

Echocardiographic Findings in Patients with Suspected Infective Endocarditis

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Objective

To assess the echocardiographic findings in patients with suspected infective endocarditis.

Methods

Two hundred sixty-two patients with suspected infective endocarditis underwent transthoracic and transesophageal echocardiographic investigation. Images of vegetations, valvular abscesses, and acute periprosthetic insufficiency were analyzed, and the correlation with clinical and laboratory data, diagnostic category, and hospital evolution was assessed.

Results

The diagnosis of endocarditis was categorized as defined in 127 (47.8%) episodes, possible in 81 (30.4%), and rejected in 58 (21.8%). In patients with the defined diagnosis, the following images were identified: 135 vegetations, 37 abscesses, and 6 periprosthetic insufficiencies. Vegetations were more frequent in patients with endocarditis due to streptococci of the viridans group and enterococci ($P=0.02$), and with symptom duration < 10 days ($P=0.001$). Abscesses were more frequent in patients with symptom duration < 10 days ($P=0.001$). Periprosthetic insufficiency was associated with a greater need for surgical treatment ($P=0.001$). In patients with the possible diagnosis of endocarditis, 8 echocardiographic images considered compatible with vegetations were identified. In patients whose diagnosis of endocarditis was rejected, no vegetations, valvular abscesses, or periprosthetic insufficiencies were demonstrated.

Conclusion

Our echocardiographic findings varied according to the diagnostic category. The contribution to both the diagnosis and prognostic evaluation should consider the pretest probability of the diagnosis of infective endocarditis.

Keywords

infective endocarditis, echocardiography

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Echocardiography has contributed to the diagnosis and therapeutic management of patients suspected of having infective endocarditis, both through the transthoracic¹ and transesophageal techniques².

Despite the progress observed, situations occur in which the diagnosis of infective endocarditis is difficult, such as in patients with acute disease, infection in cardiac valvular prostheses^{3,4}, prosthetic infection in the immediate postoperative period^{5,6}, patients with an artificial cardiac pacemaker^{7,8}, patients receiving previous antimicrobial therapy, or those whose blood cultures are negative^{9,10}.

In the different recent published studies¹¹⁻¹⁵ about the use of transesophageal echocardiography in patients suspected of having infective endocarditis, we observe case series ranging from 23 to 180 patients studied using biplanar transducers, or part of the case series being studied with multiplanar probes. In addition, they did not include the diagnostic categorization of patients.

Therefore, this study aimed at assessing the echocardiographic findings, both through the transthoracic and multiplanar transesophageal techniques, in a greater case series of patients suspected of having infective endocarditis, classified according to diagnostic categories, which also include situations of greater diagnostic difficulty.

Methods

Two hundred sixty-two patients were prospectively studied in 266 episodes of the disease, in which the differential diagnosis included the diagnostic hypothesis of infective endocarditis. The patients' age ranged from 10 to 85 years (mean, 47.6; standard deviation, 17.9), and 139 (52.2%) episodes occurred in men and 127 (47.8%) in women.

The echocardiographic examination was indicated by the clinician responsible for the patient. The patients studied initially underwent the transthoracic study, and, on the occasion of the transesophageal investigation, the examination was preceded by a new transthoracic study. All patients underwent transthoracic and transesophageal echocardiographic investigation.

The diagnosis of infective endocarditis was based on clinical findings (fever, predisposing heart disease, illicit use of intravenous drugs, cardiac murmur, vascular or immunologic phenomena), identification of the etiologic agent in at least 2 blood cultures, identification of endocardial impairment on transthoracic or transesophageal echocardiography, and histological evidence of infective

endocarditis on surgical or autopsy findings. The diagnosis of infective endocarditis followed the recommendations of the previously published criteria¹ and were categorized as defined, possible, and rejected.

The examinations were performed according to the routine of our service and previously recommended techniques^{16,17}. The transesophageal echocardiography was performed with electrocardiographic and oximetric monitoring, and no antibiotic prophylaxis was administered¹⁷. The mean duration of the transesophageal examination was 28.2 minutes (standard deviation of 6.4 minutes).

The examinations were performed on Advanced Technology Laboratory devices, Apogee CX 200, HDI 3000, and HDI 5000 models (Bothell, Washington, USA). The transesophageal examinations were performed with multiplanar transducers. The transthoracic examinations that precede the transesophageal examinations and the transesophageal examinations were recorded on VHS videotapes.

