

Relationship between depression and non-adherence to anticoagulant therapy after valve replacement

A.S. El-Gatit^{1,2} and M. Haw²

العلاقة بين الاكتئاب وعدم الالتزام بالعلاج بمضادات التخثر عقب جراحة استبدال الصمام
عبد السلام الخشيت، ماركوس هاو

الخلاصة: يعتبر التدبير العلاجي بمضادات التخثر عقب استبدال الصمام ببدائل ميكانيكي أمراً صعباً في البلدان النامية نتيجة عدم التزام المرضى بالعلاج. وقد تم تقييم تأثير الاكتئاب على الالتزام بالعلاج الدوائي وبجدول زيارات العيادات على 62 مريضاً ممن أُجري لهم استبدال الصمامات ببدائل ميكانيكية. فقد تم وصف نظام معالجة للمرضى بإعطاء الوارفارين مرة يومياً، على أن يراجعوا عيادة التدبير العلاجي لمضادات التخثر ثلاث مرات لتعديل الجرعة خلال فترة ثلاثة أسابيع. ووفقاً لمقياس الاكتئاب المعتمد لدى مركز الدراسات الوبائية، فقد كان 22 شخصاً منهم مصاباً بالاكتئاب. وقد وجد أن المرضى غير المكتئبين أكثر التزاماً من المكتئبين، فهناك ترابط عكسي بين الالتزام وبين درجات الاكتئاب. وبالرغم من أن الاكتئاب لا يرتبط بالسن والجنس والأعراض القلبية، إلا أنه يرتبط بالقلق وضعف الدعم الاجتماعي.

ABSTRACT Management of anticoagulant therapy after mechanical valve replacement is difficult in developing countries because of patient non-adherence. The effect of depression on adherence to drug therapy and to a clinic visit schedule was evaluated for 62 patients who received prostheses. All were prescribed a once-per-day regimen of warfarin and were scheduled for three appointments at the anticoagulant clinic for dose adjustment at 3-week intervals. According to the Center for Epidemiological Studies Depression Scale, 22 were depressed. Non-depressed patients were more compliant than depressed patients; adherence was inversely correlated with depression scores. While depression had no relationship with age, sex and cardiac symptoms, there was a relationship with anxiety and poor social support.

Relation entre la dépression et la non-observance du traitement anticoagulant après une intervention chirurgicale de remplacement valvulaire

RESUME La conduite du traitement anticoagulant après le remplacement valvulaire mécanique est difficile dans les pays en développement du fait de la non-observance des patients. L'effet de la dépression sur l'observance du traitement médicamenteux et du suivi médical prévu a été évalué pour 62 patients auxquels des prothèses avaient été implantées. Un traitement par la warfarine en prise unique quotidienne a été prescrit et trois visites à la clinique des anticoagulants ont été prévues pour tous les patients afin d'ajuster la dose à intervalles de trois semaines. Selon l'échelle de dépression du Centre des Etudes épidémiologiques, 22 patients étaient déprimés. Les patients non déprimés avaient une observance plus importante que les patients déprimés, l'observance étant inversement corrélée aux scores de dépression. Alors qu'il n'y avait pas de relation entre la dépression et l'âge, le sexe et les symptômes cardiaques, il y en avait une entre l'anxiété et le faible soutien social.

¹Annour Clinic, Red Crescent, Misurata, Libyan Arab Jamahiriya.

²Department of Cardiothoracic Surgery, Southampton University Hospital, United Kingdom.

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Introduction

The increased morbidity and mortality described in depressed patients with chronic medical disorders may be partly attributed to poor adherence to drug therapy and to other follow-up protocols. Previous studies have demonstrated a high prevalence of depression in patients undergoing heart operations, both before and after surgery [1-3]. With the rapid progress of cardiac surgery over a short period, there has been a corresponding growth in the awareness of the importance of psychological factors in all stages of treatment [3-5]. The importance of depression in conjunction with heart surgery lies in its association with increased morbidity and mortality [6,7]. Although the mechanism underlying the relationship between depression and increased morbidity and mortality is not fully understood, non-adherence to the prescribed medical therapy appears to play a role [8,9].

The use of anticoagulants following mechanical valve replacement surgery is highly recommended to prevent thromboembolic complications. The anticoagulant therapeutic programme is a complex task that requires frequent laboratory testing, dosage adjustment, prompt diagnosis and treatment of thromboembolic and haemorrhagic events. The clinical goal is to prevent thromboembolic events without increasing the risk of haemorrhagic complications. In Europe and the United States of America (USA), most health systems have established anticoagulant clinics that provide patient education, close monitoring of prothrombin levels and continuous clinical surveillance. Adherence to the anticoagulant therapeutic programme including frequent monitoring of the coagulation profile is a major concern of such clinics. In most developing countries, there are few anti-

coagulant clinics and there are no alternative patient registers to help maintain patient adherence to the programme.

