

According to therapeutic positioning reports published by the Spanish Agency of Medicines and Medical Devices (AEMPS), PCSK9 inhibitors are funded by the public health care system when used in patients with atherosclerotic cardiovascular disease and LDL-C > 100 mg/dL.⁵ Accordingly, and even though bempedoic acid can be combined with PCSK9 inhibitors to improve LDL-C control,³ the subgroup of patients who would derive the greatest benefit from bempedoic acid treatment would be those with an LDL-C level above recommended targets (> 70 mg/dL in our study) but below 100 mg/dL.⁴ Our results show that much remains to be done to optimize lipid-lowering therapy, and we believe that bempedoic acid can contribute to LDL-C goal attainment. Combination therapy with ezetimibe and bempedoic acid might be particularly beneficial in patients not taking statins because of intolerability issues (6% of all patients), with estimates showing an overall reduction of 38% in LDL-C.³ Addition of bempedoic acid to high-intensity statins plus ezetimibe (used in 16% of all patients) could result in an additional 7% reduction (and an overall reduction of 72% from baseline).³ Finally, patients on high-intensity statins (22%) would stand to benefit from an additional reduction of 15% if also treated with bempedoic acid, and ezetimibe could be added in certain cases.

Our results show that a significant proportion of patients could benefit from bempedoic acid. Considering that stricter LDL-C goals have now been introduced, the potential reductions are even higher (in the DA VINCI study, LDL-C goal attainment decreased from 45% to 22% in secondary prevention patients).² Because bempedoic acid is a prodrug that requires activation by long-chain acyl-CoA synthetase 1, which is expressed in the liver but not the muscles, it carries a lower risk of adverse muscle effects and may therefore provide added value as a long-term treatment due to better tolerability.³ While the ongoing CLEAR Outcomes study will clarify the effects of bempedoic acid on cardiovascular events, analysis of secondary outcomes from other studies suggests that this drug is associated with a lower risk of cardiovascular complications and new-onset diabetes.⁶

In brief, bempedoic acid is a new class of agent that will undoubtedly contribute to improved lipid control, especially in patients at higher cardiovascular risk.

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AUTHORS' CONTRIBUTIONS

V. Barrios and C. Escobar analyzed the data and wrote and approved this manuscript.

CONFLICTS OF INTEREST

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REFERENCES

1. Barrios V, Soronen J, Carter AM, Anastassopoulou A. Lipid management across Europe in the real-world setting: a rapid evidence review. *Curr Med Res Opin.* 2021;37:2049–2059.
2. Ray KK, Molemans B, Schoonen WM, et al. EU-wide cross-sectional observational study of lipid-modifying therapy use in secondary and primary care: the DA VINCI study. *Eur J Prev Cardiol.* 2021;28:1279–1289.
3. Escobar C, Barrios V, Ariza A, Campuzano R, Gámez JM, Mostaza JM. Empleo del ácido bempedoico en los pacientes con dislipemia. Una aproximación práctica. *Rev Esp Cardiol Supl.* 2021;21(C):1–7.
4. Anguita Sánchez M, Gómez Doblas JJ, Barrios Alonso V. Grado de control del cLDL tras un síndrome coronario agudo en España. ¿Se utilizan adecuadamente los recursos terapéuticos existentes? *Rev Esp Cardiol.* 2021;74:194–196.
5. Barrios V, Escobar C, Arrarte V, et al. Análisis del proceso de prescripción de inhibidores PCSK9 en los servicios de cardiología de los hospitales españoles y propuesta de optimización. Estudio IKIGAI. *Clin Investig Arterioscler.* 2021;33:296–305.
6. Wang X, Zhang Y, Tan H, et al. Efficacy and safety of bempedoic acid for prevention of cardiovascular events and diabetes: a systematic review and meta-analysis. *Cardiovasc Diabetol.* 2020;19:128.

