Depression in patients with hypertrophic cardiomyopathy: is there any relation with the risk factors for sudden death?

Artemis Igoumenou,1 Giorgos Alevizopoulos,2 Aris Anastasakis,3 Errika Stavarakaki,4 Pavlos Toutouzas,3 Christodoulos Stefanadis3

ABSTRACT

Objectives The aim of this study was to investigate whether depressive symptoms are related to the risk factors for sudden death in patients with hypertrophic cardiomyopathy (HCM).

Design 121 patients diagnosed as having HCM were assessed for depressive symptomatology using the Beck Depression Inventory and the Center for Epidemiological Studies Depression Scale (CES-D) and followed up for a period of 2 years. For the interview, the authors used the Structured Clinical Interview for DSM-III/DSM-III-R. A multidimensional longitudinal study was carried out with both somatic and psychological symptoms and signs taken into consideration. SPSS was used for the statistical analysis.

Results (1) Patients with HCM are more depressed than the general population. (2) There is no positive correlation between the occurrence of depressive symptoms and the risk factors for sudden death in patients with HCM. (3) Patients at high risk for sudden death are not more depressed than the others. (4) Time from diagnosis of the cardiac disease is not related to the presence and severity of depressive symptoms.

Conclusions Patients with HCM are more depressed than the general population. The authors suggest that depressive symptoms and risk factors for sudden death in these patients are not related. It is important to screen for mood disorders in this patient population in order to provide an early diagnosis and treatment of the psychiatric disease.

INTRODUCTION

One of the major causes of sudden death, especially in young adults, is hypertrophic cardiomyopathy (HCM). HCM is a genetically transmitted disease of myocardial tissue following the rules of autosomal dominant inheritance.1 2 3

It is a disease with variable penetrance and expressivity. HCM occurs in 0.2–0.3% of the population4 and is slightly more prevalent in males, although it usually presents at an earlier age in females.3

HCM is a progressive condition that may occur at any time, although its most common presentation is in the third decade of life. For inherited forms of the disease, the peak incidence is in the second decade of life.

Patients with HCM may be asymptomatic or have symptoms such as fatigue, dyspnoea, dizziness, chest pain, syncope, presyncope, palpitations, orthopnoea or congestive heart failure.3 4 The majority of patients have few or no cardiac symptoms, and sudden death may be the first clinical manifestation of the disease.1 2 4

Patients with HCM may have no pathological findings on physical examination (especially asymptomatic ones) or have a great variety of arrhythmias, such as atrial fibrillation or flutter, ventricular ectopy, ventricular tachycardia and ventricular fibrillation. They may also have a fourth heart sound, a double carotid arterial pulse, a systolic murmur or a split second heart sound.2

For the diagnosis of HCM, cardiologists use imaging studies and other diagnostic tests such as electrocardiography, echocardiography, continuous wave Doppler, Holter monitoring, cardiac catheterisation, radionuclide imaging (with thallium or technetium, MRI, PET) and cardiopulmonary exercise testing.1 4

Treatment targets should be the relief of symptoms and the prevention of complications.

The most notable complication is HCM-related cardiovascular death. It can be sudden death or death after heart failure or stroke. It is believed that the major mechanism of sudden death is ventricular arrhythmias. Patients with HCM may be at a very high risk of sudden death if they have1 4

- a history of cardiac arrest
- non-sustained ventricular tachycardia during Holter monitoring.

There is another category of patients with HCM who are at high risk for sudden death, characterised by1 5

- syncope
- crisis of ventricular tachycardia during Holter monitoring
- abnormal response of blood pressure during exercise (patients aged under 40 years)
- family history of sudden cardiac death
- left ventricular hypertrophy >30 mm.

Younger patients are at greater risk of sudden death. It has been suggested that the number of risk factors for sudden death is important for the prognosis. The death rate for patients with HCM is 4% per year.1 5

Previous studies have suggested that a high percentage of patients with cardiovascular disease appear to have detectable psychopathology. Depressive disorders occur most often, but substance abuse, anxiety disorders and somatoform illnesses are also possible co-morbid conditions.6 7

Depression is the most common of the mood (affective) disorders. It can occur as a single depressive episode or recurrent episodes. The
severity of depression can vary from mild to severe and it can present with or without somatic symptoms. Severe depression can also present with or without psychotic symptoms.