The examinations were analyzed by the physician who performed them, and then by a second researcher, who ignored the previous clinical diagnosis. Agreement between the different observers in the analysis of the transesophageal examinations was greater than 95% for the presence of defined images, such as vegetations, abscesses, and acute periprosthetic insufficiency (dehiscence of cardiac valvular prosthesis). When divergence in identification of the images occurred, a third observer also analyzed the examinations.

The echocardiographic findings were diagnosed according to previously published criteria¹⁸⁻²⁰.

The images obtained on transthoracic examinations were categorized according to quality, using the identification of the endocardium and the valvular structures as a criterion, as follows: a) adequate; b) regular; c) inadequate²¹.

The following characteristics of the vegetations were examined: a) location in the cardiac structure; b) dimension in their greater diameter (until 5 mm, from 6 to 10 mm, > 10 mm); c) refringence \geq that of the endocardium (with the gain of the echocardiographic device in minimum values capable of identifying the image defined as a vegetation); d) mobility (vegetation firmly adhered to the underlying structure, fixed base with free mobile border, and prolapsing).

The following characteristics were studied: a) demographic and clinical aspects: age, sex, time between symptom onset and hospitalization, previous use of antimicrobial agents, diagnostic categorization of endocarditis, etiologic agents, heart disease, treatment, evolution; b) echocardiographic findings: vegetation, perivalvular abscess; periprosthetic insufficiency; fistula between the cardiac chambers; thrombus; and pericardial effusion.

The descriptive analysis of the continuous variables was performed using the minimum and maximum values, mean, and standard deviation. The descriptive analysis of the categorical variables was performed using the absolute and relative frequencies. The comparative analysis was performed using the chi-square test or the Fisher exact test. The data were processed with the statistical analysis system of the SAS Institute, Cary, North Carolina, USA. The P values < 0.05 were considered significant.

The project was approved by the Committee on Ethics in Research of the Hospital das Clínicas of the Medical School of the Universidade de São Paulo.

Results

The demographic and clinical characteristics, including laboratory data, complications, and hospital evolution are shown in table I. The population studied was characterized by the predominance of patients with cardiac valvular prostheses, and time elapsed between symptom onset and hospitalization < 10 days. More than half of the patients required surgical treatment during in-hospital evolution.

The diagnosis was categorized as defined in 127 (47.8%) episodes as follows: 112 (88.2%) through clinical criteria, and 15 (11.8%) through anatomicopathological criteria. The diagnosis was categorized as possible in 81 episodes (30.4%), and as rejected in 58 (21.8%) episodes.

The microbiologic agents identified in the 127 episodes with the defined diagnosis of infective endocarditis were: coagulase-negative *staphylococcus* in 26 (20.5%); *staphylococcus aureus* in 21 (16.5%); *streptococcus* of the *viridans* group in 20 (15.7%); *streptococcus* not pertaining to the *viridans* group in 6 (4.7%); gram-negative bacteria in 10 (7.9%); *enterococcus faecalis* in 5 (3.9%); fungi in 3 (2.4%); and association of 2 infective agents in 3 (2.4%) episodes. No infective agents were identified in blood cultures in 33 (26%) episodes, and, in 22 patients with 33 episodes, no etiologic agent could be identified, because they had cardiac valvular prostheses.

The quality of the images of transthoracic examinations that preceded the transesophageal examinations were considered as follows: adequate in 256 (77.6%) of 330 examinations; regular in 52 (15.7%); inadequate in 22 (6.7%).

In patients with the defined diagnosis of endocarditis, 135 images of vegetations were identified as follows: through transthoracic analysis in 61 (48%) of the 127 cases of the diagnosis defined as infective endocarditis; and through transesophageal analysis in 112 (88.2%) cases. Therefore, vegetations were identified through transthoracic analysis in 61 (54.4%) of the 112 cases identified through transesophageal examination.

