Stress Echocardiography in Italian Echocardiographic Laboratories: A Survey of the Italian Society of Echocardiography and Cardiovascular Imaging

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Abstract

Background: The Italian Society of Echography and Cardiovascular Imaging (SIECVI) conducted a national survey to understand the volumes of activity, modalities and stressors used during stress echocardiography (SE) in Italy. **Methods:** We analyzed echocardiography laboratory activities over a month (November 2022). Data were retrieved through an electronic survey based on a structured questionnaire, uploaded on the SIECVI website. **Results:** Data were obtained from 228 echocardiographic laboratories, and SE examinations were performed in 179 centers (80.6%): 87 centers (47.5%) were in the northern regions of Italy, 33 centers (18.4%) were in the central regions, and 61 (34.1%) in the southern regions. We annotated a total of 4057 SE. We divided the SE centers into three groups, according to the numbers of SE performed: <10 SE (low-volume activity, 40 centers), between 10 and 39 SE (moderate volume activity, 102 centers) and ≥40 SE (high volume activity, 37 centers). Dipyridamole was used in 139 centers (77.6%); exercise in 120 centers (67.0%); dobutamine in 153 centers (85.4%); pacing in 37 centers (21.1%); and adenosine in 7 centers (4.0%). We found a significant difference between the stressors used and volume of activity of the centers, with a progressive increase in the prevalence of number of stressors from low to high volume activity ($P = 0.033$). The traditional evaluation of regional wall motion of the left ventricle was performed in all centers, with combined assessment of coronary flow velocity reserve (CFVR) in 90 centers (50.3%): there was a significant difference in the centers with different volume of SE activity: the incidence of analysis of CFVR was significantly higher in high volume centers compared to low – moderate – volume (32.5%, 41.0% and 73.0%, respectively, $P < 0.001$). The lung ultrasound (LUS) was assessed in 67 centers (37.4%). Furthermore for LUS, we found a significant difference in the centers with different volume of SE activity: significantly higher in high volume centers compared to low – moderate – volume (25.0%, 35.3% and 56.8%, respectively, $P < 0.001$). **Conclusions:** This nationwide survey demonstrated that SE was significantly widespread and practiced throughout Italy. In addition to the traditional indication to coronary artery disease based on regional wall motion analysis, other indications are emerging with an increase in the use of LUS and CFVR, especially in high-volume centers.

Keywords: Coronary flow velocity reserve, lung ultrasound, stress echocardiography

Introduction

Stress echocardiography (SE) is an efficient and cost-effective option for diagnosing and stratifying the risk of ischemic heart disease (coronary artery disease [CAD]).[1,2] Over time, SE has evolved beyond its traditional evaluation of regional wall motion analysis to encompass a broader scope of functional testing, including conditions such as valvular heart disease and cardiomyopathy.

The SE 2020 and SE 2030 multicenter studies,[3,4] endorsed by the Italian Society of Echography and Cardiovascular Imaging (SIECVI), have played a significant role in demonstrating the effectiveness of this new approach. These studies have validated emerging signs and integrated new information with established knowledge, leading to the standardization of procedures and the adoption of additional imaging evaluations beyond regional wall motion analysis. These new imaging evaluations include coronary flow velocity reserve (CFVR) on left anterior descending coronary artery (LAD)[5-7] and lung ultrasound (LUS),[8-12] making SE a more comprehensive and valuable tool in CAD and the diagnosis and assessment of various cardiac conditions including valvular heart disease and cardiomyopathy.[12-14]

With the advancements in SE and the expansion of its applications, the aim of this survey is to understand the current volumes of activity, modalities, and stressors used during SE in Italy. Analyzing the new indications for SE both within and beyond CAD, as well as the implementation of the new imaging approach, can help in building next-generation SE labs and improving patient care.

Methods

We analyzed the activity of echocardiography laboratories in 1 month. November 2022 was chosen as an ideal reference month (30 days; away from holidays).

A list of accredited echocardiographic laboratories was obtained from SIECVI. Each member of SIECVI was contacted by mail. Data were retrieved through an electronic survey based on a structured questionnaire uploaded on the SIECVI website (www.siec.it.)

