

Level of Compliance with Spanish Guideline Recommendations in the Management of Asthma

Lorena Piñel Jimenez, Álvaro Martinez Mesa, Esther Sanchez Alvarez, Javier Lopez Garcia, Ana Aguilar Galvez, Nuria Reina Marfil, Belen Gómez Rodríguez, Eva Cabrera Cesar, Jose Luis Velasco Garrido

Department of Pulmonology, Hospital Universitario Virgen de la Victoria, Málaga, Spain

Correspondence: Eva Cabrera Cesar, Department of Pulmonology, Hospital Universitario Virgen de la Victoria, Campus de Teatinos, S/N. 29010, Málaga, Spain, Tel +34 646905201, Email evacabracesar@gmail.com

Objective: To describe the clinical management of asthmatic patients and the level of compliance with the *Guía Española para el Manejo del Asma* (GEMA, Spanish Guidelines for Asthma Management) in the influential area of Virgen de la Victoria University Hospital, Málaga (Spain).

Materials and Methods: Descriptive, cross-sectional study in asthma patients from the Virgen de la Victoria University Hospital influential area, Málaga (Spain). Asthma Control Test (ACT) results, demographic and clinical characteristics, and GEMA indicators of quality asthma care were obtained from each participating patient.

Results: Two hundred and eighty-eight patients (64.2% woman, mean age 48.6 years) were included in the study. The evaluation of the level of compliance with the GEMA quality indicators showed that in 20.8% of the patients the diagnosis of asthma was confirmed by spirometry and bronchodilator test, and 52.5% of the patients with suspicion of allergic asthma performed a sensitization test. Among the smoker patients, 76.3% were recommended to stop smoking; 14.2% of the patients received a paper-based educational plan. Regarding asthma treatment, 92.3% of patients with persistent asthma received inhaled glucocorticoids (IGC). IGC and LABA were the most common treatments for asthma, used in combination (IGC + LABA) in 139 (48.3%) patients; 32.6% discontinued SABA treatment during the study period. Asthma was well controlled in 54.9% of the patients (ACT score ≥ 20), and 13.9% of the patients registered exacerbations during the previous year with a mean (SD) of 1.38 (0.74) events.

Conclusion: Most of the GEMA quality indicators of asthma care are not followed in real-world clinical practice. Specialists select the best option among the available treatments but there is an unmet need for training plans in other relevant aspects, such as diagnosis and/or disease monitoring.

Keywords: asthma, asthma control, indicators of quality care, clinical guidelines, asthma management, compliance with guidelines

Introduction

Asthma is a heterogenic chronic disease affecting more than 300 million people worldwide. The estimated prevalence in Spain is ~5%, ranged from 1% in Huelva to 4.7% in Albacete, with a tendency to increase.¹

A substantial number of patients show an inadequate control of the disease, increasing morbidity and mortality and negatively impacting health-related quality of life.²⁻⁴ A poor control of the disease represents an important percentage of the economic cost associated with asthma, estimated in ~1-2% of the total public healthcare resources in developed countries.^{4,5} These factors represent a high burden to the National Health System, and directly affect the patients, their families and society.^{6,7}

Despite the publication of international and national guidelines, such as the Global Initiative for Asthma (GINA) and the *Guía Española para el Manejo del Asma* (GEMA, Spanish Guidelines for Asthma Management),^{8,9} a high number of patients have a poor control of the disease, evidencing a low adherence to the recommendations.^{3,10-13}

In terms of economic burden, it is estimated that ~70% of the disease-associated cost is related to a poor asthma control and management.¹⁴ Therefore, an adequate management of the disease would improve symptom control and

reduce asthma-associated costs, based on the use of preventive anti-inflammatory medication, a better patients' disease-specific education, and a higher adherence to the guidelines' recommendations.^{15–17}

These evidences raised the need to determine the quality of care provided to patients with asthma in the influential area of Virgen de la Victoria University Hospital in Málaga (Spain) through the evaluation of the adherence to the GEMA guidelines. The objective of this study is to obtain real world clinical data to assess routine medical assistance and to find areas of improvement to better control asthmatic patients.

