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Short report

Mitral valve prolapse and anxiety disorders

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Summary
We investigated whether there is an association between anxiety disorders and mitral valve prolapse. We compared mitral valve prolapse prevalence in individuals with panic disorder ($n=41$), social anxiety disorder ($n=89$) and in healthy controls ($n=102$) in an attempt to overcome the biases of previous studies. Our results show no associations between panic disorder or social anxiety disorder and mitral valve prolapse, regardless of the diagnostic criteria employed, and that the relationship between these conditions seems not to be clinically relevant.

Declaration of interest
None.

For 30 years there has been discussion about the association between mitral valve prolapse and anxiety disorders, especially panic disorder and social anxiety disorder, but the evidence to date has been insufficient to establish or definitively exclude this association.[1,2] The prevalence of mitral valve prolapse in panic disorder has been reported to range between 0% and 57%,[2] and to reach 26.7%[3] in social anxiety disorder. The validity of existing results is subject to important sample biases, widely differing diagnostic criteria for mitral valve prolapse, lack of diagnostic reliability and investigators who are not masked to the participants' diagnoses.

Although the current diagnostic criteria for mitral valve prolapse were redefined at the end of the 1980s, none of the studies investigating this cardiac condition in association with anxiety disorders have used this criteria.[2] This study compared the prevalence of mitral valve prolapse in people with social anxiety disorder and panic disorder with that of healthy controls in an attempt to overcome the biases of previous studies.

Method

Participants in the social anxiety disorder and healthy control groups were selected from 263 participants of a previous study that assessed the prevalence of psychiatric comorbidities in social anxiety disorder among university students.[4] The panic disorder group was selected from 50 individuals followed up at the Ribeirão Preto University Hospital. Exclusion criteria comprised the presence of organic brain syndromes, lifetime psychoactive substance misuse and current use of psychoactive substances (medication, alcohol, drugs), current general medical conditions and other psychiatric disorders (except for remitted depressive episodes and specific phobias). Diagnoses were confirmed with the Structured Clinical Interview for DSM-IV (SCID).[5] The study was approved by the local ethics committee and all participants gave informed consent.

From the initial samples, 78 individuals were excluded because of the presence of other psychiatric disorders and 3 refused to participate. The groups were as follows: (i) social anxiety disorder: $n=89$; mean age 23.4 years (s.d. = 4.14); 59 (66.3%) were female; mean education 11.93 years (s.d. = 1.05); mean duration of illness 11.03 years (s.d. = 5.30); (ii) panic disorder: $n=41$; mean age 37.8 years (s.d. = 9.03); 19 (46.3%) were female; mean education 11.59 years (s.d. = 3.57); mean duration of illness 11.12 years (s.d. = 7.89); (iii) control: $n=102$; mean age 22.3 years (s.d. = 2.69); 67 (65.7%) were female; mean education 11.91 years (s.d. = 0.95).

Participants were evaluated by two cardiologists who specialised in echocardiography and who were masked to the group assignment. Echocardiography was performed at the Doppler Echocardiography Laboratory of the Ribeirão Preto University Hospital, and mitral valve prolapse diagnosis was based on currently standardised criteria[6] that define the presence of prolapse when one or both mitral valve leaflets present a superior displacement of more than 2 mm during systole in relation to a line connecting the annular extremities in the parasternal or apical long-axis view (PLAX).[6,7] The participants were also evaluated according to two older criteria: (i) a two-dimensional evaluation using an apical four-chamber view (Ap4C): abnormal superior systolic movement ($\geqslant 2$ mm) of mitral valve leaflets, with prolapse displacement below the annular plane and into the left atrium; (ii) a unidimensional evaluation using M-mode: posterior systolic movement of the mitral valve $\geqslant 3$ mm.

Quantitative measurements of valve thickness and of the displacement of mitral valve leaflets in the PLAX and Ap4C views were analysed as continuous data. The Hakim & Grahame questionnaire[8] was used to evaluate the presence of joint hypermobility, a benign connective tissue alteration that may act as a confounding variable in mitral valve prolapse and anxiety disorders.[2,8] None of the participants was taking cardiovascular medication. Data were analysed using Fisher's exact test, *t*-test for two independent samples, and one-way analysis of variance with Duncan's *post hoc* comparisons. The level of statistical significance was set at $P\leqslant 0.05$.

Results

The prevalence of mitral valve prolapse obtained with the PLAX view in the control group (1.0%) was not statistically different from that in the panic disorder (2.4%, $P=0.49$) and social anxiety disorder (4.5%, $P=0.19$) groups, as well as for the mean valve displacement and the prevalence of any valve displacement beyond the annular extremities during systole (online Table DS1).

