recommended by most professionals. To date, several protocols described for this purpose have included ACS patients treated by stent placement.[2] Nonetheless, aspirin desensitization may not always be possible: lack of resources at certain times (it must be done in an intensive care unit), clinically unstable patient, ongoing acute hypersensitivity reaction (asthmatic or angioedema), or a recent anaphylactic reaction.

Triflusal is a drug of the salicylate family that possesses a trifluoromethyl group, a characteristic that differentiates it from aspirin. In contrast to aspirin, triflusal inhibits cyclic adenosine monophosphate phosphodiesterase (cAMP) and cyclic guanosine monophosphate (cGMP). It is as effective as aspirin for inhibiting platelet cyclooxygenase 1 (COX-1), but it is able to maintain endothelial COX-2 expression levels.[3] Triflusal has been mainly investigated in relation to peripheral vasculopathy or cerebrovascular disease; to date, the published results in cardiovascular disease are limited. In 1 multicenter study including more than 2000 patients, triflusal was not inferior to aspirin with regard to mortality, reinfarction, or the need for repeat revascularization in acute myocardial infarction patients.[4] Furthermore, even though it is a member of the salicylate family, triflusal has proven to be safe for patients with aspirin hypersensitivity leading to exacerbation of respiratory disease.[5] In a recent study including 127 patients with a history of aspirin intolerance or hypersensitivity, 8 patients (6.3%) were treated with triflusal and 1 with thienopyridine following implantation of a coronary stent. There were no cases of stent thrombosis during the time patients were receiving DAPT, and the infarction and mortality rate at 3 years of follow-up was 3.1%.[6]

In the present series of patients with aspirin hypersensitivity treated with a coronary stent, triflusal use was associated with low rate of adverse events at long term, and there were no cases of stent thrombosis in the first year or hypersensitivity reactions to triflusal.

The main limitation of this study is the small number of patients included. In addition, aspirin challenge testing to confirm hypersensitivity was carried out in only 20% of patients, a limitation related to the retrospective nature of the study.

The association of aspirin hypersensitivity and ischemic heart disease requiring DAPT is not common in our daily practice, but it could pose a problem for adequate treatment. If aspirin desensitization cannot be carried out, triflusal use seems to be a safe and effective alternative.

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Marfan Syndrome and Loeys-Dietz Syndrome in Children: A Multidisciplinary Team Experience

Síndrome de Marfan y síndrome de Loeys-Dietz en la edad pediátrica: experiencia de un equipo multidisciplinar

To the Editor,

The main cause of morbidity and mortality in Marfan syndrome (MS) and Loeys-Dietz syndrome (LDS) is progressive aortic root dilatation.[1,2] Family study is crucial for both early diagnosis and genetic assessment: relatives should be seen by a specialized multidisciplinary team.

We present our experience with the treatment and follow-up of pediatric patients with a diagnosis of MS or LDS. From 2005 to 2016, we followed up 64 pediatric patients in pediatric cardiology: 52 (81%) with classic MS, 2 (3%) with neonatal MS, and 10 (16%) with LDS. Coordinated care involving geneticists, adult cardiologists, ophthalmologists, orthopedic surgeons, and rehabilitation medicine specialists is essential for the comprehensive care of these families.

Fifty-two patients met the criteria for classic MS according to the Ghent criteria.[3] Half of these patients (55.8%, 29/52) were investigated due to a known family history, including intrauterine history. The other half (44.2%, 23/52) were diagnosed due to their peculiar phenotype. Of these, 12 (18.8%) were de novo cases with negative genetic studies in both parents; 10 (15.6%) were index cases leading to a diagnosis in another relative. One patient was adopted and therefore the family history was unknown. In summary, 75% had an affected relative, data that coincide with the literature.[2]

Most of the patients had confirmed *FBN1* mutations (80.8%) or a study in-progress (n = 2). Seven patients did not undergo genetic testing because they met clinical and family history criteria.

Sixty-seven percent of the patients had dilatation of the sinuses of Valsalva (SV) (Table). This finding agrees with the data in the literature, which describes progressive dilatation in 50% to 83% of pediatric patients.[2] The indications for starting treatment were an aortic size adjusted by z-score[4] $> +2$, except for patients younger than 12 years, in whom slight dilatations were tolerated due to the low risk of dissection. Beta-blockers and

