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Editorial

Sudden Cardiovascular Death in Young Patients With Aortic Dissection. What Lessons Should We Learn?

Muerte súbita por disección de aorta en el joven. ¿Qué deberíamos aprender?

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Aortic dissection is one of the most serious cardiovascular complications and is associated with high mortality, especially when the ascending aorta is affected. The true incidence of aortic dissection is difficult to establish. Although aortic dissection has been thought to affect 2.9 to 3.5 per 100,000 population/y,[1,2] recent epidemiological studies have shown a substantially higher incidence.[3,4] A Swiss study, [4] which included clinical diagnosis as well as autopsy results of out-of-hospital sudden cardiac death, reported an incidence of thoracic aortic aneurysms and dissections of 16.3/100 000 population/y. One of the variables that determines the incidence of aortic dissection is the age range of the population studied. The study by Malmö[4] included more than 30 000 patients aged > 65 years and found an aortic dissection incidence of 15/100 000 population/y, 5 times higher than previously thought.[5]

There is very little evidence available on the incidence and characteristics of aortic dissection in young people. Classic studies indicated that fewer than 3.5% of dissections occurred in individuals aged ≤ 21 years.[6–8] In a retrospective analysis of the SPARCS database,[8] which included 12 142 dissections from a period spanning more than 10 years, only 45 cases (0.43%) occurred in patients younger than 21 years. Of these cases, 82% were male and 42% were of traumatic etiology. Marfan syndrome was the second most common cause (24%), and no cause was identified in 22% of the population studied. The mortality rate for dissection was 13% in young patients, similar to the 16% rate for the whole aortic dissection patient series. In the IRAD hospital registry,[9,10] 7% of patients were younger than 40 years, and in RESA-II, 2.6% of the 629 patients included were younger than 35 years.[11] These hospital registries only include patients admitted to hospital but do not provide information on patients who die before arrival. The Oxford Vascular Study (OXVASC)[12] concluded that close to 50% of patients with aortic dissection died before being diagnosed in hospital. A study published by Morentin Campillo et al.[13] analyzed the incidence of dissections and the characteristics of patients younger than 35 years who died before receiving a diagnosis of aortic dissection in hospital, and who therefore underwent autopsy. Traumatic dissections were excluded. Aortic dissection represented 5.4% of all autopsies performed due to sudden death in this age range, and of 465 sudden deaths due to aortic dissection, 7.5% were younger than 35 years. The authors determined that the incidence of sudden death due to aortic dissection in patients < 35 years was 0.09 cases per 100 000 population/y in the general population in the 3 autonomous communities that participated in the study. However, this finding reflects out-of-hospital mortality, but does not include in-hospital mortality. Therefore, the true incidence of aortic dissection remains to be determined since, in addition to patients with sudden cardiac death diagnosed at autopsy and those diagnosed in hospital, we must consider those who have a dissection but do not die or attend a hospital. This information is impossible to obtain, although considering that most dissections affect the ascending aorta, particularly in young patients, this situation should be rather exceptional.

Although the factors predisposing to aortic dissection are well established, they can vary in relation to the patient's age. In adults, hypertension and atherosclerosis are the most frequent, yet in young people the risk factors can vary substantially. Excluding trauma, the most frequent cause of aortic dissection in young patients in the IRAD[10] and SPARC[8] registries were genetic diseases such as Marfan syndrome (40%). Other prevalent factors were congenital cardiovascular anomalies and the use of cocaine, crack, or amphetamines (such drug use can lead to a severe increase in blood pressure). In the study by Morentin Campillo et al.,[13] 51% of the patients who had sudden death due to aortic dissection had a risk factor, and when the postmortem findings, such as cardiovascular anomalies, Marfanoid phenotype, or the presence of cocaine on the toxicology analysis were taken into account, they found that 80% of these young patients who had died had some predisposing factor. Both in this series and in other published cases, it is not uncommon for some of these predisposing factors, especially congenital heart disease or hereditary diseases, to be diagnosed at autopsy. Unlike clinical series, this series, which included autopsy assessment, found that 43% of patients had a bicuspid valve, 11% had a Marfanoid phenotype, and 9% had coarctation of the aorta.

One of the most striking findings in this series has to be the high incidence of bicuspid aortic valve, found in 14 patients (43%). Although it is well established that patients with a bicuspid valve may have a risk of aortic dissection 8 times higher than the general population, this risk is still low, at around 3 cases/10 000 patients/y, and only increases significantly, to 44.9 cases/10 000 patients/y, when the diameter of the ascending aorta is greater than 45 mm.[14] In the study by Morentin Campillo et al.,[13] 11 of the 14 patients with bicuspid aortic valve had aortic dilatation, although only in 4 cases was this greater than 50 mm. These findings must

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be interpreted with caution, given that the study did not provide detailed information on aortic diameter. In IRAD, 9% of the patients younger than 40 years with aortic dissection had a bicuspid valve versus just 1% of patients older than 40 years ($P < .0001$).[9,10] The high incidence of bicuspid valve at autopsy in young patients with sudden cardiac death must also be interpreted with caution, as there were other predisposing factors in 8 of them, including Turner syndrome in 2 patients, coarctation of the aorta in 1, Marfanoid habitus in 1, previous aortic valve surgery in 1, renal failure on dialysis in 1, and cocaine use in 2. However, in 4 of the remaining 6 patients with no predisposing factors, a diagnosis of left ventricular hypertrophy was made, which could indicate a history of hypertension or idiopathic aortic valve disease. Therefore, these findings do not allow us to conclude that a bicuspid valve necessarily confers a high risk of aortic dissection, since there were usually other predisposing factors that could have played a stronger role in causing the aortic dissection.