The life prevalence of depression is 10–25% for women and 5–12% for men. The point prevalence is 5–9% for women and 2–5% for men. The prevalence does not seem to differ between nations, or according to the person’s financial or marital status.8–12

Depression can occur at any stage in life, although it usually occurs around the age of 40 years. It is estimated that half the patients have their first episode between 20 and 50 years of age.

The aetiology of depression seems to be complicated by multiple factors. Experts in the area divide the aetiological factors into three broad categories: biological, genetic and psychosocial, although these factors interfere with each other.13

It seems that depressive disorders tend to persist with time and the patients may experience remissions and relapses. Studies in the field suggest that stressful life events have a role to play in the occurrence of mood disorders and the risk of relapse.13

It is worth mentioning that of the people who have depression, only half will receive treatment at some stage.7 Treatment for depression can be biological (pharmaceutical, electroconvulsive therapy, surgical), psychotherapy, social intervention or a combination of the above. Any treatment should target the potential for self-harm, the acute phase of the illness and the prevention of relapse.9,14

Clinical depression not only causes individuals to lose pleasure from daily activities, but can also complicate or even be a risk factor for cardiovascular disease.15

Cross-sectional and case-control studies have shown that rates of depression are higher among patients with coronary artery disease. It has also been found that a history of major depressive episodes was associated with the odds of myocardial infarction being more than four times higher than among patients with no history of major depressive episodes or dysphoria. This risk was independent of major coronary risk factors.16

Additionally, it has been suggested that there is a positive correlation between depression and sudden death in patients with chronic cardiac disease.6 17–20 There is evidence that patients with depression are at an increased risk of dying from sudden cardiovascular death compared with the general population.21

Cardiovascular disease and depression are associated illnesses. Safe and effective treatment of depression and cardiovascular illness can be difficult because of the interplay between them.22 It is known that the treatment of depression can cause cardiac complications.23–27 Moreover, the treatment of cardiac illness can result in symptoms of depression.22,28 That is why it is very important to recognise and treat depression and cardiovascular disease at the same time.

**METHODS**

**Selection of patients**

Patients diagnosed as having HCM, who were under the care of cardiologists at the Division of Inherited Cardiovascular Disease in Athens, Greece, were approached and informed about the study. All potential participants were outpatients at the time of recruitment. The first 121 patients who consented to participate were included in the study. These patients were diagnosed and regularly followed up by a cardiologist (usually at 6-month or 1-year intervals). The participants were from all age groups and both sexes. Therefore, our inclusion criterion was a diagnosis of HCM by a cardiologist specialised in inherited cardiomyopathies; no exclusion criteria were set.

**Risk stratification for sudden death**

Risk stratification for sudden death was based on satisfying five criteria: (1) syncope, (2) family history of sudden death, (3) crisis of ventricular tachycardia during Holter monitoring, (4) abnormal response of blood pressure during exercise and (5) left ventricular hypertrophy >30 mm.

We have adopted the criteria used by cardiologists regarding risk stratification for sudden death. Patients with HCM and no risk factors were considered as low risk for sudden death. Those with one risk factor were considered as medium risk and those with two or more risk factors as high risk for sudden death.

All the patients were assessed for depressive symptomatology, but 13 patients did not have full cardiological evaluation on risk stratification for sudden death. So, these patients were excluded from the statistical analysis when risk stratification was considered as an overall score, but they were included in the analysis of the components of the risk stratification where cardiological data were available.

**Depression scales**

For the evaluation of depressive symptomatology, Beck Depression Inventory (BDI) and the Center for Epidemiological Studies Depression Scale (CES-D) were used. Both scales were standardised Greek versions.

BDI is a scale for depression scored from 0 to 63. It involves identifying a range of depressive symptoms and estimates their severity. It is a self-administered questionnaire including 21 items that cover mood/affect, self-accusation, changes in activity and somatic symptoms. Each of the items is scored from 0 to 5 according to the given response. The overall score is obtained by the addition of the individual scores.

BDI is used in screening for mental illness, in general medicine and in research, so there are different cut-off points that indicate diagnosis of depressive symptomatology. For example, in screening BDI>13 is translated as present depressive symptomatology, in general medicine the cut-off point is BDI>10, while in research the cut-off point is BDI>21.

