

Original Article

COVID-19 quarantine and depression in patients with congenital heart disease

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Abstract: COVID-19 outbreak has brought tremendous psychological pressure to the general population, especially to those with associated cardiovascular disease. An online Patient Health Questionnaire (PHQ-9) survey on consecutive congenital heart disease (CHD) patients, was carried out to determine depression during the Spanish coronavirus disease (COVID-19) quarantine. Two-hundred forty-two out of 407 (59%) CHD patients answered the survey, 123 (51%) had mild defects, 88 (36%) moderate and 31 (13%) great defects, most of them between 18 and 24 years old and 51% were male. Patients were dichotomized to no or mild (PHQ-9 < 10) and moderate to severe (≥ 10) depressive symptoms. Thirty-four (14%) patients showed a PHQ-9 ≥ 10 and 10 of them (29%) were under anxiolytic or antidepressant treatment during the quarantine. During the study period, 9 (4%) patients had COVID-19 symptoms. Patients with a NYHA above 2 ($P=0.025$), living in houses without garden or balcony ($P=0.014$), needing psychological/psychiatric evaluation/medication in the previous 12 months or being under anxiolytic/antidepressant treatment during the confinement had, significantly, a PHQ-9 score ≥ 10 ($P < 0.001$). Being under anxiolytic/antidepressant treatment during the coronavirus pandemic [OR 3.92 (95% CI 1.05-14.66), $P=0.043$] and having previous psychological/psychiatric evaluation in the previous 12 months to the quarantine [OR 3.82 (95% CI 1.16-12.54), $P=0.027$] were the only variables that reached statistical significance, in the multivariable analysis, as predictors of a pathological PHQ-9 questionnaire (score ≥ 10). In conclusion depression was frequent during the COVID-19 quarantine among CHD patients, with only a third of them being under anxiolytic or antidepressant treatment. Needing psychological/psychiatric evaluation/treatment during the previous 12 months to the lockdown was a predictive factor for an abnormal PHQ-9 score.

Keywords: COVID-19, quarantine, PHQ-9, congenital heart disease

Introduction

On March 2020, the World Health Organization (WHO) declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease 2019 (COVID-19) outbreak, a public health emergency of international concern due to its widespread and rapid rate of transmission altering routine activity in most European countries. In this context, on March 14, 2020 the Spanish Government declared a state of alarm, which led to the imposition of a national quarantine forcing all non-essential service workers to stay

home until April 26. By May 1, 2020, more than 1.6 million cases were diagnosed in 179 countries on 5 continents, with nearly 100.000 confirmed deaths [1].

Fear and anxiety about a new disease and what could happen can be overwhelming and cause strong emotions in adults and children. In this context, the COVID-19 outbreak has brought tremendous psychological pressure to the general population, which may lead to depression [2], anxiety and psychological distress [3], especially in young individuals with chronic diseases [4].

To shed light on how confinement may have impacted psychologically to patients with congenital heart disease (CHD), a population at a higher risk of a worse outcome judging from the results seen in patients with cardiovascular disease and COVID-19 [5], we carried out an online self-administered questionnaire during the mandatory quarantine to identify major depressive disorder.

Material and methods

Study population

The link to an online survey was sent to a group of consecutive CHD patients recruited from a single hospital outpatient CHD unit between October 2018 and April 2019. The survey was conducted online to maximize reach and ensure anonymity. Information about the study objectives and the procedure was given to the participants before obtaining their consent to participate or the consent of responsible adults in the case of patients younger than 18 years old. The emails were sent on April 14, 2020 and a reminder was issued the next week, encouraging people to respond the questionnaire, which were asked to complete in two weeks. Patients that either were unable to answer the survey, or who did not want to participate, and those with co-morbidity problems that limited life expectancy were excluded from the study. The protocol of the study was approved by the Hospital's Ethics Committee.

Clinical data

Participants were asked a series of questions: age, sex, type of CHD, functional class, associated syndromes, previous cardiac intervention (surgery or percutaneous treatment), cardiac device implantation (pacemaker or implantable cardiac defibrillator), educational level (none, primary, high school, vocational training or university), marital status (single, married, cohabit, divorced, separated or widowed), pre-pandemic employment status (student, active worker, domestic worker, unemployed, retired or incapacity for work), post pandemic employment status changes (none, dismissal, temporary labour force adjustment or forced vacation), previous medical diagnosis of anxiety or depression carried out by a physician in the previous 12 months to the coronavirus pandemic, the need for psychological/psychiatric evaluation or medication previous to and dur-

ing the coronavirus pandemic, exercising at home and having COVID-19 symptoms or relatives with COVID-19 symptoms. Patients were also asked if they lived alone, if their houses had garden, or a balcony and if they lived in urban or rural areas. CHD patients were classified into diagnostic groups (simple, moderate, or great complexity) according to the newly elaborated AHA/ACC guidelines [6]. New York Heart Association (NYHA) functional class was classified according to the severity of their symptoms: class 1 means no limitation, class 2 mild limitation, class 3 marked limitation and class 4 unable to carry on any physical activity.