Materials and Methods

Patient Selection Criteria

Adult patients diagnosed with asthma and followed-up in the influential area of Virgen de la Victoria University Hospital, referral hospital in Málaga (Spain), were included in the study after signing the Informed Consent Form. The study was conducted according to the Declaration of Helsinki ethical principles and the Study Protocol approved by the Central Ethics Committee of the Regional University Hospital of Malaga on Aug 3rd, 2020 (code FIM-ASP-2020-01). Eligible patients were adult patients (≥ 18 years old) diagnosed with asthma more than one year before the inclusion in the study with clinical data available for that period. To analyse the routine clinical practice, the exclusion criteria excluded patients who had participated in any clinical trial during the year prior to data collection initiation (study period).

Patient and Public Involvement

To identify the most relevant topics and meaningful outcomes in the study, researchers considered patients' priorities, experience, and preferences and evaluated if the quality indicators of asthma care of the GEMA guidelines were followed in the study population.

Participating patients were offered to obtain information about the study results during their routine medical care upon request. A specific program for the dissemination of the study findings to the general population was not established.

Study Design

Non-Interventional, descriptive, cross-sectional study was conducted in the referral area of Virgen de la Victoria University Hospital (Málaga, Spain).

The main objectives of the study were 1) to describe the clinical management of asthmatic patients in that region and 2) to study the level of compliance with the indicators of quality assistance established by the GEMA guidelines. The indicators analysed were: a) Confirmation of the asthma diagnosis by spirometry with bronchodilator test; b) Sensitization study in allergic asthma; c) Smoking cessation (patients who stopped smoking at least 6 months before the inclusion in the study); d) Educational plan; e) Treatment of choice in persistent asthma [inhaled glucocorticoid (IGC)]; f) Asthma treatment in pregnant women; g) Periodic monitoring of the patients; h) Periodic record of exacerbations.

The secondary objectives were: 1) To describe the sociodemographic and clinical characteristics of the study population; 2) To describe the treatment patterns (maintenance treatment, reliever treatment, type of treatment) during the study period; 3) To describe the level of disease control; 4) To describe the use of health resources (emergency visits, primary care visits, specialist visits) during the study period; 5) To describe the number of patients with short-acting beta agonists (SABA) discontinuation within the last year.

The sample size was calculated based on the criterion of maximum indeterminacy, when the percentage of one category in a categorical variable is expected to be 50%. To estimate a proportion of 50%, with a margin of error of ± 6 percentage points, a confidence level of 95% and 10% non-available data, a sample size of 294 patients was required.

Study Subjects

Patients were included in 8 sites selected among the 31 centres under the influential area of Virgen de la Victoria University Hospital. Site selection was randomized using the RAND() function in Excel program.

Patients selected using the RAND() function in Excel program were informed about the study and invited to participate. Patients included in the study signed the ICF and performed a 5-items Asthma Control Test (ACT).¹⁸ All other study variables were collected from patients' electronic medical records. No additional visits were needed to complete the study.

Analysis

The primary endpoint was the percentage of patients that met each indicator of the GEMA guidelines.

The secondary endpoints were the analysis of demographic and clinical characteristics, such as age, gender, ethnicity, weight, height, body mass index, pregnancy status, smoking status, age at asthma diagnosis and patient's management (primary care/specialized healthcare).

Asthma severity grade was categorized according to the GEMA guidelines as mild intermittent, mild persistent, moderate persistent, and severe persistent.

The level of asthma control was calculated according to clinical criteria (number of SABA canisters and oral corticoids collected from the pharmacy during the study period, number of emergency and primary care visits in the previous year) and ACT score (ACT \geq 20: well-controlled asthma, ACT $<$ 20: uncontrolled asthma). The asthma therapeutic level was determined using the GEMA stepwise approach from Step 1 to Step 6.

Comorbidities included in the Charlson Comorbidity Index (CCI) were collected and the CCI score calculated.

Type and date of asthma treatments initiation, history of asthma exacerbations, and use of healthcare resources during the study period were transcribed from the patient's electronic medical charts. Health resources consumption included visits to the hospital emergency room, primary care and specialist.

For the statistical analysis, mean and standard deviation (SD) were calculated for quantitative data and number of cases and frequency (%) for qualitative data.

Results

Baseline Characteristics of the Study Population

A total of 305 patients were screened for being included in the study. Of them, 17 patients did not meet all the eligibility criteria, with a final sample size of 288 patients. Demographic and clinical characteristics of the participating patients are shown in [Table 1](#).