Table
Echocardiographic and Pharmacological Treatment Data

	Classic MS	Neonatal MS	LDS	*P*[a]
Patients, n	52	2	10	
Age at diagnosis, y	10.3 ± 4.2	0.2 ± 0.2	11.6 ± 5.7	.39
SV ≥ 2 SD	34 (67.3)	2 (100)	9 (90.0)	
SV diameter, mm	30.6 ± 1.0	23.0 ± 2.8	36.7 ± 10.3	.01[b]
SV (z-score)	+2.7 ± 1.6	+6.3 ± 1.1	+5.2 ± 1.8	<.001[b]
AA ≥ 2 SD	11 (22.0)	1 (50.0)	3 (42.9)	
AA diameter, mm	22.5 ± 5.5	15.5 ± 3.5	23.9 ± 5.4	.50
AA (z-score)	+1.0 ± 1.7	+3.7 ± 2.6	+2.5 ± 1.8	.02[b]
Treatment	28 (53.8)	1 (50.0)	9 (90.0)	
Beta-blocker	8 (22.9)	1 (50.0)	3 (30.0)	
ARB	18 (51.4)	0	5 (55.6)	
ARB + beta-blocker	2 (5.7)	0	1 (10.0)	

AA, ascending aorta; ARB, angiotensin II receptor blocker; LDS, Loeys-Dietz syndrome; MS, Marfan syndrome; SD, standard deviation; SV, sinuses of Valsalva.
Unless otherwise indicated, data are expressed as No. (%) or mean ± SD.
[a] Compares classic MS with LDS, Student *t* test for independent data.
[b] Statistically significant result.

angiotensin II receptor blockers have been reported as equally effective in adults[5] and they were prescribed equally in our patients (Table).

No patients died, and 2 required pediatric cardiac surgery (3.8%): 1 adolescent aged 13.3 years required a David procedure for aortic root replacement (SV, 47 mm; z-score, + 6.3) and 1 child aged 6 years required mitral valve replacement for severe mitral regurgitation.

The 2 patients with neonatal MS were diagnosed at birth and had a rapidly progressive clinical course. Neither had a positive family history. One died at 4.5 months, following mitral valve replacement for severe mitral regurgitation. The other is in the first year of life, with severe aortic root dilatation and moderate-severe mitral and tricuspid regurgitation that is being treated medically. Neonatal MS is uncommon and has a very severe phenotype, with aortic root dilatation in 93% and a mortality reaching 95% in the first year of life.[2]

The 10 patients with LDS diagnosed in childhood came from 8 families. Two siblings were diagnosed following the sudden death of their mother due to aortic dissection. At 12.5 years, the younger sister died due to aortic dissection (SV, 49 mm; z-score, + 7.3); she had previously declined a preventative intervention. The older brother underwent a David procedure for aortic root replacement at 14 years of age (SV, 41 mm; z-score, + 5.4) but died 5 years later due to subarachnoid hemorrhage. In the other 7 families, there were 8 affected individuals: 3 of them were diagnosed because they had affected relatives, 3 were de novo cases, and 2 were index cases leading to diagnosis in their relatives. All the patients had a positive genetic study (4 *TGFBR1*, 5 *TGFBR2*) with the exception of the adolescent who died before undergoing genetic study (her bother had a *TGFBR1* mutation).

The SV and ascending aorta dilatation was significantly more severe in the patients with LDS than in the patients with MS (Table). Only 1 patient (13 years old) had a normal sized aorta.

All patients with LDS and dilatation (z-score[4,6] > + 2) received treatment with angiotensin II receptor blockers (Table). Three patients (30%) required cardiac surgery, at 12, 14, and 17 years, in the form of aortic root replacement: 2 underwent a David procedure (SV, 42 and 41 mm; z-score, + 4.7 and + 5.4 respectively) and 1 underwent a Bentall procedure (performed in another hospital). Only 1 patient died before adulthood (the patient who declined intervention).

Loeys-Dietz syndrome confers an increased risk of aortic dissection and cerebral hemorrhage, even in childhood.[1] Regular imaging checks of the entire arterial tree are recommended, preferably with magnetic resonance angiography in children.

In conclusion, the follow-up of patients with MS and LDS in specialized hereditary heart disease units is essential for the comprehensive care of these families. In up to 20% of these pediatric patients, follow-up led to the diagnosis of an affected relative, and 55% of the pediatric patients were diagnosed because they had an affected relative. Diagnosis and treatment at an early age can change the natural course of the disease, which can be particularly severe and rapid in neonatal MS and LDS.

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Miniaccess Heart Surgery. A Spanish Multicenter Registry

Cirugía cardiaca mediante mínimo acceso. Registro multicéntrico español

To the Editor,

Minimally invasive surgery is performed in many Spanish centers, but few articles give the impression that these techniques are widely used in Spain.[1,2] We present an analysis of the data compiled in a Spanish registry including 15 centers where minimally invasive surgery is performed, mainly for aortic valve replacement and mitral valve repair or replacement (Table 1).