The patient health questionnaire (PHQ-9)

Psychological distress was evaluated using the 9-item Patient Health Questionnaire (PHQ-9). The PHQ-9 questionnaire is a self-administered tool which is used clinically as it can be rapidly completed by patients [7]. In fact, the PHQ-9 is acceptable, and as good as longer clinician-administered instruments in a range of settings, countries, and populations [8, 9] being a highly satisfactory tool to identify major depressive disorder in adult patients in Spanish primary care centres [10].

Many of the nine items align with the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria for identifying depressive disorders: anhedonia, depressed mood, insomnia or hypersomnia, fatigue or loss of energy, appetite disturbances, guilt or sense of worthlessness, diminished ability to think or concentrate, psychomotor agitation or retardation, and suicidal thoughts. The nine items of the survey score from 0 to 3 in each of the response categories of "not at all", "several days", "more than half the days", and "nearly every day", respectively. Subsequently, the PHQ-9 scores were used to categorize the severity of the depression symptoms: no symptoms (0-4), mild (5-9), moderate (10-14), moderately severe (15-19) and severe symptoms (19-27) [8]. For the statistical analysis, the patients were dichotomized to no or mild (0-9) and moderate to severe (≥ 10) depressive symptoms as a PHQ-9 score ≥ 10 has a sensitivity of 88% and a specificity of 88% for major depression [7].

Statistical analysis

Qualitative variables were expressed in percentages. Possible associations between cate-

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Table 1. Congenital cardiac defects according to anatomical complexity

Types of congenital heart disease	Number of patients
Simple defects	123
Aortic valve disease	27
Pulmonary valve disease	17
Atrial septal defect	20
Ventricular septal defect	37
Ductus	4
Other simple defects	18
Defects of moderate complexity	88
Subvalvular or supra-avalvular aortic stenosis	5
Coarctation of the aorta	21
Subvalvular or supra-avalvular pulmonary stenosis	17
Tetralogy of Fallot	40
Ebstein	2
Atrioventricular septal defects	3
Defects of great complexity	31
Dextro transposition of the great arteries	11
Levo transposition of the great arteries	8
Pulmonary atresia	4
Single ventricle	5
Double outlet right ventricle	1
Truncus	2

gorical variables were evaluated by using the Pearson chi-square test (χ^2). Binary logistic regression analysis was performed to compare patients with normal (< 10) and borderline/abnormal (≥ 10) PHQ-9 scores with those independent variables that had a *p* value lower than 0.05 in the univariate analysis. The results were expressed as odds ratios (OR) with their 95% confidence intervals (CIs). A *p* value less than 0.05 was considered statically significant. Data analysis was carried out using SPSS 24.0 (SPSS, Chicago, IL).

Results

CHD patient population

Two-hundred forty-two out of 407 (59%) patients with CHD were invited to participate in the survey. Of them, 156 did not answer, 2 did not give written consent to participate and 7 did not complete the whole PHQ-9 questionnaire. No patients were excluded due to inability to answer the survey or due co-morbidity problems.

Among all patients who completed the survey, 123 (51%), 88 (36%) and 31 (13%) patients had mild, moderate, or great anatomical CHD defects (**Table 1**). During the study period 9 (4%) out of 242 CHD patients presented with COVID-19 symptoms and, of them, only three underwent a polymerase chain reaction (PCR) test, that was negative. Meanwhile, 8 relatives referred to have COVID-19 symptoms: 4 did not undergo any PCR test, 3 had a negative PCR result and one a positive one.

PHQ-9 questionnaire in CHD patients

According to the PHQ-9 questionnaire 135 (56%) patients with CHD had minimal or no depression, 73 (32%) showed mild depression, 25 (10%) moderate depression, 5 (2%) moderate to severe depression and 4 (2%) severe depression. After dichotomization, 208 (86%) patients had a PHQ-9 score below 10 and 34 (14%) showed a PHQ-9 score equal or above 10.