Additional data related to mitral valve morphology and function included the presence of elongated chordae tendineae and mitral regurgitation, which were statistically similar across groups. Cases of mitral regurgitation were classified as mild or minimal, regardless of group. Valve thickness was also similar in all groups. Importantly, among those participants diagnosed with mitral valve prolapse, only one presented mitral regurgitation (classified as mild), and two had elongated chordae tendineae. No volunteers had significant valve thickening or classic prolapse (valve thickening >5 mm) (online Table DS1). No differences were observed among the groups regarding the presence of joint

hypermobility (panic disorder: 39.0%; social anxiety disorder: 42.7%; control: 47.1%).

For the purpose of comparison with previous studies, echocardiography examinations included measures in the Ap4C view and M-mode, although these methods are currently considered inadequate for the diagnosis of mitral valve prolapse.[2,6,9] In the Ap4C view, mean valve displacement and presence of systolic valve displacements above the mitral annulus were measured, with no significant differences between groups. When the prevalence of mitral valve prolapse established using this method was compared, healthy controls had higher values (10.8%) than the panic disorder (2.4%) and social anxiety disorder (4.5%) groups, although this difference was not statistically significant ($P = 0.18$). Similarly, no differences were found across groups when examinations were performed using M-mode (control: 4.9%; panic disorder: 2.4%, $P = 0.67$; social anxiety disorder: 6.7%, $P = 0.76$) (online Table DS1).

The agreement between the three echocardiography methods was low. Among those with mitral valve prolapse confirmed using the PLAX view, only half were diagnosed when M-mode was used and none in the Ap4C view. Additionally, the prevalence of mitral valve prolapse in the total sample was higher when the older projections were used (PLAX: 2.6%; Ap4C: 6.9%; M-mode: 5.2%).

Discussion

To the best of our knowledge, this is the first study investigating the association between mitral valve prolapse and panic disorder and social anxiety disorder using current diagnostic criteria for mitral valve prolapse. Our main finding was the absence of differences in the prevalence and continuous echocardiography measures of mitral valve prolapse among groups, whether using current or older diagnostic criteria. The prevalence rates of mitral valve prolapse were consistent with those of previous studies (2–3%).[6,7,10]

The diagnosis of mitral valve prolapse in the total sample was more frequent when older diagnostic criteria were used (twice as prevalent in M-mode and almost threefold more prevalent in the Ap4C view). Reliability across the methods was low, consistent with the results of earlier investigations.[6,9] Moreover, no group differences were found in terms of the presence of joint hypermobility, which could act as a confounding variable in the association between mitral valve prolapse and anxiety disorders.[2] The fact that the instrument used is a screening tool to assess the presence of joint hypermobility as a symptom, and not necessarily of the joint hypermobility syndrome, may explain the high rates of joint hypermobility observed in our sample.[9]

Cardiology and psychiatry guidelines and handbooks still mention the possible association between mitral valve prolapse and anxiety disorders. Psychiatrists commonly see individuals with panic disorder, social anxiety disorder or other anxiety disorders who have undergone cardiac evaluation and have been diagnosed with mitral valve prolapse. Using more accurate measures, a substantial proportion of such people might not fulfil the current criteria for the diagnosis of mitral valve prolapse.[2,9] It should be noted, however, that the present study did not assess anxiety in people with mitral valve prolapse, which affects its clinical significance. It can be hypothesised that if individuals with mitral valve prolapse are more anxious, this might enhance their self-perception and motivate the search for treatment; whereas if individuals with anxiety disorders suffer from mitral valve prolapse more often, they might live for years with an untreated cardiac abnormality that may have clinical consequences in the long run.

The main methodological limitations of our investigation concern the sample size and the fact that the panic disorder group was not balanced with the other two groups in terms of age and gender. However, considering the effect size of 2 mm (s.d. = 0.5mm),[7] the sample included in each study group was large enough to reach the power of 0.8. One possible reason for the imbalance in age and gender across groups is that participants in the social anxiety disorder group were selected from a previous study of university students, whereas participants in the panic disorder group were selected from individuals followed up at the university hospital. Nevertheless, no potential outliers were identified that could have influenced the results. Also, existing evidence from cohort studies on cardiovascular diseases shows that prolapse is not associated with gender or age, having a similar distribution over the different decades of life according to the current diagnostic criteria.[10] Our results remained unchanged when the analyses were covaried for gender and age.

In conclusion, we found no associations between panic disorder or social anxiety disorder and mitral valve prolapse, and all valve abnormalities found were either small or borderline, regardless of the diagnostic criteria employed. The purported relationship between these conditions appears to be a matter of chance and the result of a confluence of factors.

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