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DOI: 10.1007/s12160-015-9695-2

Document Version Peer reviewed version

Link to publication record in King's Research Portal

Citation for published version (APA):

Crawshaw, J., Rimington, H., Weinman, J., & Chilcot, J. (2015). Illness Perception Profiles and Their Association with 10-Year Survival Following Cardiac Valve Replacement. *Annals of Behavioural Medicine*, *49*(5), 769-775. https://doi.org/10.1007/s12160-015-9695-2

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PREPUBLICATION FINAL COPY – <u>uncorrected proof</u> <u>Annals of behavioral medicine</u> Brief Report

Illness perception profiles and their association with 10-year

survival following cardiac valve replacement

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Keywords: illness perceptions; cardiac surgery; valve replacement; cluster analysis; mortality; illness schema

Conflict of interest

Jake Crawshaw, Helen Rimington, John Weinman and Joseph Chilcot declare no conflict of interest.

Acknowledgements:

Dr Sebastian Kohlmann conducted the original cluster analysis. We thank him for additional guidance in the preparation of this manuscript.

<u>Abstract</u>

Objective: To examine whether profiles of illness perceptions are associated with 10-year survival following cardiac valve replacement surgery.

Methods: Illness perceptions were evaluated in 204 cardiac patients awaiting first time valve replacement and again one-year post-operatively using cluster analysis. All-cause mortality was recorded over a 10-year period. At one-year, 136 patients were grouped into one of four profiles (stable positive; stable negative; changed from positive to negative; changed from negative to positive).

Results: The median follow-up was 3063 days (78 deaths). After controlling for clinical covariates, including markers of function, patients who changed illness perceptions from positive to negative beliefs one year post-surgery had an increased mortality risk (HR = 3.2, 95% CI: 1.2 - 8.3, p = .02) compared to patients who held positive stable perceptions.

Conclusions: Following cardiac valve replacement, developing negative illness perceptions over the first post-operative year predicts long-term mortality. Early screening and intervention to alter this pattern of beliefs may be beneficial.

Introduction

In developed countries most heart valve disease is caused by age-related degenerative changes, or by damage from infection or abnormalities in the adjacent heart muscle. Heart valve replacement is major surgery involving the use of heart-lung bypass equipment and requires postoperative intensive care. There are two types of replacement valve: biological valves consisting of human or animal tissue and mechanical valves, made of pyrolitic carbon. Patients are usually encouraged to attend a postoperative cardiac rehabilitation programme and to attend regular outpatient monitoring of their replacement valve. Studies exploring mortality risk following valve replacement surgery have predominantly focused on clinical factors (1). However, there is a growing body of research suggesting that psychological factors, specifically perceptions patients' have about their illness, may play a part in how cardiac patients adjust and recover following treatment (2, 3).

According to Leventhal's Self Regulation Model (4, 5) patients develop personal beliefs about their illness, which regulate emotional and behavioural responses to allow them to cope and adjust to the condition. Leventhal describes five key illness perceptions: (1) *identity*, how symptoms are experienced and attributed to the illness; (2) *cause*, beliefs about causes of the illness; (3) *timeline*, beliefs about the duration of the illness; (4) *consequences*, beliefs about the likely impact of the illness on the patients life, and, (5) *control/cure*, beliefs regarding the controllability/curability of the illness. A feature of Leventhal's model regards the dynamic nature of illness perceptions, which can alter as a product of cognitive and emotional reappraisal, allowing patients to regulate how they cope with their condition. The impact of illness perceptions has been studied mainly in the context of psychosocial outcomes such as coping and adjustment (6). For example, among patients with cardiovascular disease, illness perceptions have been found to mediate the association

between disease severity and various outcomes including depression (7) and health satisfaction (8). Rimington et al (9) found that physical performance (6 minute walk test) one year following cardiac valve replacement was predicted by preoperative levels of mood and negative illness perceptions.