The methods of the survey were previously described in other survey of the SIECVI.[15-17]

For the allocation of the response, the questionnaire required general information, such as the name of the hospital, the investigator, and the interviewed person's name:

1. General information: date, hospital's name, department, name of the interviewed physician, city, and region of Italy

2. The number of SE performed
3. The stressors used
4. The number of SE with CFVR and LUS performed
5. The principal indications of SE.

Statistical analysis

The categorical data are expressed in terms of the number of subjects and percentage, whereas continuous data are expressed as mean ± standard deviation or median (minimum-maximum) depending on the variables' distribution. For continuous variables, intergroup differences were tested with a one-way analysis of variance and inter-group comparison by Bonferroni or Kruskal-Wallis, followed by the Mann–Whitney test as appropriate. The Chi-square test or Fisher exact test was used to compare the distribution of categorical variables among groups.

All statistical calculations were performed using the SPSS for Windows, release 20.0 (Chicago, Illinois, USA).

Results

Data were obtained from 228 echocardiographic laboratories, and SE examinations were performed in 179 centers (80.6%): 87 centers (47.5%) were in the northern regions of Italy, 33 centers (18.4%) were in the central regions, and 61 (34.1%) in the southern regions.

During the month of observation, we annotated a total of 4057 SE.

We divided the SE centers in three groups, according to the numbers of SE performed: <10 SE (low-volume activity, 40 centers, 22%), between 10 and 39 SE (moderate volume activity, 102 centers, 57%) and ≥40 SE (high volume activity, 37 centers, 21%). The principal data of number and indication of SE are reported in the Table 1.

Dipyridamole was used in 139 centers (77.6%), dobutamine in 153 centers (85.4%); pacing in 37 centers (21.1%) and adenosine in 7 centers (4.0%) [Figure 1].

Exercise was performed in 120 centers (67.0%): treadmill in 20 centers (16.7%), semisupine bike in 82 centers (68.3%) and with both modality in 18 centers (15.0%) [Figure 1].

A single stressor was used in 29 centers (16.2%): only dipyridamole in 3 centers, only dobutamine in 9 centers and only exercise in 17 centers. Two stressor was used in 45 centers (25.1%) and 3 or more stressors in 105 centers (58.7%).

We found a significant difference between the stressors used and volume of activity of the centers, with a progressive increase in the prevalence of number of stressors from low-to-high volume activity [Figure 2].

The traditional evaluation of regional wall motion of the left ventricle was performed in all centers, with combined assessment of CFVR in 90 centers (50.3%). There was a significant difference in the centers with different volume of SE activity: the incidence of analysis of CFVR was significantly higher in high volume centers compared to low-to-moderate volume [Figure 3]. CFVR was evaluated routinely during traditional SE in 70 centers (77.8%), in patients with known CAD and previous coronary revascularization in 80 centers (88.9%) and in the evaluation of intermediate stenosis in 81 centers (90%).

The LUS was assessed in 67 centers (37.4%). We found also for LUS use a significant difference in the centers with different volume of SE activity: significantly higher in high volume centers compared to low-to-moderate volume [Figure 4]. The principal indications of LUS evaluation during SE were: heart failure with reduced ejection fraction in 61 centers (91.0%), heart failure with preserved ejection fraction in 59 centers (88.0%), routine evaluation in 51 centers (73.9%), and in post-COVID in 46 centers (68.7%) [Figure 5].

We found a significant difference between the three groups studied in the indications for aortic and mitral valve disease, with more frequent indication in high-volume center [Table 1].

Discussion

We described the use of SE in Italian echocardiographic laboratories. SE is a widely used diagnostic tool that combines echocardiography with physical or pharmacological SE, by