The images of vegetations were identified on mitral valve prosthesis in 46 (36.1%) of 127 episodes; on aortic valve prosthesis in 33 (26%) episodes; on pulmonary valve prosthesis in 1 (0.8%); on native mitral valve in 15 (11.8%); on native aortic valve in 9 (7.1%); on tricuspid valve in 2 (1.6%); on native pulmonary valve in 1 (0.8%); on mitral valve and on aortic valve in 15 (11.8%); on the extension of artificial cardiac pacemakers in 3 (2.4%); and on ventricular endocardium in 2 (1.6%) episodes.

The dimensions of the images identified as vegetations were as follows: < 5 mm in 24 of 135 (17.8%); between 6 and 10 mm in 78 (57.8%); and > 10 mm in 33 (24.4%). The refringence of the images of the vegetations was equal to that of the endocardium in 132 (97.8%) images, and greater than that of the endocardium in 3 (2.2%). The images of the vegetations had a fixed base with free mobile border in 45 (33.3%) characterizations, and prolapsing structures in 90 (66.7%) images.

The distribution of the presence of vegetations differed with the different etiologies (more frequent for *streptococci* of the *viridans* group and *enterococci*) (P=0.02).

The presence of vegetations was more frequent with different times between symptom onset and hospitalization (more frequent



Table I – Clinical characteristics of 262 patients with 266 episodes of suspected infective endocarditis

Clinical characteristics	Diagnostic category			
	Total n (%)	Defined n (%)	Possible n (%)	Rejected n (%)
Patients	262 (100)	125 (47.7)	79 (30.2)	58 (22.1)
Episodes	266 (100)	127 (47.8)	81 (30.4)	58 (21.8)
Age in years (mean ± standard deviation)	47.6±17.9	42.9±15.7	51.8±18.8	51.3±17.1
Sex				
Male	139 (52.2)	66 (52)	42 (51.8)	31 (53.5)
Female	127 (48.8)	61 (48)	39 (48.2)	27 (46.5)
Previous heart disease				
Cardiac valvular prosthesis	147 (55.3)	80 (63)	40 (49.3)	27 (46.5)
Biological prosthesis	132 (49.6)	73 (57.5)	35 (43.2)	24 (41.3)
Mechanical prosthesis	15 (5.7)	7 (5.5)	5 (6.1)	3 (5.2)
Cardiac valvular disease	76 (28.6)	39 (30.7)	20 (24.7)	17 (29.3)
Congenital heart disease*	9 (3.3)	5† (3.9)	2 (2.5)	2 (3.4)
Artificial cardiac pacemaker	10 (3.8)	3 (2.4)	4 (5)	3 (5.3)
Other ‡	19 (7.1)	-	12 (14.8)	7 (12.1)
No previous heart disease §	5 (1.9)	-	3 (3.7)	2 (3.4)
Time elapsed between symptom onset and hospitalization (days)				
0-10	142 (53.4)	76 (59.8)	39 (48.1)	27 (46.5)
11-20	33 (12.4)	20 (15.7)	8 (9.8)	5 (8.6)
21-30	19 (7.1)	13 (10.3)	4 (4.9)	2 (3.4)
31-60	14 (5.3)	5 (3.9)	6 (7.5)	3 (5.3)
61-90	17 (6.4)	6 (4.7)	7 (8.6)	4 (6.9)
>90	41 (15.4)	7 (5.6)	17 (21.1)	17 (29.3)
Previous administration of antimicrobial agents	49 (18.4)	28 (22)	12 (14.8)	9 (15.5)
Treatment				
Clinical	124 (46.6)	34 (26.8)	51 (63)	39 (67.3)
Surgical	142 (53.4)	93 (73.2)	30 (37)	19 (32.7)
In-hospital mortality	73 (27.8)	44 (35.2)	23 (29.1)	6 (10.3)
Hospital discharge	189 (72.2)	81 (64.8)	56 (70.9)	52 (89.7)

n- number; * bivalve aortic valve in 4, tetralogy of Fallot in 2, transposition of the great vessels in 2, complex heart disease in 1; † bicuspid aortic valve in 1, tetralogy of Fallot in 2, transposition of the great vessels in 1, complex heart disease in 1; ‡ coronary artery disease in 8, dilated cardiomyopathy in 7, Chagas' disease in 2, asymmetric hypertrophic cardiomyopathy in 2; § cine coronary angiography in 2, abdominal surgery in 1.

for the time between symptom onset and hospitalization up to 10 days) ($P=0.001$).