Studies have also shown that perceptions regarding treatment control (e.g. "my treatment controls my condition") predict survival in end-stage kidney disease patients (10, 11). However, the influence of illness perceptions upon survival in cardiac patients is not yet known.

According to the Self Regulation Model, individual illness perceptions are not held in isolation but link with each other to form a patient's illness schema (illness representations) as operationalized by Clatworthy et al (12). A recent study found that Rheumatoid Arthritis (RA) patients' illness perceptions cluster to form either positive or negative schemas (i.e. representations) of illness (13). Negative representations of RA predicted greater levels of pain, functional disability and distress over time (13). There is also growing evidence that profiling patients according to their pattern of illness perceptions may be useful when designing interventions targeting subgroups of patients who hold stable negative illness perceptions (14)

Kohlmann et al (15) investigated the role of illness perceptions in predicting postoperative health status following cardiac valve replacement surgery. Illness perceptions were measured pre-surgery and at one year follow up, and at each stage, patients were categorised into either a positive or negative illness perception profile. By one year, some patients had changed their illness beliefs from positive to negative and vice versa. Patients that maintained a negative illness profile reported lower health-related quality of life compared to patients who had maintained a positive illness profile or had changed from a preoperative negative profile to a positive profile at follow up. The current study extends the work of Kohlmann et al by following up the patient cohort over a 10-year period in order to evaluate the association between illness perception profiles and all-cause mortality following valve replacement.

The following hypotheses were tested, after controlling for clinical covariates: (1) Patients with negative pre-surgical patterns of perceptions will show an increased mortality risk compared to those with positive perceptions.

(2) At one-year, patients with a negative illness perception profile will have a greater mortality risk over the study follow-up compared to those who held positive perceptions.

3) Patients with stable negative illness perceptions (i.e. negative at both baseline and 1-year) will have a greater mortality risk compared to those with stable positive perceptions.

Methods

Sample

Originally studied by Rimington et al (9) and then by Kohlmann et al (15), 225 patients from a UK cardiothoracic centre was recruited of which 204 were used for cluster analysis evaluated here. Patients received either bioprosthetic (65%) or mechanical valves and a proportion (42%) also received coronary arterial bypass graft (CABG) surgery. A summary of baseline patient characteristics is shown in Table 1 (n=204).

At one-year follow up, 204 patients remained as part of the study (15 had died, 4 withdrew consent and 2 were lost to follow up), of which 145 have data suitable for cluster analysis 1-year post operatively. Across baseline and follow-up time points, 136 had completed illness perception data (i.e. matched repeated data). Given that cluster analysis requires complete cases, analysis was conducted in this sample of 136 patients, which had illness perception data at both baseline and at 1-year follow-up. Patients not included in the cluster analysis at both time points (baseline and 1-year) did not differ significantly to those included with regards to baseline ejection fraction, New York Heart Association (NYHA) class, pulmonary arterial pressure, six-minute walk test performance and general distress (p-

values all \geq .05). There was no association between inclusion in the cluster analysis (or not) with gender. However those included in the cluster analysis had significantly lower EuroSCORES (mean difference=1.6, s.e=4.3 p<.01), Parsonnet scores (mean difference=4.9, s.e=1.2, p<.01) and were younger (mean difference=6.2, s.e=1.6, p<.01) compared to not included.

Clinical Measures

Preoperative risk assessment was measured using both the EuroSCORE and the Parsonnet screening tools. To indicate heart function, patients underwent a transthoracic echocardiogram, which measured left ventricular ejection fraction and pulmonary arterial pressure (PAP). The NYHA class, and functional performance via a six-minute walk test (6MWT) were used to determined health status, which was evaluated at baseline and also at 1-year follow-up. Attendance at cardiac rehabilitation (yes/no) offered at six weeks post-surgery as part of routine clinical care was also recorded. Attendance was recorded as "yes" if they attended at least one session. All attenders received an exercise homework sheet, although adherence to this was not recorded.