Level of Compliance with Assistance Quality Indicators Established by the GEMA Guidelines

The quality indicators of asthma care established by the GEMA guidelines were analysed. Level of compliance with the recommendations for each item is shown in [Table 2](#).

Sixty patients (20.8%) performed a spirometry and bronchodilator test at diagnosis, being only the pre-bronchodilator values available in most of the cases (only 3 patients have all post-bronchodilator values available). For these patients, the mean percentage (SD) pre-bronchodilator spirometry forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) was 89.4% (17.07) and 85.73% (16.62), respectively. Mean (SD) FEV1/FVC ratio was 78.15% (23.06). History of allergic asthma was present in 122 patients (42.4%); of them, 64 patients (52.5%) made a sensitization to allergen study.

A total of 38 patients (13.2%) were smokers at study entry. These patients smoked a mean (SD) of 12.05 (8.27) cigarettes a day during a mean (SD) of 25.53 (15.31) years. Twenty-nine of the smoking patients (76.3%) were advised on the importance to stop consuming.

Forty-one patients (14.2%) were registered in an asthma education program that includes indications on how to use the medication in case of symptom appearance. The mean (SD) time since patient attended an educational program was 8.09 (2.94) years.

The treatment of choice for persistent asthma was IGC in 84 patients (92.3%). Forty patients (13.9%) suffered exacerbations during the study prior, with a mean (SD) of 1.38 (0.74) exacerbations per year. Finally, 26 (9.0%) had a scheduled monitoring visit during the study period, with a mean (SD) of 1.73 (1.87) visits per year.

Table 1 Demographic and Clinical Characteristics of the Patients Included in the Study

Characteristics		
Mean age at the time of the study visit (SD) (years)		48.59 (14.91)
Female gender, n (%)		185 (64.2%)
Ethnicity	Asian, n (%)	1 (0.3%)
	Latino or Hispanic, n (%)	15 (5.2%)
	White, n (%)	272 (94.4%)
Mean weight (SD) (kg)		85.83 (22.24)
Mean height (SD) (cm)		161.95 (11.69)
Mean BMI (SD) (kg/m ²)		34.06 (11.36)
Pregnancy status (Yes) (n %)		3 (1.6%)
Mean age at asthma diagnosis (SD) (years)		34.64 (16.25)
Mean Charlson Comorbidity index score (SD)		1.39 (1.78)
Type of comorbidities	Chronic pulmonary disease, n (%)	56 (19.4)
	Rheumatologic disease, n (%)	21 (7.3)
	Diabetes mellitus without organic affectation, n (%)	20 (6.9%)
	Cancer without metastasis, n (%)	11 (3.8%)
Patient's management ^a	Primary care, n (%)	269 (93.4%)
	Specialized healthcare, n (%)	39 (13.5%)
Asthma severity degree according to GEMA guidelines	Mild intermittent, n (%)	197 (68.4%)
	Mild persistent, n (%)	45 (15.6%)
	Moderate persistent, n (%)	34 (11.8%)
	Severe persistent, n (%)	12 (4.2%)
Current asthma therapeutic level according to GEMA stepwise therapy	Step 1, n (%)	178 (61.8%)
	Step 2, n (%)	16 (5.6%)
	Step 3, n (%)	47 (16.3%)
	Step 4, n (%)	27 (9.4%)
	Step 5, n (%)	14 (4.9%)
	Step 6, n (%)	6 (2.1%)

Notes: ^aMultiresponse.

Abbreviations: SD, standard deviation; GEMA, Guía Española para el Manejo del Asma.

Pharmacological Management of Patients with Asthma

IGC and long-acting bronchodilator inhalers (LABA) combination was used in 139 patients (48.3%). ICG alone were used in 153 patients (53.1%), regardless the asthma severity grade. Biologic treatments were used in 50% of the patients with severe persistent asthma (n=12).

Immunomodulators were the less commonly used treatment (1.7%). The maintenance/long-term and reliever treatment prescribed for asthma is shown in [Table 3](#).