For the purposes of our study, we translated the results from the BDI, apart from treating them as continuous data, as follows. Patients who scored 0–10 belonged to category 0 (non-depressed), those who scored 11–20 to category 1 (very mild depression), those who scored 21–30 to category 2 (mild depression) and those who scored 31–63 to category 3 (depression or severe depression).

CES-D is a scale for depression scored from 0 to 60. The cut-off point for the diagnosis of depression is 15, so patients whose score is above 15 are depressed. This scale does not give information about the severity of the depressive illness. It is a self-administered questionnaire that targets the general population. It is mainly used in people with co-morbid physical conditions (sensitivity 81%, specificity 78%). It evaluates the symptomatology during the last month before the administration.

CES-D includes 20 items, each scored from 0 to 3, and the overall score is calculated by adding the scores for the individual items. Apart from the full version that we used in the presenting research, there are short versions consisting of 10, 8 or 4 items, which are not widely used.

Patients who scored 16 or above in the CES-D were interviewed in order to ascertain the diagnosis. For the interview, we used the Structured Clinical Interview for DSM-III/ DSM-III-R (SCID). The SCID provides the researcher not only with the current diagnosis but also with the lifetime diagnosis, according to DSM-III-R. In our research, we used parts of the SCID related to the diagnosis of depression, dysthymia and suicidality.
The assessment for depressive symptomatology for each participant took place after a consultation with the cardiologist. The first assessment followed their consent to participate and the second one happened a year later, again following consultation and examination by the cardiologist. For both assessments, the cardiologists provided us with the updated cardiological data. All psychiatric data were collected by the main researcher to avoid bias and to ascertain that the same standards were followed. The main researcher has received training in administering and rating the scales used as well as performing the psychiatric interview.

RESULTS
Clinical data for the overall study group are shown in table 1.

Most of the patients were men (57.9%). The age range was 16–82 years. Of the 121 patients included in the study, 45.5% were at low risk, 31.4% were at medium risk and 23.1% were at high risk for sudden death. Thirteen (10.7%) patients were at low risk, 31.4% were at medium risk and 12.4% were at high risk for sudden death. Thirteen (10.7%) patients were not assessed for risk stratification, as they were not assessed for one or more of the five risk stratification criteria.

Among the risk factors for sudden death, ventricular tachycardia was the most common (18.2%), while family history of sudden death and syncope were found to have the same percentage (14.9%). Abnormal response of blood pressure during exercise (11.6%) and hypertrophy over 30 mm (5.3%) were less common.

Depressive symptomatology was first assessed with the BDI, which is a scale for depression scored from 0 to 63. As mentioned above, we have transformed this ratio scale into an ordinal one. So, patients who scored from 0 to 10 were listed in category 1 (extra mild depression), those who scored from 11 to 20 were in category 2 (mild depression), those who scored from 21 to 30 were in category 2 (mild depression), and those who scored from 31 to 63 were in category 3 (moderate or severe depression). In our statistical analysis, we treated the results from the BDI as continuous and subsequently as ordinal data.

Of the patients with HCM 47.1% were not depressed, 37.2% were very mildly depressed, 11.6% were mildly or moderately depressed and 4.1% were severely depressed. Using the CES-D scale we found that 52.9% were not depressed and 47.1% were depressed. None of the participants were treated for depression or had a historical diagnosis of depression at the time of recruitment.

We examined each risk factor for sudden death separately and tried to find out whether there was any relation with the diagnosis of depression. For the statistical analysis we used SPSS (χ² test and ANOVA). We found that:

- left ventricular hypertrophy over 30 mm was not related with depressive symptomatology (p=0.840 for BDI and p=0.335 for CES-D);
- for family history of sudden death, both χ² test and ANOVA showed that there was no relation with depression (p=0.440 for BDI and p=0.494 for CES-D);
- similar results were obtained for ventricular tachycardia (p=0.798 for BDI and p=0.105 for CES-D) and for abnormal response of blood pressure (p=0.236 for BDI and p=0.882 for CES-D);
- the history of syncope was also not related with depression in patients with HCM (p=0.574 for BDI and p=0.762 for CES-D).

We also examined whether there was any relation between depression and the total risk stratification for sudden death. Using the χ² test we found that there was no positive correlation between depressive symptoms and the risk stratification for sudden death (p=0.316 when using BDI for the diagnosis of depression and p=0.603 when using CES-D).

