

CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

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Case 25-2025: A 93-Year-Old Woman with Dyspnea and Fatigue

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PRESENTATION OF CASE

Dr. Leigh H. Simmons: A 93-year-old woman was evaluated by her primary care physician because of dyspnea.

The patient had been in her usual state of health, which included being independent with respect to activities of daily living and participating in light exercise daily, until 1 month before the current presentation, when dyspnea developed.

Seven years before the current presentation, echocardiography was performed to assess a systolic murmur that radiated to the carotid arteries, and aortic stenosis was diagnosed. Five years before the current presentation, osteoarthritis that had been refractory to treatment resulted in total knee replacement; while the patient was hospitalized, arrhythmia was detected on telemetry and atrial fibrillation was diagnosed. During that hospitalization, repeat echocardiography was performed.

Dr. Nathanael Tran: Transthoracic echocardiography showed stable aortic stenosis, with a mean aortic-valve gradient of 18 mm Hg (<20 is mild), a peak aortic velocity of 2.8 m per second (<3.0 is mild), and an aortic-valve area of 1.5 cm² (>1.5 is mild) (Fig. 1 and Video 1).

Dr. Simmons: Anticoagulant therapy was not started at that time. However, 15 months before the current presentation, atrial flutter developed and treatment with apixaban and metoprolol was started. Echocardiography was performed.

Dr. Tran: Transthoracic echocardiography showed progression of aortic stenosis, with a mean gradient of 23 mm Hg, a peak velocity of 3.0 m per second, and an aortic-valve area of 0.9 cm².

Dr. Simmons: At the current presentation, the patient reported that the onset of dyspnea had been gradual and had progressed steadily during the past month. She stated that she had previously maintained a regular schedule of physical activity that had included dancing and daily walks but that the shortness of breath now prevented her from participating in these activities. She had no chest pain, palpitations, weight gain, leg swelling, or orthopnea, and she did not awaken at night with shortness of breath. She reported no melena or blood in the stool.

Author affiliations are listed at the end of the article.

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 transthoracic
 echocardiography
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Figure 1. Transthoracic Echocardiogram Obtained 5 Years before the Current Presentation.

A parasternal short-axis view of the aortic valve shows mild aortic stenosis. The mean aortic-valve gradient is 18 mm Hg (<20 is mild), the peak aortic velocity is 2.8 m per second (<3.0 is mild), and the aortic-valve area is 1.5 cm^2 (>1.5 is mild).

Additional medical history included stage 3a chronic kidney disease, type 2 diabetes mellitus, sensorineural hearing loss in both ears (for which she used hearing aids), Hashimoto's thyroiditis, vitamin B₁₂ deficiency, obstructive sleep apnea, and depression. Granulomatosis with polyangiitis was diagnosed 17 years before the current presentation and had been treated with cyclophosphamide, followed by azathioprine and low-dose prednisone, which had led to remission; treatment with azathioprine was stopped 9 years before the current presentation, and low-dose prednisone therapy was continued. The most recent screening colonoscopy was performed when the patient was 78 years of age (15 years before the current presentation), and no polyps were seen. Other surgical history included hysterectomy and total replacement of one knee at 85 years of age and the other at 88 years of age.

Other medications included aspirin, calcium carbonate, vitamin D, vitamin B₁₂, citalopram, glipizide, and levothyroxine. The patient had no known adverse reactions to medications. Approximately 2.5 years before the current presentation, she had moved to an assisted-living facility after the death of her husband. She was a lifelong non-smoker and did not drink alcohol or use illicit drugs.

On examination, the temporal temperature was 36.2°C , the blood pressure 123/62 mm Hg,

the pulse 61 beats per minute, the respiratory rate 12 breaths per minute, and the oxygen saturation 100% while the patient was breathing ambient air. The body-mass index (the weight in kilograms divided by the square of the height in meters) was 23.2. She appeared mildly fatigued but was in good spirits. The jugular venous pressure was estimated at 5 cm of water. The heart rhythm was regular, with normal heart sounds, and S2 was normal. A grade 4/6 systolic murmur that did not obscure the second heart sound was noted. The lungs were clear on auscultation. The skin was not pale. She had no leg edema. An electrocardiogram (ECG) showed sinus rhythm. Imaging studies were obtained.