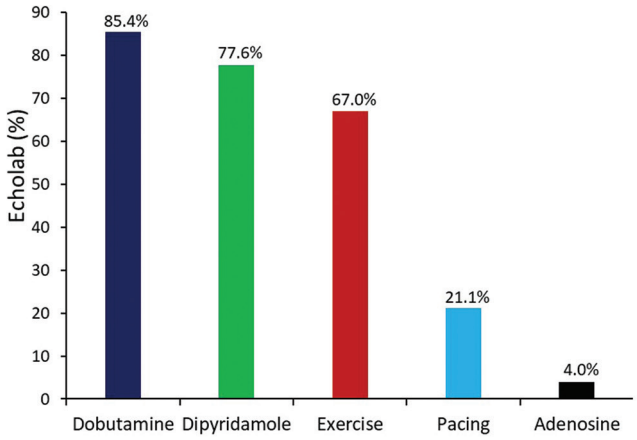

Figure 1: Percentage of stressors used in stress echocardiography

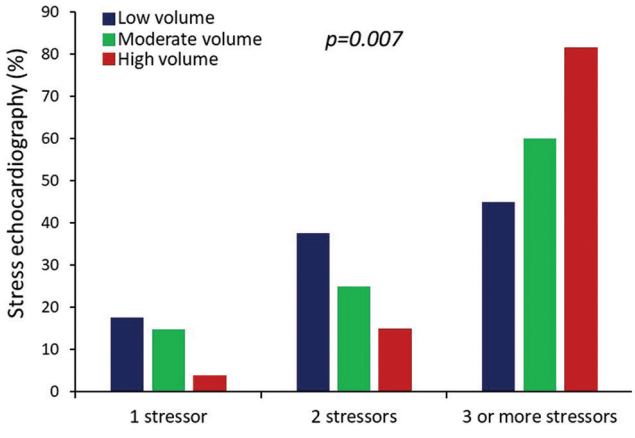

Figure 2: Numbers of stressors used during stress echocardiography in low, moderate, and high volume centers

Table 1: Stress echocardiography and principal indications in the study groups

	Overall (*n*=179)	Low-volume (*n*=40)	Moderate-volume (*n*=102)	High-volume (*n*=37)	*P*
SE (*n*)	22.7±24.3	4.6±2.2	15.8±6.7	61.0±28.0	<0.001
SE and CFVR evaluation (*n*)	8.9±17.2	1.3±2.1	5.3±7.0	26.8±29.9	<0.001
SE and CFVR evaluation, *n* (%)	90 (50.3)	13 (32.5)	57 (41.0)	27 (73.0)	0.001
SE and B-Lines evaluation (*n*)	6.0±13.8	1.5±3.2	3.6±7.2	17.6±24.7	<0.001
SE and CFVR evaluation, *n* (%)	67 (37.4)	10 (25.0)	36 (35.3)	21 (56.8)	0.013
Regional distribution in Italy, *n* (%)					
Northern	85 (47.5)	16 (40.4)	48 (47.1)	21 (56.8)	0.510
Center	33 (18.4)	10 (25.0)	19 (18.6)	4 (10.8)	
Southern	61 (34.1)	14 (35.0)	35 (34.3)	12 (32.4)	
Use of contrast, *n* (%)					
Never	83 (46.4)	21 (52.5)	46 (45)	16 (43.2)	0.611
Rare	55 (30.7)	13 (32.5)	31 (30.4)	11 (29.7)	
Frequent	26 (14.6)	5 (12.5)	15 (14.7)	6 (16.2)	
Routinely	15 (8.4)	1 (2.5)	10 (9.8)	4 (10.8)	
Indication CAD, *n* (%)					
Never	4 (2.2)	2 (5.0)	2 (2.0)	0	0.053
Rare	10 (5.6)	5 (12.5)	4 (3.9)	1 (2.7)	
Frequent	131 (73.2)	29 (82.5)	74 (72.5)	28 (75.7)	
Routinely	34 (19.0)	4 (10.0)	22 (21.6)	8 (21.6)	
Indication HCM, *n* (%)					
Never	55 (30.7)	16 (40.0)	33 (32.4)	6 (16.2)	0.134
Rare	81 (45.3)	17 (42.5)	47 (46.1)	4 (10.8)	
Frequent	41 (22.9)	6 (15.0)	21 (20.6)	14 (37.8)	
Routinely	2 (1.1)	1 (2.5)	1 (1.0)	0	
Indication HF, *n* (%)					
Never	47 (26.3)	14 (35.0)	26 (25.5)	7 (18.9)	0.058
Rare	82 (45.8)	22 (55.0)	47 (46.1)	13 (35.1)	
Frequent	45 (25.1)	3 (7.5)	26 (25.5)	16 (42.2)	
Routinely	5 (2.8)	1 (2.5)	3 (2.9)	1 (2.7)	
Mitral disease, *n* (%)					
Never	34 (19.0)	13 (32.5)	20 (19.6)	1 (2.7)	0.006
Rare	63 (35.2)	12 (30.0)	39 (38.2)	12 (32.4)	
Frequent	78 (43.5)	15 (37.5)	39 (38.2)	24 (64.8)	
Routinely	4 (2.2)	0	5 (3.9)	0	
Aortic disease, *n* (%)					
Never	22 (12.3)	7 (17.5)	13 (12.7)	2 (5.4)	0.050
Rare	73 (40.8)	17 (42.5)	45 (44.1)	11 (29.7)	
Frequent	82 (45.8)	10 (25.0)	42 (41.1)	24 (64.8)	
Routinely	2 (1.1)	0	2 (2.0)	0	