Table 2 shows demographic and clinical data in CHD according to the PHQ-9 questionnaire. Patients with a NYHA functional class > 2 (*P*=0.025), those who lived in houses without a garden or balcony (*P*=0.014), who had been diagnosed with depression or anxiety or had required psychological or psychiatric treatment or evaluation in the previous 12 months to the coronavirus pandemic (*P* < 0.001) and used anxiolytic or antidepressant treatment during the quarantine (*P* < 0.001), scored significantly higher on the PHQ-9 questionnaire. By contrast, age, gender, presenting with COVID-19 symptoms, CHD complexity, having a syndrome or a previous cardiac procedure, the educational level, the marital status, or the working life did not reach a statistically significant association with the result of the PHQ-9 questionnaire. Furthermore, a multivariate analysis showed that being under anxiolytic or antidepressant treatment during the coronavirus pandemic [OR 3.92 (95% CI 1.05-14.66), *P*=0.043] or requiring psychological or psychiatric evaluation in the previous 12 months to the quarantine [OR 3.82 (95% CI 1.16-12.54), *P*=0.027] were risk factors associated with a PHQ-9 questionnaire score ≥ 10 (**Table 3**).

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Table 2. Demographic and clinical data in CHD with a PHQ-9 score above and below 10

	PHQ-9 score		P
	< 10	≥ 10	
Number of patients (n)	208	34	
Age (time period), n			0.520
14-17 years	18 (9)	2 (6)	
18-24 years	65 (31)	16 (47)	
25-34 years	54 (26)	9 (26)	
35-44 years	38 (18)	3 (9)	
45-54 years	26 (13)	4 (12)	
> 55 years	7 (3)	0 (0)	
Sex (male), n	111 (53)	13 (38)	0.102
CHD complexity, n			0.688
Mild	106 (51)	17 (50)	
Moderate	74 (36)	14 (41)	
Great	28 (13)	3 (9)	
Functional class (NYHA >2), n	25 (12)	9 (26)	0.025
COVID-19 symptoms, n	7 (3)	2 (6)	0.472
Relatives with COVID-19 symptoms, n	6 (3)	2 (6)	0.365
Syndromes, n			0.494
Down	14 (7)	0 (0)	
Others (Williams, Noonan, Turner,...)	20 (10)	3 (9)	
Previous cardiac intervention, n			0.455
None	37 (18)	7 (20)	
Cardiac surgery ≤ 14 years old	121 (58)	23 (68)	
Cardiac surgery > 14 years old	33 (16)	3 (9)	
Percutaneous procedure	17 (8)	1 (3)	
ICD or pacemaker device, n	16 (8)	6 (18)	0.061
Educational levels, n			0.895
None	7 (3)	2 (6)	
Primary	30 (14)	6 (18)	
High school	86 (42)	12 (35)	
Vocational training	58 (28)	11 (32)	
University	27 (13)	3 (9)	
Marital status, n			0.346
Single	158 (76)	28 (82)	
Married or cohabit	38 (18)	6 (18)	
Divorced, separated, or widowed	12 (6)	0 (0)	
Pre-pandemic employment status, n			0.373
Student	70 (34)	12 (35)	
Active worker	73 (35)	7 (21)	
Domestic worker	13 (6)	3 (9)	
Unemployed or retired	24 (12)	8 (23)	
Incapacity for work	28 (13)	4 (12)	
Post-pandemic employment status changes, n			0.270
None	159 (77)	31 (91)	
Dismissal or temporary labor force adjustment	30 (14)	2 (6)	
Forced vacation	19 (9)	1 (3)	
Living alone at home, n	17 (8)	1 (3)	0.281

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House with garden or balcony, n	153 (74)	18 (53)	0.014
Living in an urban area, n	110 (53)	12 (35)	0.057
Exercising (sporadically or regularly) at home, n	153 (74)	23 (68)	0.473
Previous medical diagnosis [‡]			< 0.001
Anxiety	2 (1)	3 (9)	
Depression	3 (1)	11 (32)	
Psychological/psychiatric evaluation or medication [‡]	12 (6)	12 (35)	< 0.001
Anxiolytic or antidepressant treatment during the pandemic	8 (4)	10 (29)	< 0.001

NYHA: New York Heart Association, COVID-19: coronavirus disease 2019, ICD: implantable cardioverter defibrillator. [‡]In the previous 12 months to the coronavirus pandemic.

Table 3. Predictive clinical variables of a pathological PHQ-9 questionnaire (score ≥ 10)

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P	OR (95% CI)	P
NYHA functional class > 2 (yes)	2.63 (1.10-6.28)	0.029	2.43 (0.91-6.50)	0.078
House with terrace, garden, or balcony (yes)	0.40 (0.193-0.85)	0.017	0.48 (0.21-1.01)	0.083
Living in an urban area (yes)	2.06 (0.97-4.37)	0.061		
Previous anxiety or depression (yes) [‡]	0.62 (0.37-1.06)	0.079		
Psychological/psychiatric evaluation or medication (yes) [‡]	8.90 (3.57-22.21)	< 0.001	3.82 (1.16-12.54)	0.027
Anxiolytic or antidepressant treatment during the coronavirus pandemic (yes)	10.47 (3.75-28.93)	< 0.001	3.92 (1.05-14.66)	0.043

OR: Odds ratio, CI: confidence interval. NYHA: New York Heart Association. [‡]In the previous 12 months to the COVID-19 quarantine.