In patients with the possible diagnosis of endocarditis, images interpreted as vegetations were identified on transesophageal examination in 8 (9.8%) of 81 episodes, and in 2 (2.5%) with the use of transthoracic echocardiography. Of those 8 cases, all had negative blood cultures, 5 received antibiotic therapy for a short period of time (under 14 days), with remission of the findings and maintenance of the images on later transesophageal examination. They were discharged from the hospital and clinically followed up for at least 6 months, with no other possible diagnosis of infective endocarditis. Of the 8 patients with an image interpreted as vegetation, 3 underwent surgical treatment, and neither macroscopic, nor histological material compatible with vegetation was found. The image saw as vegetation on echocardiography was then attributed to surgical suture thread. Of the 8 cases, 7 had a bioprosthesis (5 in the mitral position, 2 in the aortic position). One patient had an image on the native aortic valve. All 8 patients had no previous history of an episode of infective endocarditis.

In the episodes in which the diagnosis of endocarditis was rejected, no image of vegetation was identified on echocardiography.

In patients with the defined diagnosis of infective endocarditis, 357 complications due to infection occurred as follows: acute renal failure, 67 episodes; congestive heart failure, 52 episodes; cardiac valve abscess, 31 episodes; stroke, 29 episodes; extracerebral embolism, 21 episodes; complete atrioventricular block, 13 episodes; cerebral embolism, 7; mycotic aneurysm, 7; pulmonary embolism, 3; and other complications, 127. Stroke was

more frequent in patients whose vegetations were > 10 mm ($P = 0.02$).

No greater need for surgical treatment was observed in patients in whom vegetations were identified.

The mortality rate was not greater in patients with vegetations.

No statistical significance was observed between refringence and the following parameters: sex, age, abscess, flow of acute periprosthetic insufficiency, time elapsed between symptom onset and hospitalization, previous use of antibiotic therapy, complications, treatment, and condition at hospital discharge.

In the episodes with the defined diagnosis of infective endocarditis, 5 cases of valvular ring abscesses were identified by using transthoracic echocardiography (4 in the aortic ring, and 1 in the mitral ring). On transesophageal echocardiography, 37 images of valvular ring abscess were identified as follows: 24 in the aortic ring, 7 in the mitral ring, and 6 in other locations. A perivalvular abscess was identified during surgery in 31 cases (22 in the aortic ring, 7 in the mitral ring, and 2 in the mitroaortic junction). In the 6 cases, in which a perivalvular abscess was identified on transesophageal echocardiography, but was not confirmed during surgery, previous surgical manipulation had occurred.

Valvular ring abscess was more frequent in patients with endocarditis, who had vegetations with dimensions > 10 mm ($P=0.01$) and prolapsing mobility ($P=0.02$).

No statistical significance was found between the presence of a perivalvular abscess and the different etiological agents.

The distribution of the presence of abscesses differed according to the different times between symptom onset and hospitalization

(time between symptom onset and hospitalization up to 10 days) ($P=0.001$). No statistical significance was found between the presence of abscesses, sex, and age.

In patients with the possible diagnosis of endocarditis or in those whose diagnosis of endocarditis was rejected, no perivalvular abscess was identified on echocardiography.

Renal failure was more frequent in patients with the defined diagnosis of infective endocarditis who had an abscess of the valvular ring ($P=0.04$).

The need for surgical treatment was greater among patients in whom perivalvular abscesses were identified ($P=0.004$).

The mortality rate was greater in patients with perivalvular abscesses ($P=0.003$).

In patients with a defined diagnosis of infective endocarditis, periprosthetic insufficiency was evidenced in 2 cases on transthoracic echocardiography, and in 6 on transesophageal echocardiography (tab. II). Of the 6 episodes, a new cardiac murmur was reported in 3. The greater number of transthoracic and transesophageal examinations predominated in patients with the defined diagnosis of endocarditis, with a relative decrease in the number of those examinations in patients with the possible and rejected diagnoses of endocarditis.

A greater need for surgical treatment was observed among patients in whom acute periprosthetic insufficiency was identified ($P=0.001$).