This study in the Libyan Arab Jamahiriya examined the relationship between depression and adherence to the anticoagulant programme—the prescribed medication and the scheduled clinic visits—for patients who had undergone valve replacement surgery.

Methods

The study sample was a series of 62 patients who had undergone aortic valve replacement surgery with a mechanical prosthesis at different centres and who attended the anticoagulant clinic of Annour Clinic for elective dose adjustment and follow-up. All patients had undergone surgery within the last 18 months. There were 38 men and 24 women. The mean age of all patients was 48.7 ± 10.6 years. The exclusion criteria were known major psychiatric illness, stroke, dementia and illiteracy. The demographic and clinical data of patients are shown in Table 1.

Diagnosis of current depression was based on the Center for Epidemiological Studies Depression Scale (CES-D), which is a 20-item self-report scale designed to measure symptoms of depression [10]. The scoring system of CES-D ranges from 0 to 60 with higher scores indicating greater depressive symptoms. All patients completed testing with CES-D during interviews with a senior psychologist. A score of 16 was considered as the cut-off point for clinical symptoms of depression.

Anxiety was assessed using the Spielberg State-Trait Anxiety Inventory (STAI). STAI is comprised of two different self-report inventories, one measuring temporary state anxiety and the other more

Table 1 Demographic and clinical data of depressed and non-depressed patients

Variable	All patients (n = 62)	Depressed patients (n = 22)	Non-depressed patients (n = 40)
Male (%)	61.3	54.6	65.0
Mean age (years)	48.7 ± 10.6	51.0 ± 7.1	47.5 ± 11.0
Mean left ventricle ejection fraction (%)	55.8 ± 3.8	55.5 ± 4.1	56.7 ± 3.0
Mean NYHA class	3.2 ± 0.12	3.1 ± 0.15	3.4 ± 0.17
% with history of:			
Myocardial infarction	9.7	9.0	10.0
Stroke	4.8	4.5	5.0
Hypertension	8.0	9.0	7.5
Diabetes mellitus	12.9	13.6	12.5

All mean values are ± standard deviation.

n = total number of patients.

NYHA = New York Heart Association. Classification of symptoms in relation to activity: range from 1 (symptoms with more than ordinary activity) to 4 (symptoms at rest).

No significant differences between depressed and non-depressed patients.

general and long-standing trait anxiety. Scores range from 20–80 with higher scores reflecting greater anxiety [11].

Social support was evaluated using the Perceived Social Support Scale (PSSS), which is a 12-item self-report scale designed to measure perception of social support from family, friends and significant others. Scores range from 12 to 48 with lower scores reflecting poorer social support [12].

All patients included in this study had already been started on a regimen of anticoagulant therapy with warfarin following surgery. Following the psychometric testing, they were informed of the importance of taking warfarin regularly and were warned of the risks of negligence in taking warfarin in the prescribed dose and of irregularity in attending the anticoagulant

clinic. All patients were prescribed a single dose of warfarin (Coumadin, Bristol-Myers Squibb) per day ranging from 3–5 mg to achieve and maintain an international normalized ratio (INR) of 2.5–3.5. Adherence to anticoagulant therapy was assessed by supplying warfarin to all patients in the form of pill bottles in the cap of which was a microprocessor that registered the exact date and time of opening of the bottle. Adherence was defined as the percentage of days on which the patient took warfarin.

During the 9-week study course, each patient was given three follow-up appointments at 3-week intervals to test their INR and adjust the warfarin dose accordingly. Adherence to this schedule was defined as the percentage of appointments at which the patients attended the clinic on the given day.

All statistical analyses were performed using Graphic Prism software on a personal computer. Comparisons were made using simple *t*-test. Correlations were made between the corresponding values and the results expressed as r^2 and *P*-values. *P*-values below 0.05 were considered significant.

Results

Of the 62 patients who were eligible for the study, 22 (35.5%), 12 males (19.4%) and 10 females (16.1%), met the CES D criteria for depression (scores ≥ 16). Comparisons of demographic and clinical variables between depressed and non-depressed patients are shown in Table 1. There were no significant differences between groups for any of these variables. No patients were prescribed antidepressants.

The non-depressed patients adhered to the prescribed regimen on an average of 97.0% of the days studied compared with an average of 86.2% for the depressed patients ($P < 0.0001$) (Table 2). The non-depressed patients adhered to the follow-up schedule an average of 96.7% of the anticoagulant clinics studied compared with an average of 53.1% for the depressed patients ($P < 0.0001$).

There were significant inverse correlations between depression and adherence to the prescribed regimen ($r^2 = 0.8980$, $P < 0.0001$) and to the follow-up schedule ($r^2 = 0.8014$, $P < 0.0001$). Higher depression scores were associated with significantly lower adherence (Figure 1).