SE: Stress echocardiography, CFVR: Coronary flow velocity reserve, CAD: Coronary artery disease, HCM: Hypertrophic cardiomyopathy, HF: Heart failure

adhering to the SE recommendation, that to be familiar with all the forms of physical and pharmacological SE.[13]

One notable advancement in SE is the simultaneous assessment of CFVR on LAD and LUS. This approach significantly expands the diagnostic and prognostic potential of the traditional evaluation, which was primarily based on identifying regional wall motion abnormalities (RWMA).

ABCDE stress echocardiography

The upgrade of SE to the ABCDE protocol represents a significant advancement in the field, aiming to provide a more comprehensive assessment of patients with ischemic heart disease and other cardiac conditions. The ABCDE protocol involves five steps that offer a more integrated evaluation of patient vulnerability beyond the detection of anatomical CAD.[18,19]

Cardiac functional testing with ABCDE SE allows to gain a comprehensive insight on patient vulnerability still with an extraordinarily simple and feasible test with low cost, minimal risk, zero radiation, and near-zero environmental impact.

This approach is likely to enhance the diagnostic accuracy and prognostic value of SE in clinical practice, leading to better patient management and outcomes.[19]

This new approach was rapidly implemented by the Italian echocardiography laboratories and, as emerged from the survey, is now an integral part of the evaluation of the patient

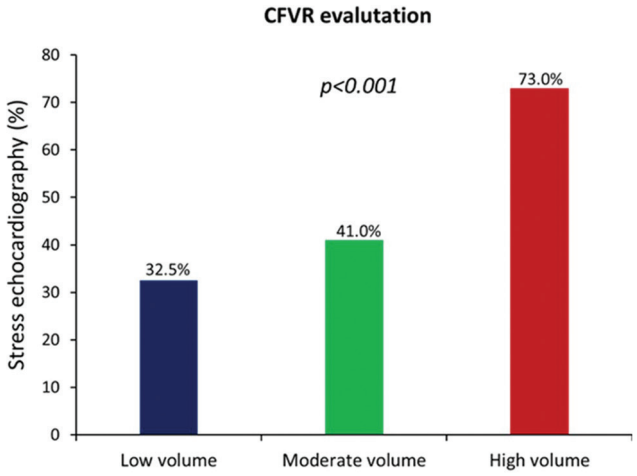

Figure 3: Percentage of coronary flow velocity reserve evaluation during stress echocardiography in low, moderate, and high volume centers

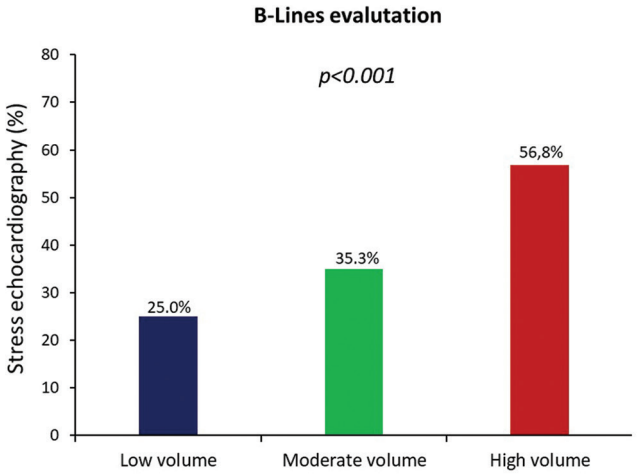

Figure 4: Percentage of lung ultrasound evaluation during stress echocardiography in low, moderate, and high volume centers

in ischemic heart disease and beyond ischemic heart disease, especially in high-volume centers. It has also allowed an extension of the indications to SE, beyond ischemic heart disease, as in cardiomyopathies and valvulopathies.