Dr. Andrea C. Furlani: Chest radiography (Fig. 2) showed a normal cardiomeastinal silhouette and no pulmonary edema, along with pleuroparenchymal scarring in the lung apices with upper-lung volume loss — a finding that was unchanged from that seen on computed tomography (CT) that had been performed in the remote past. In addition, the radiograph showed coronary and aortic-valve calcifications.

Dr. Simmons: Diagnostic tests were performed, and management decisions were made.

DIFFERENTIAL DIAGNOSIS

Dr. Suzanne V. Arnold: I am aware of the final diagnosis in this case. This 93-year-old woman with moderate aortic stenosis and paroxysmal atrial fibrillation and flutter presented with dyspnea that had progressed over the course of 1 month. Slowly progressive dyspnea is a common presenting symptom that may be caused by cardiac or noncardiac processes.

CARDIAC CAUSES OF DYSPNEA

Progressive stable angina manifesting as exertional dyspnea is a possible diagnosis in this patient's case, and nonspecific symptoms of coronary ischemia are common in older women. Atrial arrhythmias can cause progressive dyspnea but would generally need to be persistent to account for this patient's symptoms. It is important to note that atrial flutter with adequate heart-rate control — or even atrial fibrillation — can be missed on physical examination, particularly when heart rates are slow and irregularity is more difficult to ascertain. However, this patient's ECG showed sinus rhythm.

Sick sinus syndrome with chronotropic incompetence leading to an abnormally slow heart rate should be considered in this older woman.¹ Frequent premature ventricular contractions (>15%

of total heartbeats), even in the context of a normal ejection fraction, can also cause exertional intolerance but would be unlikely in this patient who had no evidence of ectopy on examination or ECG. In patients in whom chronotropic incompetence or frequent premature ventricular contractions are suspected, short-term continuous rhythm monitoring can be useful.

Heart failure and valvular disease can also cause subacute dyspnea. The absence of signs of hypervolemia on examination of this patient makes heart failure an unlikely diagnosis, although a low-flow state can cause dyspnea in the absence of overt hypervolemia. In older patients, age-related hypertrophic obstructive cardiomyopathy, infiltrative cardiomyopathy, mitral stenosis due to mitral annular calcification, degenerative mitral regurgitation, tricuspid regurgitation, and aortic stenosis are all relatively common causes of subacute dyspnea. Atrial dilatation and resultant functional mitral or tricuspid regurgitation should be considered in this patient with atrial arrhythmias. It is important to note that, in this patient, the presence of a murmur associated with severe tricuspid regurgitation could easily be obscured by the murmur associated with her aortic stenosis. Progression of aortic stenosis is a probable diagnosis in this patient. However, preservation of the second heart sound on cardiac auscultation makes progression to severe aortic stenosis unlikely.

NONCARDIAC CAUSES OF DYSPNEA

Interstitial lung disease, pleural effusion, or hiatal hernia can cause dyspnea. The normal chest radiograph in this patient makes these pulmonary causes of dyspnea unlikely. In patients with chronic kidney disease, such as this patient, acute kidney injury can cause dyspnea, either through hypervolemia or metabolic acidosis. Anemia, neuromuscular disorders, and hyperthyroidism can lead to exercise intolerance that is often described by patients as dyspnea. Furthermore, these systemic symptoms of stress can lead other cardiac conditions to become symptomatic. For example, chronic coronary disease, cardiomyopathy, or valvular disease may not be symptomatic unless a patient has increased systemic stress from another condition such as sepsis or anemia.