Table 2 Level of Compliance with the Recommendations Included in the Guía Española Para El Manejo Del Asma (GEMA) Guidelines for the Management of Asthmatic Patients

Assistance Quality Care Indicators Established By GEMA Guidelines	Percentage of Compliance
Asthma diagnosis confirmed by spirometry and bronchodilator test	20.8%
Sensitization to allergen study in patients with history of suspected allergic asthma	52.5%
Smoker patients who were advised on the importance of stopping this habit	76.3%
Patients who were included in an educational plan.	14.2%
Patients who were receiving inhaled glucocorticoids at inclusion date for persistent asthma treatment	92.7%
Patients who had an evaluation and documentation of exacerbations	13.9%

Table 3 The Maintenance/Long-Term and Reliever Treatment Prescribed for Asthma According to Asthma Severity Grade and Level of Control of Asthma

	Asthma Severity Grade n (%)					Exacerbations n (%)	
	Mild Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent	Total	Controlled	Uncontrolled
SABA	44 (22.3%)	11 (24.4%)	16 (47.1%)	5 (41.7%)	76 (26.4%)	51 (20.6%)	25 (62.5%)
LAMA	1 (0.5%)	2 (4.4%)	6 (17.6%)	5 (41.7%)	14 (4.9%)	12 (4.8%)	2 (5.0%)
ICG	67 (34.0%)	41 (91.1%)	31 (91.2%)	12 (100.0%)	153 (53.1%)	119 (48.0%)	34 (85.0%)
LTRA	10 (5.1%)	4 (8.9%)	8 (23.5%)	3 (25.0%)	25 (8.7%)	17 (6.9%)	8 (20.0%)
LABA + GCI	60 (30.5%)	39 (86.7%)	28 (82.4%)	12 (100.0%)	139 (48.3%)	106 (42.7%)	33 (82.5%)
Biologic	0	0	0	6 (50.0%)	6 (2.1%)	4 (1.6%)	2 (5.0%)
Immunomodulator	2 (1.0%)	1 (2.2%)	1 (2.9%)	1 (8.3%)	5 (1.7%)	5 (2.0%)	0
OCS	15 (7.6%)	7 (15.6%)	11 (32.4%)	2 (16.7%)	35 (12.2%)	7 (2.8%)	28 (70.0%)
Other	4 (2.0%)	1 (2.2%)	4 (11.8%)	2 (16.7%)	12 (4.2%)	8 (3.2%)	4 (10.0%)
N valid	197	45	34	12	288	248	40

IGC alone and the combination of IGC + LABA were also the most common treatments for patients with exacerbations. For uncontrolled exacerbations, 34 patients (85.0%) were on IGC treatment and 33 (82.5%) were treated with IGC + LABA; for controlled exacerbations, 119 patients (48.0%) were treated with IGC and 106 (42.7%) with IGC + LABA. Only one pregnant woman was included in the study, receiving SABA, but she did not maintain the treatment during pregnancy.

Treatment was adjusted based on the severity of asthma. Patients with mild intermittent disease received Step 1 treatment level in most of the cases (84.8%); on the other hand, patients with severe disease were mostly receiving Step 5 and Step 6 treatment levels (91.7%) (Table 4).

Control of Asthma, Monitoring and Use of Healthcare Resources in the Previous Year to Study Inclusion

ACT score was available in all the patients included, mean (SD) 19.10 (5.34); 157 (54.5%) patients had the score already calculated in the last month before study initiation and in 131 subjects (45.5%), the ACT score was obtained at study

Table 4 Cross-Table Between Current Asthma Therapeutic Level and Asthma Severity Degree According to GEMA Guidelines

		Asthma Severity Degree			
		Mild Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent
Total patients (n=298)		198 (68.4%)	45 (15.6%)	34 (11.8%)	12 (4.2%)
Current Asthma Therapeutic Level According to GEMA Stepwise Therapy	Step 1	168 (84.8%)	7 (15.5%)	3 (8.8%)	0 (0.0%)
	Step 2	3 (1.5%)	10 (22.2%)	3 (8.8%)	0 (0.0%)
	Step 3	23 (11.6%)	14 (31.1%)	9 (26.5%)	1 (8.3%)
	Step 4	2 (1.0%)	12 (26.7%)	13 (38.2%)	0 (0.0%)
	Step 5	1 (0.5%)	2 (4.4%)	6 (17.6%)	5 (41.7%)
	Step 6	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (50.0%)

entry. One hundred and fifty-eight (54.9%) patients had an ACT score ≥ 20 (well-controlled asthma), and 130 (45.1%) patients < 20 (uncontrolled asthma).