There are three possible reasons of this rapid reshape of SE practice. First, the culture of SE has deep clinical and cultural roots in Italy, since several Italian laboratories were early adopters of the technique in the eighties and established the practice of SE well before it was recognized and endorsed by the international guidelines. Second, the last wave of SE innovation with the addition of B-lines and CFVR was again started in Italy in 2002 and 2004, and progressively accepted worldwide. Third and possibly more importantly, the new ABCDE protocol received the official endorsement of the SIECVI, which allowed a more efficient dissemination of the project, harmonization of protocols across different laboratories, and rapid uptake of the technique by leading edge laboratories. Stress echo 2030 is a flagship project of SIECVI, and over 20 Italian laboratories are currently active parts and recruiters of the study. When innovation starts in the clinically oriented laboratories, daily practice is aligned with the state of the art protocols, and the dissemination of innovation becomes easier and faster.

B-lines LUS identify pulmonary congestion at rest[8,9] and, more frequently, during stress[10,11] in a variety of cardiovascular conditions, characterized by the possible occurrence of increased pulmonary artery wedge pressure and accumulation of extravascular lung water. Stress B-lines were more frequent than rest B-lines, indicating that SE can be useful to unmask a condition of latent pulmonary congestion, undetectable at rest, and shared by different cardiovascular conditions: CAD, heart failure with preserved and reduced ejection fraction, valvulopathy.[9,11]

CFVR on LAD offers an integrated assessment of epicardial coronary artery stenosis and coronary microcirculation.[20] Large evidences supporting the usefulness of CFVR, especially for risk stratification in CAD and HF and its endorsement in SE recommendations by the European Society of Echocardiography.[13] Starting 2016, CFVR was adopted in the ABCDE protocol of the stress echo 2020 first and after, stress echo 2030 study as the new clinical standard of the technique.[3,4]

CFVR during SE is feasible with high success with vasodilator than with dobutamine or exercise test.[5,21] Reduced CFVR is more prevalent in the patients with inducible RWMA or extensive CAD, but can be found also in patients with normal coronary arteries.[5] Reduced CFVR is a marker of altered coronary microvascular function and/or epicardial artery stenosis, which integrates and complements stress-induced RWMA which are more specific for a reduction of CFVR due to epicardial artery stenosis.[6,7] The risk is lowest for patients with preserved CFVR and no RWMA, intermediate in patients with only reduced CFVR and highest for patients with RWMA and reduced CFVR.[5]

Comparison with previous studies

Compared to previous Italian SE survey of 2015,[22] we had more centers involved (179 vs. 125 centers, respectively): SE activity was present in 81% of Italian centers, higher data compared to previous Italian survey with 67% of the centers, 61% in UK[23] and 49% in Austria.[24]

Exercise was performed in 67% of labs, with an increase compared to the previous value of 2015 in Italy (56%), similar from UK practice, exercise was used in 67% of laboratories, while in Austria exercise was lower employed (only 26% of laboratories).

Dobutamine was widely used in 91% and vasodilators by 82% of the centers in the previous Italian survey, grossly comparable with 85% and 78%, respectively, of the centers involved in this survey.

Dobutamine was largely used in the UK (100%) and Austria (91%), whereas vasodilators were underused in