In a pattern similar to depression, anxiety scores correlated inversely with adherence to anticoagulant therapy ($r^2 = 0.8366$, $P < 0.0001$) and to the follow-up clinic schedule ($r^2 = 0.7898$, $P < 0.0001$, Figure 2).

Social support scores significantly correlated in a directly proportional manner to adherence to anticoagulant therapy ($r^2 = 0.7373$, $P < 0.0001$) and to follow-up visits ($r^2 = 0.5023$, $P < 0.0001$). Poor social support was thus associated with fewer adherences (Figure 3).

Anxiety and social support significantly affected the depression scale in a manner opposite to social support. Anxiety scores correlated directly with depression ($r^2 = 0.8837$, $P < 0.0001$), while social support scores correlated inversely with depression ($r^2 = 0.8837$, $P < 0.0001$, Figure 4). This indicates that higher anxiety and poorer social support precipitated higher depression scores that in turn were associated with

Table 2 Adherence to anticoagulant drug therapy and clinic visits for depressed and non-depressed patients

Adherence	Depressed patients (n = 22)		Non-depressed patients (n = 40)		P-value
	Mean \pm s	Range	Mean \pm s	Range	
Adherence to drug therapy (% of days)	86.2 \pm 4.0	79-94	97.0 \pm 2.8	92-100	< 0.0001
Adherence to clinic schedule (% of visits)	53.1 \pm 32.0	0-100	96.7 \pm 10.0	67-100	< 0.0001

s = standard deviation.

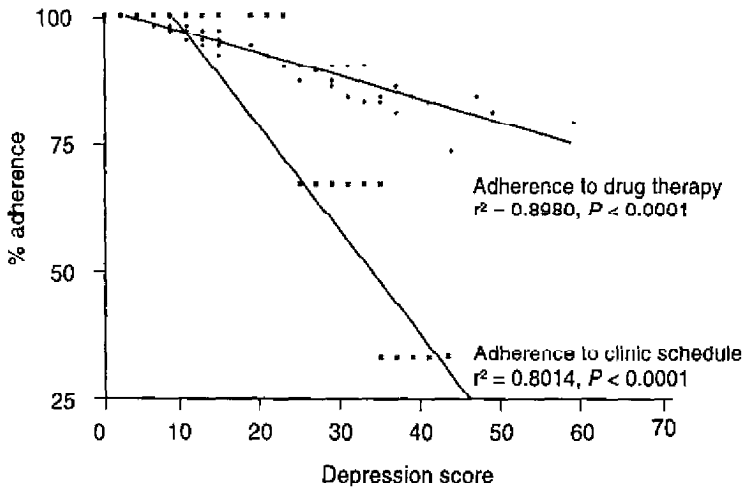


Figure 1 Relationship between depression scores and adherence to anticoagulant therapy and to follow-up clinic schedule

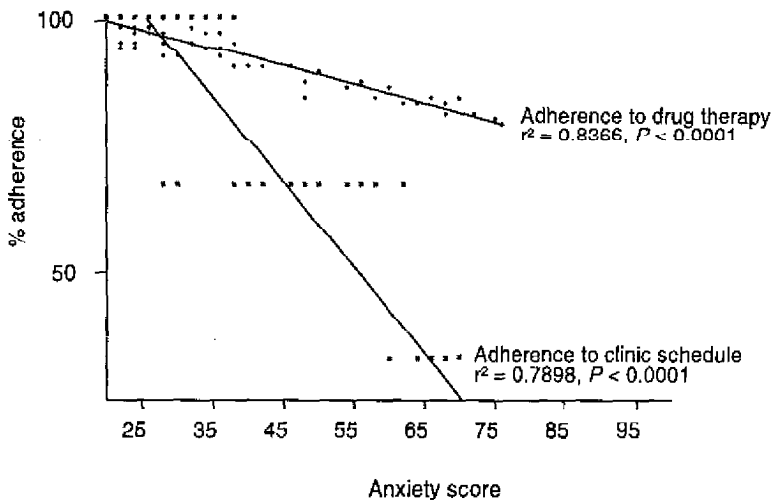


Figure 2 Relationship between anxiety scores and adherence to anticoagulant therapy and to follow-up clinic schedule