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Survival after out-of-hospital cardiopulmonary resuscitation before ambulance arrival in the Basque Country



Supervivencia tras reanimación cardiopulmonar extrahospitalaria previa a la llegada del primer recurso asistencial en el País Vasco

To the Editor,

The chances of surviving an out-of-hospital cardiopulmonary arrest (CPA) can be increased by the execution of 1 task by nonprofessional bystanders: immediate activation of the emergency services, good quality cardiopulmonary resuscitation (CPR), and, when possible, the use of a public-access defibrillator.

Execution by bystanders of these first links in the survival chain, without waiting for the ambulance to arrive, can maximize the chances of a successful outcome of subsequent advanced life-support interventions.

The goal of this study was to determine the differences in survival and other epidemiological characteristics between CPA patients who received CPR before ambulance arrival and those who did not.

We report the results of an observational study conducted in the Basque Country. The study population included all CPA patients with an indication for CPR who were attended by the emergency ambulance services between June 2016 and May 2018 (digitized data are not available after this date). The study was approved by the Basque Research Ethics Committee. Informed patient consent was not required because the data were extracted

from an anonymized database. This centralized out-of-hospital CPA database is compiled by the emergency services coordination unit of the Basque Health Service (*Emergentziak-Osakidetza*) from standardized documents provided by the public medical emergency system (*Sistema de Emergencias Médicas*; SEM).

Information was collected on patient sex and age; the place, date, and time of the CPA; the presence of witnesses; whether a nonprofessional bystander performed CPR; and if so whether CPR was initiated with or without telephone support. The study examined in-ambulance electrocardiography data and patient outcome, defined in terms of patient death, immediate survival, and survival to hospital discharge. Outcomes were related to neurological status, assessed according to the Glasgow-Pittsburgh Cerebral Performance Categories (CPC), and to the time elapsed between activation of the SEM and ambulance arrival.

Patient characteristics are presented as absolute numbers and percentages for qualitative variables and as the median [interquartile range] for quantitative variables. Median values were compared by the Kruskal-Wallis test, and associations between qualitative variables were assessed by the chi-square test; differences were considered significant at a 2-sided P value $< .05$.

During the study period, 1603 out-of-hospital CPA patient events requiring CPR were recorded. Of the patients, 923 (57.6%) did not receive CPR before ambulance arrival. Of the remaining patients, 407 (25.4%) were given CPR by a bystander who did not require telephone support, and 273 (17%) received bystander-initiated CPR with telephone support from the SEM.

Bystander CPR was more frequent among patients younger than 65 years (52.7% vs 35.5%; $P < .001$) (table 1). Patients receiving bystander CPR had a higher prevalence of defibrillation rhythms (33.7% vs 19.1%; $P < .001$). Public-access semiautomatic external defibrillators (SAED) were more frequently used by bystanders who did not require telephone support than by those who did (6.8% vs 2.4%; $P < .001$).

Telephone support for CPR was more frequent when the CPA was witnessed (25.6%; $P < .002$) or when the event occurred in the

patient's home (71.1%; $P < .001$). In these situations, there was a longer interval between SEM activation and ambulance arrival.

Bystander CPR initiated without the need for telephone support was associated with better immediate patient survival (35.1%; $P < .001$) and a better clinical condition at discharge (CPC 1-2 in 13% of patients in this category; $P < .001$). There was no difference in survival between patients who received unguided out-of-hospital CPR and those not receiving CPR before ambulance arrival (24.2% vs 26.4% for immediate survival; $P < .45$, 7.8% vs 6.2% for survival to discharge; $P < .39$).

These results demonstrate that the simple act of starting CPR before ambulance arrival does not ensure survival after CPA. Survival after bystander CPR was significantly improved if there was no need for telephone support (probably because the intervening bystander was already familiar with the procedure); however, CPR performed with telephone support did not have the same effect.