At this point in the patient's clinical course, progression of aortic stenosis would be my lead-

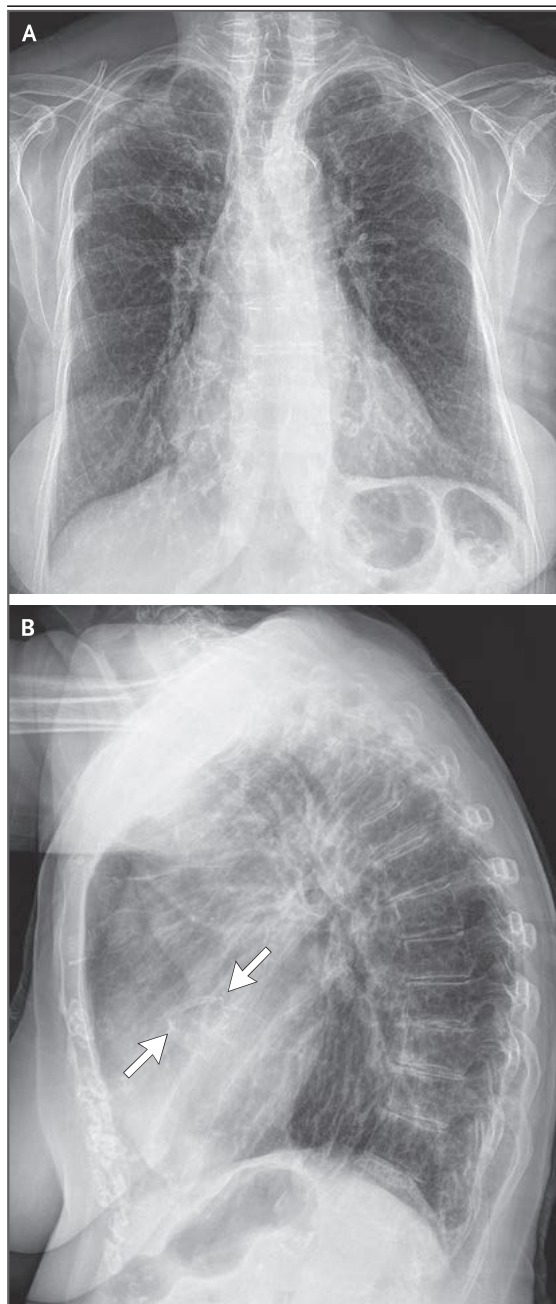


Figure 2. Chest Radiographs.

A frontal radiograph of the chest (Panel A) shows a normal cardiac silhouette without pulmonary edema. Stable pleuroparenchymal scarring is present in the lung apices. Coronary and aortic-valve calcifications are seen on a lateral radiograph (Panel B, arrows).

ing diagnosis. If basic laboratory testing ruled out noncardiac causes of dyspnea, I would obtain an echocardiogram to evaluate the degree of aortic stenosis.

DR. SUZANNE V. ARNOLD'S DIAGNOSIS

Aortic stenosis.

DIAGNOSTIC TESTING

Dr. Simmons: A complete blood count was performed, and the level of hemoglobin was 7.7 g per deciliter (reference range, 12.0 to 16.0), which had decreased from a level of 10.6 g per deciliter obtained 2 months earlier. The remainder of the complete blood count was normal. The blood levels of iron and ferritin were normal, and the reticulocyte count was 1.1% (reference range, 0.5 to 2.0); the corrected reticulocyte count was 0.8% (reference range, 0.5 to 2.0), and the reticulocyte production index was 0.4 (reference value, >3.0). When the patient was asked again about stool color, she reported that her stools had occasionally been dark. Treatment with apixaban and aspirin was stopped. One unit of packed red cells was transfused. After transfusion, the blood level of hemoglobin increased to 9.0 g per deciliter and dyspnea resolved.

A diagnosis of slow gastrointestinal bleeding due to Heyde's syndrome (the triad of aortic stenosis, gastrointestinal bleeding, and acquired von Willebrand's disease) was considered. Further evaluation by means of esophagogastroduodenoscopy and colonoscopy was discussed, but the patient's preference was to avoid these procedures unless absolutely necessary. Treatment with apixaban was resumed, but aspirin was not restarted. Echocardiography was repeated.