With regard to asthma control level according to clinical criteria, the mean (SD) number of SABA canisters and OCS acquired in the pharmacy during the study period was 0.66 (1.71) and 1.33 (17.72) units, respectively. On the other hand, the mean (SD) number of emergencies and unscheduled primary care visits due to asthma was 0.07 (0.32) and 0.13 (0.39), respectively.

A record of scheduled visits to monitor asthma was confirmed for 26 (9.0%) patients, with a mean (SD) of 1.73 (1.87) visits per year. Forty patients (13.9%) registered exacerbations during the study period with a mean (SD) of 1.38 (0.74) exacerbations.

The mean (SD) of visits to primary care department related to asthma were 0.12 (0.55) scheduled visits and 0.13 (0.39) unexpected visits. The specialty with more visits during the study period were allergology and pneumology with a mean (SD) of 0.19 (0.77) and 0.12 (0.42) visits, respectively.

SABA Discontinuation

A total of 28 (32.6%) patients discontinued the SABA treatment during the study period. Patients with SABA treatment had an ACT score mean (SD) of 17.05 (5.64) vs 19.10 (5.34) for all patients. Of the 58 patients that did not discontinue SABA treatment, 37 (63.8%) were uncontrolled (ACT score < 20) and 21 (36.2%) were controlled (ACT score ≥ 20); these patients acquired a mean (SD) of 2.69 (2.90) canisters during the study period vs 1.25 (0.84) in the group of patients that discontinued SABA treatment.

Discussion

Optimum diagnosis and control of asthma is fundamental to improve patients' quality of life and reduce the high public burden associated to this disease, with a prevalence in Spain estimated in 5%. To achieve that, it is recommended to follow the guidelines published at international and national levels, such as the GEMA guidelines in Spain.⁸

According to GEMA guidelines, spirometry test should be the preferred pulmonary function test to demonstrate a compatible alteration in children and adults with symptoms of asthma. Despite this recommendation, only in 20.8% of the patients included in our study this test was accomplished, meaning that a considerable percentage of patients may not be correctly diagnosed, with the consequent impact it has on the health system and patients' life. For allergic asthma, GEMA guidelines recommend assessing the allergens that trigger the development of asthma and/or its exacerbation through a sensitization test, and reviewing the seasonal variation of symptoms and the location where they appear (home, work, free time), together with patient's personal/familiar history of atopy (or suspected). In our series, 42.4% of the patients had history of allergic asthma (or suspected) but only half of these patients (52.5%) performed an allergen

sensitization test. Allergic asthma confirmation determines the treatment and disease control measures, such as the reduction of the exposure to the allergen, if it is identified.

Once the diagnosis of asthma is confirmed, GEMA guidelines recommend a series of actions to modify patient's lifestyle (non-pharmacological treatment), such as stop smoking habit and follow educational programs. In our study, 13.2% of the patients were smokers at study entry but almost 25% of them were not advised on the importance of stopping this habit. Considering that it can be a key action to control the course of the disease in patients with asthma, this topic must be always reviewed and discussed with the patient after asthma diagnosis and during disease management.

It is also important to provide the patients with additional information related to their disease, such as information about asthma and its treatment, a disease control plan, or the inhalation technique. However, only 14.2% of the patients participating in the study were included in an educational plan. To improve this quality-of-care indicator, it is recommended to use all visits to review and reinforce the information provided, and increase patient's knowledge about asthma and its treatment, environmental avoidance measures, inhalation technique, therapeutic compliance, and all the topics included in the educational plan. All medical personnel should be involved in the administration and management of the patient's educational program.

Regarding the treatment in persistent asthma, daily use of inhaled IGC should be the first treatment choice, according to GEMA guidelines. This treatment improves the clinical, functional, and bronchial inflammation parameters, promotes a better quality of life, and reduces the risk of exacerbations and hospitalizations.¹⁹ This recommendation was followed by most of the physicians since 92.3% of the patients under treatment for persistent asthma were receiving IGC at inclusion date. In fact, IGC and LABA were the most common treatments for asthma, regardless the asthma severity grade. This finding shows a high adherence to the guideline recommendations about the treatment, which contrasts with the poor results obtained for diagnosis.