Psychological Measures

Illness Perceptions: Illness perceptions were measured using the Illness Perception Questionnaire – Revised (IPQ-R) (16). The IPQ-R measures several illness beliefs: *identity* (number of symptoms attributed to the condition), *consequences* (e.g. "my condition has major consequences on my life", α =.69^a), *emotional representations* (e.g. "I get depressed when I think about my condition" α =.86), *timeline* (e.g. "my condition will last for a long time", α =.85), *cyclical timeline* (e.g. "my symptoms come and go in cycles", α =.85), *illness coherence* (e.g. "my condition is a mystery to me", α =.85), *personal control* (e.g. "I have the power to influence my condition", α =.69) and *treatment control* (e.g. "my treatment can

^a Cronbach's alpha calculated from the IPQ-R data reported here

control my condition", α =.60). Following the previously reported hierarchical cluster analysis [see; (15)], two illness perception clusters (positive and negative cluster) were used in the present study. Cluster selection was used using standard criteria see;(17, 18). Data from all subscales of the IPQ-R (identity, timeline, consequence, personal control, treatment control, coherence, timeline cyclical, emotional representations) at pre-surgery stage were included in the analysis. As a cluster method, Ward's minimum variance with Euclidean distance was chosen as this method is recommended to generate classification(17). Agglomeration schedule and dendogram were examined to determine the appropriate number of clusters. To test the reliability of the cluster solution a k-means clustering was performed as well as a hierarchical analysis with a randomly divided sample. To examine the stability of patterns over time and to define illness perception profiles, independent cluster analyses with illness perceptions assessed before and one year after surgery were calculated

The two-cluster solution revealed that pre-operative patients were categorised into either a positive (n = 120) or negative (n = 84) illness perception profile. Compared to the negative profile group, patients categorised in the positive illness perception profile reported less health concerns, attributed less symptoms to their illness, feared fewer consequences, perceived their illness as predictable, had greater controllability and a better overall understanding of their illness.

Mood Assessment: Mood was measured using the 14-item Hospital Anxiety and Depression Scale (HADS) (19). Since the HADS has been shown to poorly separate depression and anxiety (20) a total score was used with higher scores indicating greater general psychological distress (possible score range 0-42). Cronbach's α for the HADS total score used here was .74.

Study Outcome

All-cause mortality was the outcome measure over the 10-year study period (Jan 2003 – Mar 2013). Date of surgery was considered time-zero for analysis whilst receiving details of patients' survival status signified the end-of-study. Right-censoring was employed meaning cases were censored if patients were alive at the end-of-study or had been lost to follow up.

Statistical Analysis

Profiles identified from hierarchical cluster analysis, conducted by Kohlmann et al (15) were used here. This analysis was conducted on the baseline and 1 year follow-up data, to identify the two clusters at both time points, thus allowing four groups of patients to be defined; 1) negative IP profile at baseline and at 1 year, 2) positive IP profile at baseline and at 1 year, 3) negative IP profile at baseline, but a positive profile at 1 year, and 4) positive IP profile at baseline, but a negative profile at 1 year. Univariate associations between preoperative variables and survival were measured using Kaplan-Meier tests (with log-rank tests) and Cox regression. In the survival models, the stable positive illness perception cluster was used as the reference category. Data was analysed using IMB SPSS version 20.

Results

Description of survival data

The median follow up time was 3063 days (interquartile range 868 days). At the end-of-study, there were a total of 78 deaths from the 204 patients with illness perception data at baseline (38.2%). Of the 136 patients who had illness perception profiles available at both baseline and 1 year postoperative, there were 37 deaths (27.2%).