Dr. Tran: Transthoracic echocardiography revealed moderate-to-severe aortic stenosis; the mean gradient had increased to 32 mm Hg, the peak velocity was 3.6 m per second, and the aortic-valve area was 0.6 cm².

Dr. Simmons: The blood level of hemoglobin remained stable on monthly checks, and dyspnea did not recur.

Dr. Tran: Nine months later, transthoracic echocardiography revealed severe aortic stenosis; the mean gradient had further increased to 39 mm Hg, the peak velocity was 4.1 m per second, and

the aortic-valve area was 0.5 cm² (Fig. 3 and Video 2).

Dr. Simmons: The patient was referred to the cardiology clinic affiliated with this hospital, and management decisions were made.

DISCUSSION OF MANAGEMENT

Dr. Arnold: Shared decision making with regard to the management of aortic stenosis in this patient begins with an understanding of multiple factors. These include the expected progression of aortic stenosis over time, the challenges in defining the severity of aortic stenosis, the way in which transcatheter aortic-valve replacement (TAVR) has increased the available options for intervention, and this particular patient's preferences, values, and goals of care.

PROGRESSION OF AORTIC STENOSIS

Most cardiac conditions involve varying patterns of progression over time. For example, a patient with dilated cardiomyopathy may have stable disease for many years without a decline in ejection fraction. In these patients, the severity of mitral regurgitation may remain moderate or even severe without the need for intervention.² In contrast, aortic stenosis will reliably progress from moderate to severe and then further progress to symptomatic disease. On average, in patients with aortic stenosis, the mean gradient increases by 4.1 mm Hg per year (with greater increases seen as aortic stenosis progresses), and the aortic-

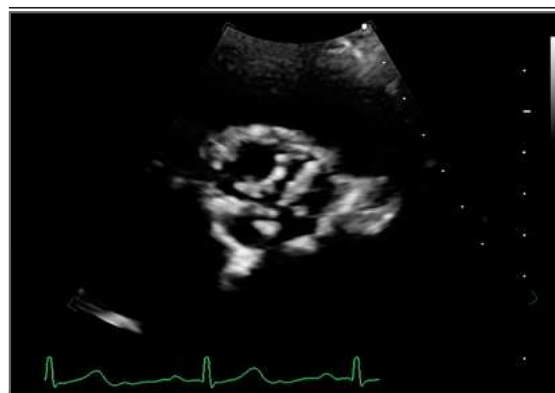


Figure 3. Transthoracic Echocardiogram Obtained 9 Months after the Current Presentation.

A parasternal short-axis view of the aortic valve shows severe aortic stenosis. The mean gradient has increased to 39 mm Hg, the peak velocity is 4.1 m per second, and the aortic-valve area is 0.5 cm².

valve area decreases by 0.08 cm² per year.³ Historical data suggest that it takes 2 to 5 years for aortic stenosis to progress from asymptomatic severe disease to symptomatic severe disease,⁴ but more recent data suggest that the true time to progression may be shorter. The results of a recent trial involving patients with asymptomatic severe aortic stenosis who had been randomly assigned to undergo either clinical surveillance or early intervention with TAVR showed that the median time from randomization to conversion to the intervention was only 11.1 months among patients in the surveillance group.⁵ Within 2 years after randomization, approximately 70% of these patients had progressively worsening symptoms and underwent TAVR.⁵

The predictable and fairly rapid progression from asymptomatic severe aortic stenosis to symptomatic severe aortic stenosis may support a strategy of treating patients earlier in the disease process. Severe aortic stenosis may cause upstream cardiac damage (e.g., ventricular fibrosis, atrial enlargement, pulmonary hypertension, or right ventricular dysfunction), and earlier intervention before the secondary effects of aortic stenosis occur may contribute to improved clinical- and health-status outcomes after TAVR.^{6,7} However, a strategy of careful surveillance in asymptomatic patients is still reasonable given the current evidence.