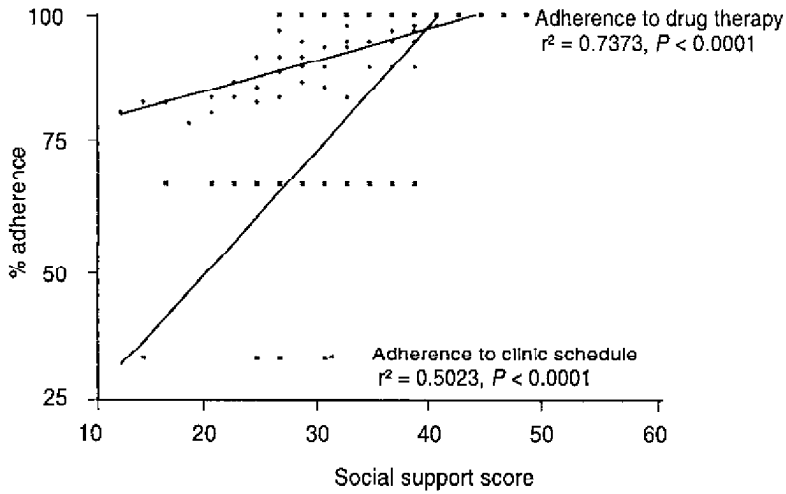


Figure 3 Relationship between social support scores and adherence to anticoagulant therapy and to follow-up clinic schedule

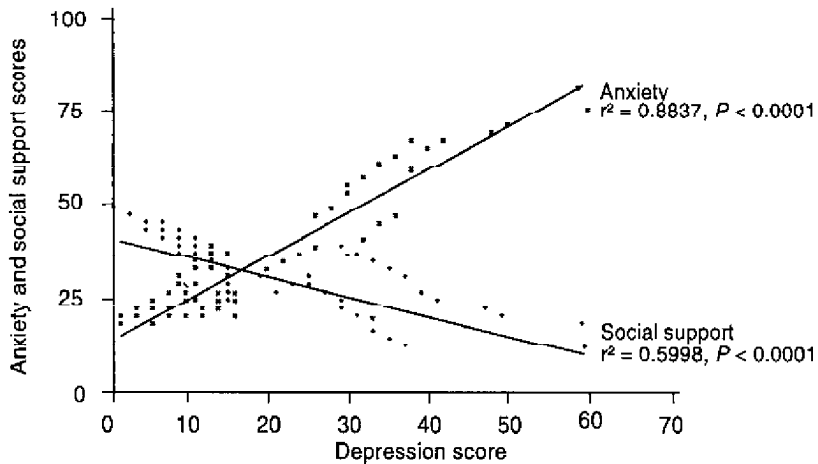


Figure 4 Relationship between depression scores and anxiety and social support scores

less adherence to anticoagulant therapy and to the clinic follow-up schedule.

At the follow-up interviews, none of the patients reported any side-effects from warfarin. All patients reported that they understood the importance of taking warfarin daily for the prevention of thromboembolic complications.

Discussion

The current study demonstrated that patients with depression following a heart operation adhered to a prescribed regimen of anticoagulant therapy and to a schedule of clinic visits significantly less than did comparable non-depressed patients. There are some studies that have demonstrated that depression in general is associated with reversible impairment of attention, concentration and memory [13], anxiety [5], and poor social support [14], all of which have been shown to affect adherence to medical therapy [15-18]. Previous studies have demonstrated the possible link between depression and non-adherence in patients who have had heart operations [8,9]. However, the reasons why depression reduces adherence is not yet fully understood. In this study, anxiety and poor social support appeared to be significantly involved along with depression in precipitating the tendency towards non-adherence to anticoagulant therapy. Age and sex did not show a significant association with depression or to adherence. Our sample, however, did not include elderly people among whom the prevalence of depression is high. Furthermore, our sample was probably not large enough to demonstrate a sex influence. A larger sample with older people would therefore be required to support our findings related to age and sex.

The annual risk of thromboembolism ranges between 1% and 4% with a slightly

higher incidence in patients with mechanical prostheses on warfarin than in those with bio-prosthetic valves on aspirin [19]. Careful follow-up is thus required for all patients who have received a prosthetic valve due to the risk of developing valve-related complications including thromboembolism, endocarditis, anticoagulant-related haemorrhage and valve degeneration [19]. Although there were no valve-related complications in either group in this relatively short follow-up period, differences of this magnitude in adherence to medical therapy (97.0% versus 86.2%) and in adherence to follow-up clinic schedule (96.7% versus 53.1%) are clinically significant. The follow-up in this study was designed to test the relation between depression and adherence.

The clinical importance of the current study was the significant role that depression may play in precipitating thromboembolic disorders following valve replacement surgery using mechanical prostheses. In developing countries where there are almost no reliable patient registers and where adherence to the anticoagulation programme is solely the patient's responsibility, this finding is alarming. Special attention should be given to patients with signs of depression. None of the patients classified as depressed in this study were on any kind of psychiatric follow-up or on regular antidepressant medication. Thus early recognition and treatment of depression, better education, and reassurance and improved social support to patients undergoing heart surgery may prove cost-effective. Further studies in this field should be performed to explore other factors that reduce the adherence of patients to the anticoagulant therapy and to set up a strategic plan to assure adherence as a fundamental aspect of quality anticoagulant therapy.

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