No statistical significance was observed between the presence of acute periprosthetic insufficiency and the following parameters: sex, age, and the different etiologic agents. No statistical significance was observed between the different times between symptom onset and hospitalization. Neither the presence of complications, nor the mortality rate was greater. In patients with the possible or rejected diagnosis of endocarditis, no acute periprosthetic insufficiency was identified on echocardiography.

In the cases with the defined diagnosis of infective endocarditis, in addition to vegetations, the following characteristics were observed on echocardiography: thrombi in 6 cases (all of them with surgical confirmation, 2 on transthoracic examination); sponta-

neous contrast in 10 cases (2 on transthoracic echocardiography); perforation of the mitral leaflet in 2 (with surgical confirmation and no evidence on transthoracic examination); early closure of the mitral valve in the case of acute aortic valve insufficiency in 1 (only transthoracic echocardiography was performed); destruction of the mitroaortic junction in 8 (all of them with surgical confirmation, and identification on transthoracic examination in 1 case); fistulas from the aorta to the right atrium in 2 (1 case identified on transthoracic echocardiography and confirmed on surgery); and rupture of the chordae tendineae in 5 (all with surgical confirmation and identification on transthoracic echocardiography).

Discussion

The case series studied was characterized by predominance of patients with cardiac valve prostheses (63%), patients undergoing surgical treatment (73.2%), and a high mortality rate (35.2%), which show the severity of the disease in those cases.

The data obtained by use of transthoracic echocardiography contributed to the diagnosis in 61 (48%) of the 127 patients with the defined diagnosis of endocarditis. The information provided by transesophageal echocardiography enabled the addition of diagnostic information in 112 (88.2%) of these 127 patients, obtaining the diagnosis of vegetation in 51 (40.1%) other cases, more than the 61 diagnosed on the transthoracic examination. This diagnostic increment takes into consideration the population involved in the study, in which patients with cardiac valvular prostheses predominate. In specific groups, such as that of patients with cardiac valvular prostheses, the transesophageal echocardiographic investigation may be regarded as a method of initial diagnostic investigation, due to the greater diagnostic accuracy of the transesophageal technique as compared with that of transthoracic echocardiography^{2,14}. Patients with greater diagnostic difficulty require repetition of the echocardiographic examinations². In the present study, the transthoracic echocardiographies were repeated until the sixth examination, and the transesophageal echocardiographies until the fifth examination. No addition of diagnostic information

Table II – Transthoracic and transesophageal echocardiographic findings in 262 patients with 266 episodes suspected of infective endocarditis

Clinical characteristics	Diagnostic category			
	Total n (%)	Defined n (%)	Possible n (%)	Rejected n (%)
Episodes	266 (100)	127 (47.8)	81 (30.4)	58 (21.8)
Transthoracic examinations (n/mean per group)	629/2.4	363/2.8	170/2.1	96/1.6
Vegetation	63 (23.7)	61 (48)	2 (2.5)	-
Cardiac perivalvular abscess	5 (1.9)	5 (3.9)	-	-
Acute periprosthetic insufficiency	2 (0.75)	2 (1.6)	-	-
Thrombus	4 (1.5)	2 (1.6)	1 (1.2)	1(1.7)
Pericardial effusion	26 (9.8)	16 (12.6)	6 (7.4)	4 (6.9)
Intercavitary fistula	1 (0.4)	1 (0.8)	-	-
Rupture of the chordae tendineae	5 (1.9)	5 (3.9)	-	-
Transesophageal examinations (n/mean per group)	330/1.2	183/1.4	87/1.1	60/1
Vegetation	120 (45.1)	112 (88.2)	8 (9.9)	-
Cardiac perivalvular abscess	37 (13.9)	37 (29.1)	-	-
Acute periprosthetic insufficiency	6 (2.2)	6 (4.7)	-	-
Thrombus	18 (6.8)	6 (4.7)	3 (3.7)	3 (5.1)
Pericardial effusion	27 (10.1)	16 (12.6)	6 (7.4)	5 (8.6)
Intercavitary fistula	2 (0.7)	2 (1.6)	-	-
Rupture of the chordae tendineae	5 (1.9)	5 (3.9)	-	-

n- number.



was observed after the third examination, either transthoracic or transesophageal ²².