To our knowledge, this is the first study published in Spain to stratify survival according to the type of bystander CPR (with or without telephone support). The results contrast with those of another recent study conducted in a different national setting,¹ and indicate that the quality of resuscitation maneuvers performed by bystanders receiving telephone support may not be sufficient to generate cerebral circulation. The insufficient quality of CPR performed by bystanders with no life-support training has been reported previously,² and there is also documented evidence of significant room for improvement in the telephone instructions provided by medical emergency systems.³ A further point of interest is the low rate of SAED use in bystander CPR, despite current legislation authorizing SAED use by members of the public and the mandatory installation of SAED devices at strategic locations⁴; in the Basque Country, there are currently 104 public-access SAED devices per 100 000 inhabitants.

With the aim of improving survival after CPA, Spanish medical authorities have prioritized the installation of public-access defibrillators and the adoption of recommended practice for the

Table 1

Characteristics of cardiopulmonary arrest events according to the type of care received before ambulance arrival

	Total (n = 1603)	No bystander CPR (n = 923)	Bystander CPR		P	Missing records
			No telephone support (n = 407)	With telephone support (n = 273)		
Women	439 (27.4)	274 (29.7)	96 (23.6)	69 (25.3)	.05	0
Age, y	68 [56-79]	71 [59-81]	65 [53-77]	62 [52-73]	< .001	
Age \geq 65 y	917 (57.2)	595 (64.5)	207 (50.9)	115 (42.1)	< .001	
Nocturnal CPR (between 22:00 and 08:00)	343 (21.4)	223 (24.2)	59 (14.5)	61 (22.3)	< .001	0
CPR outside the patient's home	621 (38.8)	325 (35.2)	217 (53.3)	79 (28.9)	< .001	1
Witnessed CPA	279 (17.5)	147 (16.1)	80 (19.7)	70 (25.6)	.002	12
Nontraumatic etiology	1032 (93.8)	561 (92.3)	289 (95.4)	182 (96.3)	.055	503
First detected rhythm nondefibrillable	1198 (74.7)	747 (80.9)	255 (71)	196 (71.8)	< .001	0
Use of a public-access SAED	52 (4.7)	—	46 (6.8)	6 (2.4)	< .001	505
Time elapsed between activation of the medical emergency system and ambulance arrival, min	9.00 [7.00-13.00]	9.00 [7.00-13.00]	9.00 [5.00-13.00]	10.00 [7.00-14.00]	.045	
Clinical outcomes						
Out-of-hospital death	1.150 (71.7)	679 (73.6)	264 (64.9)	207 (75.8)	.001	0
In-hospital death	308 (19.2)	172 (18.6)	87 (21.4)	49 (17.9)	.42	0
Discharge with CPC 1-2	134 (8.4)	69 (7.5)	53 (13)	12 (4.4)	< .001	0
Discharge with CPC 3-4	11 (0.7)	3 (0.3)	3 (0.7)	5 (1.8)	.03	0

CPA, cardiopulmonary arrest; CPC, Glasgow-Pittsburgh Cerebral Performance Category score of patient clinical condition (1-2, no incapacity; 3-4 mild-to-severe incapacity); CPR, cardiopulmonary resuscitation; SAED, semiautomatic external defibrillator. Data are expressed as No. (%) or median [interquartile range].

telephone support of bystander CPR by emergency call centers.⁵ Further efforts are needed, however, to increase skills in CPR technique among members of the general public.

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AUTHORS' CONTRIBUTIONS

S. Ballesteros-Peña designed the study, performed the statistical analysis, and wrote the first draft of the article. M.E. Jiménez-Mercado debugged the database and contributed to text writing. I. Fernández-Aedo contributed to statistical interpretation of the data and to text writing.

CONFLICTS OF INTEREST

None.