Illness Perception Profiles

Pre-surgical Baseline (n=204): Patients in the positive illness perception profile group were older (mean difference=4.6, s.e=1.7, t(202) = -2.8, p = 0.006), walked further (mean difference=40.4, s.e=20.2, t(188) = -2.0, p = 0.048) and were more likely to be male

 $(\chi^2(1, N = 204) = 4.2, p = 0.042)$ compared to patients in the negative profile group. Patients in the negative illness perception profile group had higher HADS total (mean difference=6.1 s.e=1.0, t(202) = 6.0, p = 0.001) compared to those in the positive illness perception group. The illness perception profile groups did not differ with regards to EuroSCORE (t[202]=-1.0, p=.32), ejection fraction (t[202]=-1.2, p=.24) and parsonnet scores (t[202]=1.4, p=.17).

Profiles one-year post-surgery (n=136): A proportion of patients (n = 48, 35.6%) had changed illness perception profile. The patients were categorised into one of four groups (stable positive, n = 54; stable negative, n = 34; change from positive to negative, n = 23; change from negative to positive, n = 25). In the positive to negative cluster, timeline (illness chronicity) perceptions significantly increased over the 1-year (mean difference 6.1, s.e.=1.5, p<.01), whereas personal control perceptions significantly reduced (mean difference -2.7, s.e.=1.0, p=.02). In the negative to positive cluster, cyclical timeline (mean difference -3.8, s.e.=.50, p<.01), perceived consequences (mean difference -5.0, s.e.=.70, p<.01), illness identity (mean difference -3.4, s.e.=.60, p<.01) and negative emotions (mean difference -4.8, s.e.=.90, p<.01) significantly reduced over the 1-year, with both personal (mean difference 1.72, s.e.=.81, p=.04) and treatment control (mean difference 2.0, s.e.=.52, p<.01) increasing over time.

There were significant differences between the four illness perception profiles groups with regards to age (F(3,132)=2.8, p=.04), gender ($\chi^2(1, N = 136) = 7.9$, p = 0.047), baseline general distress (F(3, 132) = 10.0, p = 0.001), baseline 6MWT performance (F(3, 120) = 3.9, p = 0.11) and baseline NYHA classification (F(3, 132) = 3.8, p = 0.01), (see table 2 for descriptive statistics); differences which also existed at 1-year. Patients' baseline EuroSCORE, parsonnet score, and ejection fraction did not differ between the four clusters.

Univariate Survival analysis

Kaplan-Meier analysis revealed that there were no significant differences in risk of mortality between positive and negative illness perception profiles at baseline, χ^2 (1, N = 204) = 3.0, p = 0.081, or at one-year follow up, χ^2 (1, N = 136) = 2.7, p = 0.103.

When patients were categorised into one of the four IP profiles clusters, group membership had a univariate association with survival (χ^2 (3, N = 136) = 9.4, p = 0.025, figure 1). Table 1 shows that age, valve type, EuroSCORE, Parsonnet, PAP, ejection fraction, 6MWT performance, NYHA classification and rehabilitation attendance also had univariate associations with survival (using Kaplan-Meier or Cox models). All of these significant variables were used as covariates in subsequent adjusted survival models.

Adjusted Survival analysis

In adjusted Cox survival models that controlled for age, valve type, baseline NYHA category, 6MWT, ejection fraction, EuroSCORE, Parsonnet, PAP and general distress scores, patients whose illness perceptions changed from positive to negative were found to have a 3.2 times increased mortality risk (HR = 3.2, 95% CI: 1.2 - 8.3, p = .02) compared to the stable positive group. None of the other illness perception profile groups predicted survival. Since, a change in illness perceptions from positive to negative beliefs may reflect worsening physical health over time and whether patients attended rehabilitation, a second model was run which adjusted for age and the following prospective factors; cardiac rehabilitation attendance, changes in NYHA score (Δ NYHA), 6MWT (Δ 6MWT), and general distress (Δ HADS total score) over 1-year. The results remained largely unchanged with those in the profile group who changed from positive to negative illness perceptions having a higher mortality risk (HR = 3.0, 95% CI: 1.1 - 7.8, p = .02) compared to those with stable positive perceptions.