Another finding of note in this study, which was not studied in great detail in other autopsy series, is that cocaine could have acted as a predisposing factor in 6 male patients: 5 who were known to have taken cocaine (2 with positive toxicology) and 1 other who was not known to have taken it, but who had positive toxicology. Some clinical series have demonstrated an association between cocaine use and aortic dissection.[10]

Diagnosing aortic dissection in the emergency department is not easy and requires a high index of clinical suspicion, particularly in young patients. Symptoms are often interpreted as atypical chest pain of unknown cause or related to other conditions. One of the most interesting aspects of the study by Morentin Campillo et al.[13] is that, before dying, 24 patients had some symptom that could be associated with aortic dissection. Chest pain was the most frequent symptom and was reported in 12 patients, back pain in 3, abdominal pain in 3, and pain in the neck region in another 3; 16 patients (67%) sought medical attention, but aortic dissection was not suspected in any of them, even though 1 patient had known risk factors for aortic dissection. Some of the symptoms reported were classified as nonspecific mechanical chest wall pain, acute pericarditis, esophagitis, gastroenteritis, and renal colic. Clinical suspicion of this serious complication has increased significantly in recent years, and advances in imaging techniques now provide fast, accurate, and accessible diagnosis. Nonetheless, we are still far from the systematic application of the clinical guidelines on the diagnosis and treatment of aortic disease,[15] which recommended using a scoring system based on evaluation of risk factors, pain characteristics, and clinical examination findings. These recommendations have proven very useful in clinical practice,[16] and we must insist on their use not only in emergency departments but also in primary care. One of the key messages of this study is that more than half of the patients sought medical attention yet serious cardiovascular disease was not suspected. The study does not allow us to analyze the pain characteristics or examination findings; nonetheless, it is essential to increase clinical suspicion from a detailed history and full examination of the patient, if possible with a screening echocardiogram and, if in doubt, to send the patient to the emergency department promptly.

Another interesting finding is that all of the dissections were Stanford type A with pericardial rupture. None of the cases affected the descending aorta exclusively (Stanford type B), and only 6 cases, of the 20 in whom this information was available, involved extension to the abdominal aorta. Although type A dissection is more common than type B (65%-70% of dissections), it is surprising that all were type A and only 6 extended to the abdominal aorta. In published clinical series, this extension pattern occurs in less than 20% to 30%.

There is little information on the risk of dissection or aortic rupture in children and young people with aortic disease involving aortic dilatation. Unlike aortic aneurysms in adults, in young patients, the aortic diameter that confers a high risk of complications is unknown. Likewise, the cutoff points for indication for surgical treatment are not well established. For adult patients, absolute aortic diameter values are used to assess the risk of aortic complications and as an indication for surgery, set at 45, 50, or 55 mm, depending on the disease and concomitant risk factors. However, in children and young patients, who are still growing, it is essential to normalize these values for the body surface area and the z-score.[17] Some authors deem that surgery is indicated when the aorta is double its normal diameter in the absence of other risk factors, and when it is 1.5 times its normal value if other risk factors or significant valve disease are present. Currently, there are no studies that allow us to confidently define the right strategy for aortic disease in children and young people.

Although aortic dissection has, very rarely, been described in children, in this study, there were no patients who had sudden cardiac death and aortic dissection who were aged younger than 19 years. This supports the concept that risk of dissection is low in children and that most relate to syndromic genetic disease that is investigated and followed up in hospital.

The article by Morentin Campillo et al.[13] contributes significantly to the knowledge on aortic dissection in a population subgroup in whom there is little information. This study confirms the low incidence of sudden death secondary to this disease in young patients and demonstrates that the risk factors for aortic dissection differ from those in adults. The main risk factors included congenital cardiovascular anomalies such as bicuspid valve, coarctation of the aorta, Noonan syndrome, Marfanoid phenotype, and a not insignificant incidence of cocaine use. Although this was a historic series that began in 1991, the current vision of the subject is lacking a postmortem genetic study. Identifying a genetic cause would allow other family members to undergo testing, which would help ensure appropriate treatment and follow-up and, in turn, improve prognosis.

The study shows that more than half of the patients sought medical attention for their symptoms but were not diagnosed or sent to the emergency department. These findings alert us to the need to increase clinical suspicion of this cardiovascular disease and take a thorough history and physical examination before labeling the symptoms as nonspecific or secondary to other more trivial conditions. Considering the high number of patients with aortic dissection who die before reaching hospital, it would be very interesting to be able to analyze the over-30-year-old population in whom this disease results in sudden death. We do not have any other way to determine the number and particularly the characteristics of aortic dissections that are not recorded in clinical registries created from hospital data.

CONFLICTS OF INTEREST

None declared.

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