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REFERENCES

1. Siman-Tov M, Strugo R, Podolsky T, Rosenblat I, Blushtein O. Impact of dispatcher assisted CPR on ROSC rates: A National Cohort Study. *Am J Emerg Med*. 2021;44:333–338.
2. Ballesteros-Peña S, Fernández-Aedo I, Vallejo-De la Hoz G, Etayo Sancho A, Alonso Pinillos A. Quality of dispatcher-assisted vs. automated external defibrillator-guided cardiopulmonary resuscitation: a randomised simulation trial. *Eur J Emerg Med*. 2021;28:19–24.
3. Ballesteros-Peña S, Fernández-Aedo I, Vallejo-De la Hoz G, Etayo-Sancho A, Alonso-Pinillos A. Analysis of dispatcher-assisted cardiopulmonary resuscitation instructions to laypersons in an out-of-hospital cardiac arrest. *An Sist Sanit Navar*. 2020;43:203–207.
4. Ballesteros-Peña S, Fernández-Aedo I, De la Fuente-Sancho I. Regulación de la desfibrilación externa semiautomática fuera del entorno sanitario en las comunidades autónomas de España: revisión de la situación actual. *Emergencias*. 2019;31:429–434.
5. García-del Águila J, López-Messa J, Rosell-Ortiz F, et al. Recomendaciones para el soporte telefónico a la reanimación por testigos desde los centros de coordinación de urgencias y emergencias. *Med Intensiva*. 2015;39:298–302.

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A new mutation in the ACTA1 gene possibly associated with dilated cardiomyopathy without concomitant myopathy



Una nueva mutación en el gen ACTA1 posiblemente asociada a miocardiopatía dilatada sin miopatía concomitante

To the Editor,

Dilated cardiomyopathy (DCM) is a myocardial disease typified by left ventricular or biventricular dilation and dysfunction that cannot be explained by abnormal loading conditions, and which provokes heart failure (HF), arrhythmias, or sudden cardiac death (SCD). A familial association has been demonstrated in a high percentage of cases, highlighting the importance of genetic studies of family members. We present a family with a previously undescribed mutation in the ACTA1 gene. Informed consent were obtained from all patients and approval was obtained from the ethics committee. Figure 1 shows the family tree.

The index case is a 36-year-old man, with bronchial asthma as the only relevant medical history. His family history includes a paternal grandfather and uncle with SCD, and his father and 2 other paternal uncles with DCM. Onset was a first episode of HF in April 2005. During admission, the patient was diagnosed with DCM, with an echocardiogram showing left ventricular dilation with severely depressed global systolic function and severe mitral regurgitation. Coronary disease was ruled out and, despite treatment optimization, symptoms persisted. The patient underwent follow-up at our HF and Inherited Heart Disease Unit, with progressive deterioration of left ventricular ejection fraction

(LVEF) and, in July 2008, he died after rapidly progressing cardiogenic shock.

In 2019, a 55-year-old man, a cousin of the index patient, was referred to our unit (figure 1, case III.7) for familial screening. His sister (figure 1, case III.5), who was under follow-up at another center, experienced onset of DCM in 2008, and had an implantable cardioverter-defibrillator that produced appropriate shocks during follow-up. A massive parallel sequencing of 121 genes found no presence of pathogenic mutation but did uncover a variant of uncertain significance in the ACTA1 gene. This patient rapidly developed advanced HF, requiring a heart transplant in the same year as diagnosis.

During the same period, a 47-year-old woman attended our clinic (figure 1, case III.16). The patient was the cousin of the index case and cases III.5 and III.7. Cardiac diagnosis tests found a mildly depressed left ventricular ejection fraction (46%) without ventricular dilation, and magnetic resonance imaging showed the presence of linear midmyocardial late gadolinium enhancement of the anteroseptal-septal-inferoseptal and medial basal segments (figure 2).

Cardiac diagnosis tests of case III.7 found no evidence of structural heart disease and targeted genetic testing of both this patient and case III.16 found both to be carriers of the heterozygous variant NM_001100.3:c.757G>A; p. (Gly253Ser) of the ACTA1 gene, which coincided with the mutation previously described in the transplanted patient. During the following year, the familial screening was extended to include first-degree relatives, among whom the most outstanding finding was the 3 daughters of case III.16, who are all ACTA1 mutation carriers but do not currently have associated structural heart disease.