In special situations such as pregnancy, the GEMA guidelines recommend maintaining the treatment that was being used, like agonists β_2 -adrenergic and IGC. In our series, only one pregnant woman was receiving treatment for asthma and she did not maintain her treatment during the pregnancy. We could not get any conclusions due to the minimum number of cases.

Finally, patients should be monitored with periodic follow-up visits to detect, among other parameters, exacerbations of the disease. This GEMA recommendation was followed by a small percentage of specialists since only 9% of the patients had a record of scheduled visits to monitor asthma, while 13.9% of the patients had exacerbations registered during the year prior to patient's inclusion in the study.

All these findings reveal that the adherence to the GEMA guidelines among the professionals in the area where the study was conducted is incomplete. There is an unmet need to implement training programs for the specialists to optimize patients' management.

When analysing the level of disease control, 54.9% of the patients had their disease controlled according to the ACT score. Although the percentage of uncontrolled patients is high, this result is in concordance with previous publications in our country.¹² Regarding the use of healthcare resources (emergencies, primary care and specialist visits), most of the patients did not consult the emergency service, but attended unscheduled primary care visits or modified their treatments during the study period, even having some of them well-controlled asthma.

Finally, one-third of the patients discontinued the SABA treatment during the year before study entry. On the other hand, 63.8% of the patients that continued with SABA treatment were uncontrolled (ACT score <20) despite the treatment. In this group of patients, an alternative treatment, or a most intensive monitoring, could be valued.

Our series meets the sociodemographic characteristics of asthmatic patients. It has been described that the prevalence of asthma varies with the age (being more frequent in young people), gender (more frequent in female) and race.²⁰ In our study, in concordance with previous publications, most of the patients were women (64.2%) with a mean age of 49 years at study entry (mean age at asthma diagnosis was 34.64 years) and 94.4% were white. Other clinical characteristics such as obesity or presence of previous comorbidities have also been related to disease complications and a worse control of the symptoms.²¹ In our series, these characteristics were not especially frequent, only 11.36% of the patients were obese and 7.3% were also diagnosed with rheumatologic disease (most common comorbidities), in accordance with the mean age of the population included, relatively young. About the severity of the disease, it has been published that between 3.9% and 7% of all cases of asthma are severe;^{7,22,23} this is in line with our results as 4.2% of the patients had a severe

disease, being most of the patients diagnosed with mild intermittent asthma (68.4%) and receiving Step 1 treatment, following GEMA stepwise therapy. In conclusion, the patients included in the study were representative of the population in terms of clinical and demographic characteristics.

The limitations of the study are linked to the retrospective design. The number of spirometry tests used to diagnose asthma may be underestimated. The spirometry tests used for diagnosis were not included in the database. In addition, other variables retrospectively collected from the medical charts may not be routinely recorded or inconsistently recorded by the clinicians (eg, inaccurate filling of the medical records).

Conclusions

An optimum control of asthma is fundamental to reduce disease associated costs and to provide a better clinical assistance to the patients. Most of the specialists know the best treatment of choice, in accordance with the GEMA guidelines; however, this study warns the need for training plans in other GEMA recommendations, such as an accurate diagnosis and a periodic monitoring of the patients. The clinicians' educational plans, which could include courses, seminars, and congresses, can help to have an ample view of the disease in its different dimensions, from diagnosis and treatment to a periodic monitoring of the disease, in which prevalence continues to increase.

Although GEMA recommendations are clear regarding the diagnosis and management of patients with asthma, this study focused on the influential area of the Virgen de la Victoria University Hospital of Malaga reveals that, in a real-world setting, most of the GEMA indicators of quality asthma care are not met. More training and dissemination of the clinical guidelines is necessary for a better care of our patients.

These findings could reflect the current management of asthma in Spain. It would be interesting to analyse if the results found in a specific area are also reproduced in other geographical areas. Prospective multicentre studies to establish causal relationships of the level of adherence to the guidelines could overcome the limitations of retrospective studies.

Data Sharing Statement

The corresponding author can provide the details of the participant's inclusion dates, Study Protocol, Statistical Analysis Plan, Informed Consent Form, Clinical Study Report and Analytic Code, and it is available upon request.

Ethics Approval

The present study was approved by the Central Ethics Committee of the Regional University Hospital of Malaga on Aug 3rd, 2020 (code FIM-ASP-2020-01).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflict of interest.

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