Discussion

The aim of this study was to determine whether illness perceptions profiles and their stability over 1 year post-surgery, predict long-term mortality following cardiac valve replacement. Our hypothesis that negative perceptions held before surgery, at 1 year, or at both time points would be associated with mortality was not supported. Rather we demonstrated that a change in illness perceptions post surgery from positive to negative predicted poor survival over a 10-year period. Changing from positive to negative illness perceptions predicted approximately a 3.2 times increase in mortality risk compared to patients who held stable positive perceptions, after controlling for numerous factors associated with poor long-term outcomes in valve disease (1). These data support the work of others showing the prognostic utility of illness perceptions (10, 11), albeit these studies investigated individual illness perceptions, not clusters as modelled here. Further, unlike the findings of these past studies, it was the shift in illness perceptions that predicted long-term survival, not baseline perceptions. Interestingly, the illness perception profile that had been previously associated with worse NYHA classification at one year - stable negative, did not show an increased risk of mortality. Further, our findings do not appear to be explained by rehabilitation attendance or changes in functional performance (6MWT) or general distress, since these were controlled for in adjusted survival models. However given the sample size and ability to detect clinical changes overtime, its likely that some of the effect shown is the result of a change in health status. Any health effect is also not likely the solely explanation however, since no attenuation of the effect was observed when controlling for a change in functional status at 1 year. Therefore it appears that developing negative illness perceptions is associated with poor prognosis beyond any changes in health status. Reasons for why it is this change, as opposed to stable negative perceptions, remains speculative and somewhat

surprising. In this group, it was observed that perceived personal control decreased over time, whereas perceptions regarding the chronicity of the condition increased. It is possible that for some, unrealistic perceptions held pre-operatively led to poor self-regulatory control and less motivation to engage in recommended health-related behaviour. However, further work is needed to replicate these findings and elucidate mediators in order to better evaluate the results of the present study.

In sum, the results of this study demonstrate that illness perceptions can be profiled, do change overtime, and predict patient outcome. Screening for negative patterns of illness beliefs may become a useful tool to identify those patients who may be at risk of poor outcomes. Clinical determinants of postoperative outcomes such as heart function cannot be readily changed therefore studying potentially modifiable factors is an area of interest and clinical importance (21). Patients having elective valve replacement surgery are usually on a waiting list for a few weeks, which may be one opportunity to optimise postoperative outcomes by a preoperative intervention designed to challenge potentially maladaptive thoughts and feelings. However, since it is the change in beliefs over the first post-operative year, further research is needed to understand why some patients develop more negative beliefs, and how these impact on their recovery.

This study had several limitations to consider when interpreting our findings. First, the survival models were not adjusted for co-morbidity. Second, all-cause mortality was used as the end-point in this study meaning that specific relationships between predictors and particular causes of death cannot be inferred. A larger sample size with a higher mortality rate would be required to draw further conclusions between certain predictive factors and cardiac-specific causes of death. Third, only patients with complete illness perceptions data sets were included in the cluster analysis and subsequent survival models. As a consequence, some may have been omitted if they did not fully participate at both time points. It must be noted

however, that patients not included in cluster analysis did not appear to have poorer health status in terms of NYHA-class, ejection fraction and 6MWT compared to those included, although those included were younger and had lower EuroSCORES and Parsonnet scores. Further, although we included rehabilitation attendance in the survival models, it was a relatively crude marker that did not account for the level of adherence to the programme, which could have influenced the findings reported here. In terms of sample representativeness, participants in this study were predominantly white English-speaking participants undergoing aortic valve replacement, which limits the generalisability of the reported findings. Furthermore the study did not measure other potentially important factors such as social economic status (SES), which is known to predict outcomes in cardiac patients (22).