As shown in figure 1, risk stratification does not seem to be related to depressive symptoms, as diagnosed using the BDI.

Furthermore, a comparison of the two diagnostic tools used in this study—the BDI and the CES-D (t test)—shows that the two scales did not give identical results but they did have a positive correlation (figure 2).

DISCUSSION
The main aim of this study was to assess associations between depressive symptomatology and clinical features of HCM. For psychiatric evaluation, standard measures were used (BDI, CES-D, SCID). HCM diagnosis and risk stratification for sudden death were done by cardiologists who were specialists in hereditary cardiac diseases. The sample consisted of 121 men
and women from all over Greece who were diagnosed as having HCM. The existing literature on depression and depressive symptomatology in hereditary cardiovascular disease, and especially in HCM, is scarce. There are only few studies on quality of life and well-being in patients with dilated cardiomyopathy or HCM. These studies suggest that dilated cardiomyopathy is associated with anxiety and depression, while HCM is associated with substantial restrictions in health-related quality of life. So, it was a pleasant surprise to find an article on depression, anxiety and quality of life in patients with obstructive HCM. However, this article was very specific to a HCM subpopulation as the researchers examined anxiety and depressive symptoms before and 3 months after alcohol septal ablation. More specific studies have also been found in the literature such as the study on the effect of depressive symptoms on survival after heart transplantation in patients with ischaemic or dilated cardiomyopathy.

In our study, patients with HCM appeared to be more depressed than the general population and almost as depressed as patients with coronary artery disease. Depressive symptomatology was not associated with the severity of cardiac illness, and patients who were at high risk for sudden death were not more depressed than the others. Although they were informed about the severity of their illness, and their daily activities were restricted due to the risk of dying suddenly, they did not seem to be more psychologically affected than others with the same diagnosis but without the risk of sudden death. Patients with a family history of sudden death were not more depressed and did not experience more psychological distress. The explanation for this observation is not clear and it does not support the belief that the sudden death of a relative with the same disease can affect mood status.

Individuals with syncope were not more depressed than patients with HCM who had no such experience. The explanation for this observation is also unclear. It seems that the experience of a syncop tic episode may cause restrictions in social functioning but not in psychological well-being.

The other risk factors for sudden death were crisis of ventricular tachycardia during Holter monitoring, abnormal response of blood pressure during exercise and left ventricular hypertrophy over 30 mm. We suggest that these risk factors are also unrelated to depressive symptomatology, possibly because these findings are not ‘felt’. Patients do not realise the severity of their disease because they do not have any symptoms. Furthermore, we observed that there was a discrepancy in the diagnosis of depression between the two diagnostic scales (BDI and CES-D). Thus, individuals who were depressed according to the BDI were not depressed according to the CES-D. The explanation may be that CES-D has two categories, depressed and non-depressed, and some patients fall into the category of non-depressed, while according to the BDI they are mildly depressed. We should also not ignore that the CES-D does not have questions on somatic symptoms, while the BDI may overestimate such symptoms.

This study was longitudinal and involved patients who were diagnosed as having HCM. These patients were recently diagnosed as having HCM or had typically been diagnosed for several years. We explored the hypothesis that depressive symptomatology is related to the time from the diagnosis of HCM, especially as it is an inherited heart disease, and that patients diagnosed as having HCM should change their everyday activities in order to prevent sudden death. We found no correlation between the time of the diagnosis and the presence and severity of depressive symptoms. In our study, patients recently diagnosed as having HCM were not more depressed than those diagnosed more than 5 years ago.

One of the limitations of this study is its duration. Long-term follow-up of the participants could give some insight into the mortality related to this co-morbid condition. The sample size, as well as the characteristics of the Greek population, can be another limitation. Further similar research involving bigger and more diverse populations is needed.

The results from this study suggest that patients with HCM are more depressed than the general population, and that depressive symptoms and risk factors for sudden death in these patients are not related. We could safely suggest that since depression occurs frequently in these patients, they should be assessed regularly for depressive symptoms and treated when necessary. Effective communication between health professionals and support from the family and social environment is of paramount importance. Both illnesses should be treated simultaneously in order to improve the person's quality of life and well-being.

Competing interests None.

Ethics approval Ethics approval was provided by National and Kapodistrian University of Athens. Provenance and peer review Not commissioned; internally peer reviewed.

REFERENCES