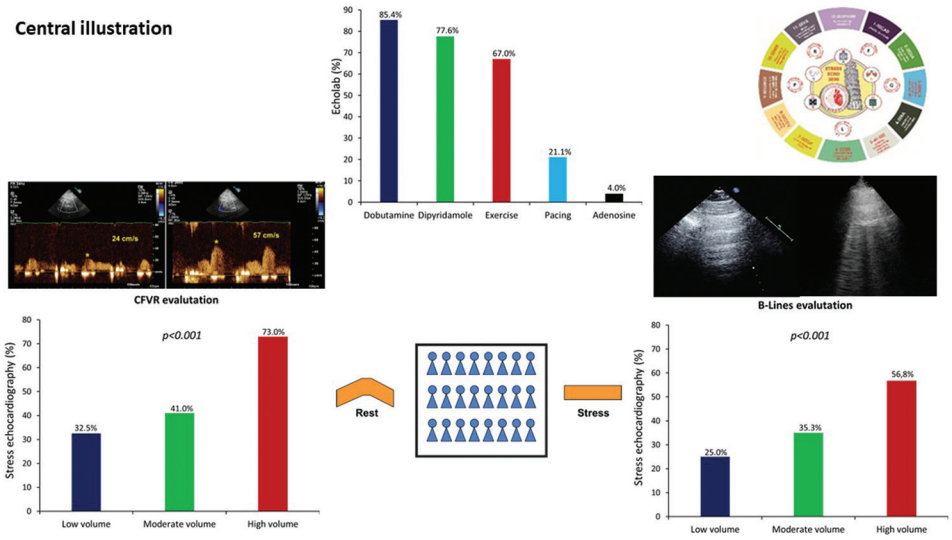

Figure 5: Percentage of stressors used in stress echocardiography (SE) on the center up. The symbol of stress echo 2030 on the right top. In the bottom on the left, an example of coronary flow evaluated at rest and at peak stress and percentage of coronary flow velocity reserve evaluation during SE in low, moderate and high volume centers. In the bottom on the center a picture of standard evaluation of regional wall motion with normal at rest and abnormal at peak stress. In the bottom on the right an example of lung ultrasound (LUS) evaluation at rest and at peak stress, and the percentage of LUS during SE in low-, moderate-, and high-volume centers

Austria (11%) and in UK (20%), a markedly lower percentage compared to the Italian data.

As an extraconsideration, the drug cost is not separately reimbursed in Italy, and therefore, the drug cost can represent an issue. In addition, in some European countries, intravenous dipyridamole is not commercially available.

The noninvasive pacemaker stress echo was used by 21% of laboratories, while only 6% in the previous Italian survey. The percentage was much higher in the UK (40%) and lower (2%) in Austria.

This option is particularly beneficial for patients with permanent pacemakers, as it allows for stress testing to be performed in a few minutes without the need for an intravenous line.[25] The described stress test is fast, safe, and requires minimal interaction with the electrophysiology outpatient lab. This means that it can be carried out efficiently and with fewer resources, making it a convenient and practical option for assessing cardiac function and response to stress in patients with pacemakers.

Study limitations

We used the electronic mailing list of the Italian Society of Echocardiography, which covers most - but certainly not all - the SE activities in Italy.[15] In fact, certification is not mandatory, and it is also run in parallel and independently by the European Association of Cardiovascular Imaging, and many cardiologists are directly accredited by international societies and do not pass through the Italian society. Some of these extra-SIECVI centers are also of large volumes and high quality standards. Therefore, the survey might have underestimated the dissemination of SE activities in Italy but has likely mirrored the quality and pattern of practice in a realistic fashion. As always in a survey, there are nonresponders for several reasons, including lack of time or unwillingness to participate to the study. No independent, external validation of the data provided by the cardiologist head of the participating lab was possible.[15-17]

Conclusions

The survey described the state of the art of SE in Italy and the SE community, characterized as being open to innovation and efficient in integrating scientific evidence into everyday clinical practice with minimal time-lag. The framework established by this community is seen as culturally and logistically suitable for developing the new generation of SE, exploring various aspects of SE, both within and beyond CAD. The community is embracing new parameters, such as B-lines and CFVR, in addition to traditional RWMA.

Furthermore, SE is extending its applications beyond CAD to evaluate conditions such as dilated and hypertrophic cardiomyopathy and valvular heart disease. This expanded scope makes SE a more versatile and comprehensive tool for assessing various cardiac pathologies.

The stage is now set for prospective, large-scale, multicenter effectiveness studies, as SE2020 first and SE 2030 studies endorsed by SIECVI are crucial for determining the clinical utility and diagnostic accuracy of this multiparametric approach with ABCDE SE.

By embracing these new approaches, the SE community is striving to improve patient care, enhance diagnostic capabilities, and ultimately contribute to better patient outcomes.

As the field of SE continues to evolve and incorporate new findings, it reinforces the importance of evidence-based medicine and the collaborative efforts of researchers, clinicians, and the medical community to advance cardiovascular care.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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