Conclusions

We have demonstrated that illness perceptions predict long-term outcomes following valve replacement. Further work is needed to understand which factors are associated with the development of unhelpful perceptions over time. Attempts to alter unhelpful illness beliefs could be an important interventional target and should be the focus of future studies.

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Table 1.

Preoperative (baseline) Demographic and Clinical Variables with Univariate Statistical Calculations

(n=204)

	Univariate survival			
	Descriptive statistics	test statistics ^a		
Variable	(baseline)		p-value	
Mean age \pm SD (range)	67.1 ± 12.1 (26 - 89)	HR = 1.07 (CI: 1.05 – 1.10)	p < 0.001	
Male, n (%)	155 (68.9)	$\chi^2 (1, N = 225) = 0.15$	p = 0.70	
Bioprosthetic replacement, n (%)	146 (64.9)	χ^2 (3, N = 224) = 9.83	p = 0.020	
Mean EuroSCORE ± SD (range)	6.6 ± 3.2 (0 - 19)	HR = 1.19 (CI: 1.13 – 1.26)	p < 0.001	
Mean Parsonnet ± SD (range)	16.3 ± 8.9 (0 - 39)	HR = 1.09 (CI: 1.06 – 1.11)	p < 0.001	
NYHA II, n (%)	131 (58.2)	χ^2 (3, N = 224) = 9.83	p = 0.02	
Combined CABG, n (%)	94 (41.8)	$\chi^2 (1, N = 225) = 0.44$	p = 0.51	
PAP > 30mmHg, n (%)	39 (17.3)	$\chi^2 (1, N = 225) = 17.41$	p < 0.001	
Ejection Fraction ± SD (range)	59.9 ± 14.9 (15 - 85)	HR = 0.97 (CI: 0.96 – 0.99)	p < 0.001	
$6MWT \pm SD$ (range)	298.3 ± 138.5 (8 - 577)	HR = 0.996 (CI: 0.994 – 0.997)	p < 0.001	
Rehabilitation non-attendance n $(\%)^1$	83 (37)	$\chi^2 (1, N = 204) = 5.73$	p = 0.02	

Notes. SD: Standard deviation HR: Hazard ratio CI: Confidence interval (95%) NYHA: New York Heart Association CABG: Coronary arterial bypass graft PAP: Pulmonary artery pressure mmHg: Millimetres of mercury 6MWT: Six-minute walk test ^a Kaplan-Meier with log-rank test or Cox regression

¹Cardiac rehabilitation attendance (yes/no) was recorded six weeks post-surgery

Table 2: Differences between illness perception profiles

	Illness Perception Profile				
	Stable-	Stable-	Positive-	Negative-	
	Positive	negative	negative	positive	
	(n=54)	(n=34)	(n=23)	(n=25)	
Age	66.8 (9.2)	60.2 (13.4)	67.7 (13.4)	63.3 (13.4)	
Gender (female, n)	11 (20%)	14 (41%)	3 (13%)	9 (36%)	
Baseline					
6MWT	358.7 (113)	249.1 (146.3)	296.9 (158.6)	297.8 (155.7)	
NYHA classification	2.0 (.5)	2.4 (.7)	2.0 (.7)	2.1 (.7)	
Distress (HADs total)	9.4 (6.3)	17.5 (9.5)	9.5 (4.4)	14.5 (7.6)	
Follow-up (1-year)					
6MWT	471.4 (79.6)	385.9 (122.1)	422.0 (128.3)	426.7 (117.2)	
NYHA classification	1.4 (.50)	1.9 (.6)	1.7 (.70)	1.5 (.60)	
Distress (HADS total)	5.8 (4.8)	15.0 (9.5)	9.5 (5.7)	9.9 (5.8)	

6MWT: six-minute walk test

NYHA: New York Heart Association

Unless otherwise stated descriptive statistics are means (s.d.), rounded to 1 d.p



Figure 1. Kaplan-Meier survival trajectories for each illness perception profile (p<.05).