A greater frequency of stroke was observed in patients with endocarditis in whom vegetations with dimensions > 10 mm were identified, although a greater frequency of peripheral embolic phenomena correlated with the dimensions of the vegetations was not observed. A greater frequency of stroke or peripheral embolism correlated with the mobility of the vegetations or location of the vegetation was not observed. Up to 65% of the embolic events may affect the central nervous system ², with a lower frequency in the different organs and places ^{23,24}. Previous studies ²⁴⁻³⁰ about the frequency of embolic phenomena in regard to the dimensions and mobility of vegetations are considered controversial. Some studies ²⁴⁻²⁷ report a greater frequency of embolic phenomena in patients with vegetations with dimensions > 10 mm, with great mobility, and with involvement of the mitral valve ²⁶. Other series do not report a greater frequency of embolic phenomena in patients with vegetations > 10 mm ²⁸⁻³⁰ and with great mobility ^{28,30}. The different series diverge in regard to the results and the echocardiographic methods used for identifying the vegetations. Some series used only the transthoracic investigation ^{25,27,29}, while others the transesophageal ^{24,26,28,30}.

Patients with time between symptom onset and hospitalization < 10 days had a greater incidence of the following: vegetations and cardiac valvular abscesses, defined diagnosis of endocarditis, 76 (59.8%) of 127 cases, heart failure, stroke, renal failure, and extracerebral embolic phenomena, 28 (53.8%) of 52 cases, 19 (65.5%) of 29 episodes, 37 (55.2%) of 67, and 12 (57.1%) of 21, respectively. These data show the importance of the initial clinical signs and symptoms and of the diagnostic investigation in patients in whom the diagnosis of infective endocarditis is possible.

The identification of 132 (97.8%) of 135 images of vegetation with refringence similar to that of the endocardium shows recent endocardial involvement, because the greater structural refringence may represent calcium accumulation due to the greater time of occurrence of the event.

The identification of cardiac perivalvular abscesses was also more frequent in patients with vegetations > 10 mm and with greater mobility. The vegetations with greater dimensions and mobility may represent greater endocardial involvement, with a greater potential to develop cardiac valvular abscesses.

The diagnosis of perivalvular abscesses and periprosthetic insufficiency was very important because of therapeutic and prognostic

implications. Patients with perivalvular abscesses had a greater need for surgical treatment and a higher incidence of renal failure, with higher mortality, and, patients with periprosthetic insufficiency had a higher need for surgical treatment.

In 8 patients with the possible diagnosis of endocarditis, structures identified as vegetations due to infective endocarditis were visualized on transesophageal echocardiography. These structures were either not confirmed on the anatomicopathological examination or had clinical improvement after treatment for a short period of time. In the series of patients in which echocardiographic criteria were introduced for the diagnostic categorization of endocarditis ¹, images defined as vegetations were identified in 11 (7%) cases with the possible diagnosis of endocarditis and in 4 (8%) cases with the rejected diagnosis of endocarditis. The differential diagnosis of vegetations resulting from infective endocarditis is made with natural structures, such as valvular thickening and degeneration, chordae tendineae, and nodular structures found mainly in the native aortic valve, such as the Lambl excrescences and the Arantius nodule. Structures with morphology similar to that of the vegetation of infective endocarditis may also be found in the following conditions: marantic (thrombotic) endocarditis; noninfective Libman-Sacks endocarditis; small tumors, such as papillary fibroelastomas; and in the presence of cardiac thrombi. The morphological differentiation of small vegetations from surgical suture thread or structures denominated fibrin filaments is more difficult ^{31,32}. In our study, all structures identified as vegetations, which underwent surgery and were not confirmed as such, were surgical suture thread with a postoperative period < 2 months.

In our case series, most patients had cardiac valvular prostheses with the suspected diagnosis of infective endocarditis and echocardiographic investigation performed in a tertiary hospital specializing in cardiology, and this may not represent other clinical circumstances with a possible diagnosis of endocarditis. The indications for performing echocardiographic investigation were heterogeneous and based on the need for diagnostic investigation and appreciation of the attending physician.

In conclusion, in patients with suspected infective endocarditis undergoing echocardiographic assessment, the echocardiographic findings varied according to the following diagnostic categories: defined, possible, and rejected. The contribution of the echocardiographic information, both for the diagnosis and prognostic assessment, should take into consideration the pretest probability of the diagnosis of infective endocarditis.

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