In total, 1245 patients undergoing on-pump surgery were analyzed. Aortic valve replacement was performed using a ministernotomy as the preferred approach in 963 patients (Ao group) and mitral valve replacement, mitral repair, or another procedure was performed using a right anterior minithoracotomy in 282 patients (MT group).

The preoperative variables in both groups are shown in Table 2. The preferred technique in the Ao group was a ministernotomy, used in 945 patients (98%), which consisted of a vertical incision measuring 6 to 12 cm (in 75%, 7–8 cm) in the most cephalad portion of the sternum. Only 2% underwent surgery using a right anterior minithoracotomy approach, described as being as effective as ministernotomy for aortic valve replacement, but technically more demanding.[3]

Table 1
Centers Participating in the Registry, With the Number of Patients Included per Center

Hospital	Ao group	MT group	Total
Complejo Hospitalario de A Coruña	212	0	212
Clínico Universitario Virgen de la Arrixaca, Murcia	167	37	204
Princesa, Madrid	90	25	115
12 de Octubre, Madrid	0	112	112
Virgen de la Victoria, Malaga	64	41	105
Germans Trias i Pujol, Badalona	102	0	102
Puerta de Hierro, Madrid	92	0	92
Sant Pau, Barcelona	70	15	85
Virgen Macarena, Seville	80	0	80
Virgen del Rocío, Seville	20	38	58
Hospital Infanta Cristina, Badajoz	46	5	51
Bellvitge, L'Hospitalet de Llobregat	7	7	14
Hospital de Navarra, Pamplona	8	0	8
Vithas Xanit Internacional, Malaga	4	0	4
Hospital Son Espases, Palma de Mallorca	0	2	2
TOTAL	962	282	1.244

Ao group, valve replacement alone, using a miniaccess; MT group, right anterior minithoracotomy for mitral replacement/repair, tricuspid repair, atrial septal defect closure, or atrial myxoma resection

Patients in the MT group underwent surgical treatment through a right anterior minithoracotomy for the following purposes: mitral valve replacement in 48%, mitral valve repair in 27%, closure of an atrial septal defect in 15%, and myxoma resection in 5%. The tricuspid valve was treated in 10% of patients.

The procedure-related information and data on morbidity and mortality in both groups are shown in Table 2. The revision rates for bleeding were low (Ao, 2.80% and MT, 3.90%). The rate of surgical wound infections was also reduced, with a value of only 1.80% in both groups.

Current technological advances, such as transesophageal echocardiography (regularly used in many types of cardiac procedures in almost all centers performing cardiac surgery), new instrumentation specifically designed for small approaches, and thoracoscopy techniques that provide excellent vision, have allowed the development of miniaccess surgery without increasing operative risk. Aortic and mitral valve surgery using small incisions has several advantages: lower bleeding rates, transfusion requirements, and wound infection rates; fewer respiratory complications; and shorter intensive care unit stay and overall length of hospital stay.[4] The pioneers of the technique in Cleveland analyzed 832 patient pairs[5] and found no significant differences in mortality, which was very low (0.96% in both groups). However, they reported differences in the number of bleeding episodes, transfusions, respiratory complications, and the percentage of patients extubated in the operating room in the ministernotomy group, as well as postoperative pain reductions, shorter hospital stay, and shorter duration of on-pump circulation and aortic clamping. Furthermore, all these advantages imply a significantly lower in-hospital cost expenditure per patient.

Similar advantages have been described for the MT approach, which is associated with reductions in morbidity and mortality, length of hospital stay, and repeat interventions for bleeding, as well as less pain, faster recovery, and, of course, evident aesthetic advantages that are particularly appreciated by younger patients.[6]

In the database analyzed, mortality in the Ao group was lower than would be expected attending to the logistic EuroSCORE and EuroSCORE IIrisk scores: the median [interquartile range] was 1.5% vs 5 [3-7] and 2 [1-3], respectively. Similar results were found in the MT group, which had an observed mortality of 2.20%, whereas the expected mortality was 2.7% [1.5-6.8] for the logistic EuroSCORE and 1.7% [0.8-2.3] for EuroSCORE II.

An analysis of the patients undergoing surgery starting from 2014 showed an even greater reduction in mortality. In the Ao group, the observed mortality was 1.2% whereas the expected mortality was 5.86% [3.40-8.44] according to the logistic EuroSCORE and 1.76% [1.16-2.87] according to EuroSCORE II. There were similar findings in the MT group, where the observed mortality starting from 2014 was 1.6%%, whereas the median risk was 2.08% [0.98-4.38] determined by the logistic EuroSCORE and 1.76% [0.98-2.48] by EuroSCORE II.