication adherence of older heart failure patients was almost 99%. This estimate was based on self-report question asking about all medications simultaneously. This level of adherence is not supported by the present data on adherence to ACEI and other studies that have used more objective measures of adherence (1). It is likely that self-reports about general
medication adherence may be particularly prone to error, perhaps due to social desirability or recall biases of study participants.

There are also considerable data showing that depression (9) and measures of social support (8, 24) are associated with non-adherence to medication and other aspects of self-care and secondary prevention. It is possible that the illness beliefs associated with non-adherence in this study were more typical of those with higher levels of depression, however emotional beliefs about the illness such as feeling depressed about the illness were not different in the adherent and non-adherent groups in the present study and there were no differences in adherence between married and unmarried patients. It is possible that depressed and non-depressed patients and those with high and low levels of social support have a different set of beliefs about illness and treatment, which may in turn determine adherence. Social support in the form of informal care may be particularly important for understanding the self-management of heart failure (25) and beliefs about illness and treatment may be shaped by those in the patient’s immediate social environment. Future studies could examine the mediating role of illness and treatment beliefs in explaining the associations between depression and social support and adherence to heart failure medications. The evidence showing that beliefs about illness can be changed to improve return to work and angina symptoms in coronary heart disease patients (16) suggests that beliefs about illness may be important targets for intervention work to improve adherence (26) and subsequent health outcomes in heart failure patients. Future work should first however, identify illness beliefs that consistently predict adherence in heart failure patients.

There are a number of important limitations to the present study which should be acknowledged. The data set did not provide the statistical power to permit the use of large
multivariate models with multiple adjustments for other known predictors of medication adherence. Further data on patient beliefs about heart failure and multiple measures of adherence (both self-report and objective measures) are required from larger samples of heart failure patients. The study did not include a measure of beliefs about medications (13), which may be more proximal predictors of medication adherence than beliefs about the illness. Including beliefs about medications in future studies of heart failure patients would also allow investigators to observe how beliefs about illness and beliefs about medications interact to determine adherence behaviour. It is also possible that adherence behaviour and beliefs about the illness reciprocally determine each other making the interpretation of cross-sectional associations problematic; however this is an acknowledged difficulty of all observational studies of psychological factors and adherence behaviour. On the other hand there are clear strengths to the present study in terms of the objective measurement of adherence to ACEI, the sample of older heart failure patients (mean age 80.2 years SD: ±4.6) who are often underrepresented in clinical research despite being most at risk (27) and the use of systematically developed psychological theory and measurement, which can provide a framework around which a cumulative body of findings on patients beliefs about heart failure and its treatment and adherence behaviour in heart failure can emerge. Such a body of knowledge is necessary to develop interventions that target heart failure beliefs to enhance adherence behaviour.

**Conclusion**

The present study adds to evidence suggesting that adherence to medication is sub-optimal in older heart failure patients and that adherence is associated with beliefs about the condition. Further research using the measures included in this study will confirm which beliefs consistently predict medication adherence in heart failure patients. The next
generation of work in this area will establish whether changing beliefs about heart failure and treatment of the condition can improve adherence to medication and medical advice and consequently reduce morbidity and mortality from heart failure.
Reference List


5. Struthers AD, Anderson G, MacFadyen RJ, Fraser C, MacDonald TM. Nonadherence with ACE inhibitor treatment is common in heart failure and can be detected by routine serum ACE activity assays *Heart* 1999;82:584-588.

6. Struthers AD, Anderson G, MacFadyen RJ, Fraser C, MacDonald TM. Nonadherence with ACE inhibitors is common and can be detected in clinical practice by routine serum ACE activity. *Congest Heart Fail* 2001;7:43-46.


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caregiver burden and emotional distress. *Eur J Cardiovasc Prev Rehabil*


Table 1
Demographic and clinical characteristics of the study population (n=58).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years ± SD)</td>
<td>80.2 ± 4.6 (58)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>43% (25)</td>
</tr>
<tr>
<td>Married</td>
<td>38% (22)</td>
</tr>
<tr>
<td>Mean school leaving age (SD)</td>
<td>14.3 (± 1.27)</td>
</tr>
<tr>
<td>Left Ventricular Ejection Fraction</td>
<td></td>
</tr>
<tr>
<td>Mild/ Moderate/ Severe.</td>
<td>26% (15) / 33% (19) / 41% (24).</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>II / III</td>
<td>59% (34) / 41% (24)</td>
</tr>
<tr>
<td>Ischemic aetiology</td>
<td></td>
</tr>
<tr>
<td></td>
<td>74% (43)</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>17% (10)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10% (6)</td>
</tr>
<tr>
<td>COPD</td>
<td>19% (11)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>60% (35)</td>
</tr>
<tr>
<td>Angina Pectoris</td>
<td>35% (20)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>16% (9)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>17% (10)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>100% (58)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>24% (14)</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>33% (19)</td>
</tr>
<tr>
<td></td>
<td>Percentage (%) (Number)</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Digoxin</td>
<td>28% (16)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>86% (50)</td>
</tr>
</tbody>
</table>

Six minute walk distance (Metres ± SD) 257 ± 111

BMI (kg/m²) (mean ± SD) 26.8 ± 4.6
Table 2 Logistic regression predicting adherence to ACEI (1= adherent, 0 =non-adherent).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate</th>
<th></th>
<th>Multivariate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Time-line acute</td>
<td>0.40</td>
<td>0.15-1.00</td>
<td>0.40</td>
<td>0.15-1.08</td>
</tr>
<tr>
<td>Time-line cyclical</td>
<td>0.87</td>
<td>0.38-2.02</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Consequences</td>
<td>0.36</td>
<td>0.12-0.99</td>
<td>0.38</td>
<td>0.14-1.05</td>
</tr>
<tr>
<td>Personal control</td>
<td>1.36</td>
<td>0.46-4.02</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Treatment control</td>
<td>2.19</td>
<td>0.48-9.99</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Illness coherence</td>
<td>0.95</td>
<td>0.45-2.00</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Emotional representations</td>
<td>1.05</td>
<td>0.37-2.98</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Identity</td>
<td>0.94</td>
<td>0.75-1.20</td>
<td>--------------</td>
<td>--------------</td>
</tr>
</tbody>
</table>
Figure 1. The comparison of the mean scores of illness beliefs between ACEI adherent (n=42) and non-adherent groups (n=16). Bars represent stand error of the mean.
Example items from the IPQ-R questionnaire.

**Time-line acute/chronic (TL-acute, α = 0.85):** My illness will last a short time.

**Time-line cyclical (TL-cyclical, α = 0.78):** The symptoms of my illness change a great deal from day to day.

**Consequences (Conseq, α = 0.73):** My illness has major consequences on my life.

**Personal control (α = 0.66):** What I do can determine whether my illness gets better or worse.

**Treatment control (α = 0.57):** My treatment will be effective in curing my illness.

**Illness coherence (0.81):** My illness doesn’t make any sense to me.

**Emotional representations (reps, α =0.76):** When I think about my illness I get upset.

**Identity (α = not applicable):** Breathlessness/Fatigue/ etc… is related to my illness.

Range for all scales 1-5, except Identity: 0-14. 
(α = Cronbach’s alpha)