Discussion

In 2014 and 2017, the European Health Survey included the eight-item Patient Health Questionnaire depression scale (PHQ-8) to assess the presence and prevalence of depressive symptoms in the population aged 15 and over [11]. The PHQ-8 and the PHQ-9 total scores are similar and, although sensitivity may be slightly reduced when using the PHQ-8 test, the specificity of both questionnaires is similar [12]. According to the 2017 survey, 6.7% and 6.6% of the Spanish population suffered from anxiety and depression, respectively. These results are similar to our findings, where the prevalence of anxiety and depression, twelve months prior to the onset of the coronavirus pandemic, was 2% and 6% respectively. Nonetheless, during the quarantine, 34 out of 242 (14%) patients with CHD showed a PHQ-9 ≥ 10 despite only 10 of them (29%) were under antidepressants or anxiolytics.

The COVID-19 pandemic may be stressful to people but, mostly, to patients at a higher risk of a worse clinical outcome [13, 14]. On top of the perceived risk of being infected, recent evidence suggests that people who are kept in isolation or quarantine experience higher levels of anxiety, anger, confusion, and stress. In fact,

many studies that have examined the psychological disorders during the COVID-19 pandemic have reported that the affected individuals may show several symptoms of mental trauma, such as emotional distress, depression, mood swings, irritability, insomnia, attention deficit hyperactivity disorder or post-traumatic stress [14]. In this context, Gonzalez-Sanguino et al. [15] reported that the psychological impact of the COVID-19 outbreak was evident in a sample of the Spanish population: 18.7% revealed depressive, 21.6% anxiety and 15.8% post-traumatic stress disorder symptoms, and were associated with being female, having previous mental or neurological problems, and having COVID-19 symptoms or relatives infected with the virus. Similarly, we found that being under anxiolytic or antidepressant treatment, having a history of anxiety or depression or needing previous psychological/psychiatric evaluation was associated with a PHQ-9 score above 10. Nonetheless, unlike previous reports [16], we found no association between gender, marital or employment status, which could be explained by the younger age of our patients with CHD, many of them still living with their parents. In fact, according to the latest Spanish National Statistics Institute (INE) survey 53% of adults between 25 and 29 years old and 25% of those between 30 and 34 years old still lived with

their parents, irrespectively of their study levels [17], a status weighed down by unemployment and the precariousness and instability of the labour market in Spain. We also found that having COVID-19 symptoms was not significantly associated with depression [14, 18], although the number of affected is small (only 9), probably due to the low prevalence of the disease in the Canary Islands, one of the regions least affected by the pandemic not only in Spain but also in Europe. Finally, patients who lived in a house with a garden or a balcony or who lived in a rural area showed a PHQ-9 score under 10 more frequently. The reason for this can be that neighbourhoods characterised by the presence of poor-quality buildings and services, as it occurs in many cities, are associated with a greater likelihood of depression [19].

In relation to the multivariate analysis, being under anxiolytic or antidepressants, or needing previous psychological or psychiatric help, were the only variables that reached statistical significance as predictors of a PHQ-9 score ≥ 10 . This result is in agreement with the view that psychiatric patients are more likely to develop recurrences or deterioration of pre-existing signs and symptoms. Moreover, individuals with 'high health anxiety' are more likely to misinterpret harmless bodily symptoms and feelings leading to an alteration of the behaviour and of the capacity of decision-making [20].

There are, however, limitations in our study that may impact our findings. Firstly, the PHQ-9 survey may overestimate the prevalence of depression, although PHQ-9 sensitivity, when compared with semi-structured diagnostic interviews, has been shown to be greater than that shown in previous conventional meta-analyses [21]. Secondly, the PHQ-9 questionnaire was carried out online. Nonetheless, remote or in-person PHQ-9 surveys seem to be a reliable procedure for assessing depression [22]. Finally, CHD patients represent a very heterogeneous population so it may be difficult to draw final conclusions in the global set of patients with CHD.

In conclusion, fourteen percent of our CHD patients showed a pathological PHQ-9 score, twice as high as expected [11]. However, less than one third reported being under anxiolytic or antidepressant treatment during the coronavirus quarantine. Needing previous psychologi-

cal or psychiatric evaluations should make us think about the possibility of relapses during confined states.

Disclosure of conflict of interest

None.

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