CHALLENGES IN DIAGNOSING SEVERE AORTIC STENOSIS

Aortic stenosis is defined as severe when the peak velocity is 4 m per second or greater, the mean gradient is 40 mm Hg or greater, or the aortic-valve area is 1.0 cm² or less (or ≤ 0.6 cm² per square meter of body-surface area). However, it is common for a patient to meet some but not all the criteria for a severity classification, and additional data such as the dimensionless velocity index, the stroke volume index, and the detection of aortic-valve calcification on CT must be considered. The occurrence of errors in the measurement of certain variables is also possible and is especially common when the left ventricular outflow-tract area is measured. Paradoxical low-flow, low-gradient severe aortic stenosis is another consideration when evaluating for severe aortic stenosis, particularly in older women with small left ventricular cavities or restrictive ventricular filling. This condition results in a low

stroke volume despite a normal ejection fraction, which can affect the capacity to generate high gradients across a stenotic aortic valve.

In this patient, the aortic-valve area met the criterion of 1.0 cm² or less on an echocardiogram that had been obtained 15 months before the current presentation, although the mean gradient and peak velocity were in the moderate range. Nonetheless, given that the aortic stenosis was asymptomatic during this time, a plan of careful surveillance was appropriate. However, it is important to recognize that categorizing the severity of aortic stenosis may be challenging in patients with inconsistent measurements. In older patients with vague symptoms, careful consideration of supporting data and evaluation for measurement errors is needed to avoid the possibility of missing hemodynamically and prognostically important severe aortic stenosis.

CHANGES IN OPTIONS FOR INTERVENTION

Since the introduction of TAVR, the total annual number of aortic-valve interventions performed in the United States has doubled, with a decrease in the annual surgical volume of approximately 45%, indicating that the use of TAVR has led to a substantial increase in the number of patients undergoing intervention.^{8,9} Among patients older than 80 years of age, the annual number of surgical aortic-valve replacements has decreased by 96% from 2012 to 2022⁹ because these patients are almost exclusively choosing between TAVR and medical management. Although the long-term outcomes in older patients are similar with TAVR and surgical aortic-valve replacement, the difference in short-term recovery between these approaches has markedly changed the discussion as to whether an older person wants to undergo surgical intervention or receive medical management.

When TAVR was first approved in the United States in 2011, the median length of stay in the hospital after the procedure was 7 days and 50% of patients had a poor outcome at 1 year (30% had died and 20% had a persistently poor quality of life).¹⁰ Since the introduction of TAVR, there has been marked improvement, with the median length of stay after TAVR having decreased to 1 day, although variability is seen with older age, coexisting conditions, the vascular access site, the urgency of the procedure, and complications affecting the length of hospital stay.⁸

Short-term mortality and major complications are also relatively low with TAVR (30-day mortality, <4%; incidence of stroke, <2%; incidence of major bleeding, <3%), and most patients have clinically significant improvement in health status within a month after the procedure.⁸ Given the relatively short recovery time, combined with the low risk of major complications, few patients are considered to be inappropriate candidates for TAVR on the basis of age or coexisting conditions. As such, it is becoming less common for patients to choose medical management in the context of symptomatic severe aortic stenosis. However, it is still important to engage with the patient in shared decision making regarding all alternative treatment methods, including palliative care.

APPROACH TO MANAGEMENT

In patients with symptomatic severe aortic stenosis, aortic-valve replacement is a class I indication to prolong survival and improve health status, with TAVR being the preferred treatment for patients older than 80 years of age (on the basis of U.S. guidelines⁴) or older than 75 years of age (on the basis of European guidelines¹¹). This patient was symptomatic when hemodynamic stress from anemia was present, but she had minimal symptoms after red-cell transfusion. Given her history of symptoms during a time of increased hemodynamic stress, proceeding with TAVR was a possible option. Another option was to wait until symptoms recurred in the absence of additional stressors and then proceed to TAVR. A third option was to wait until symptoms developed and then pursue medical management with palliative care and eventually hospice. Although TAVR has greatly expanded the pool of patients who are willing and able to undergo intervention, many patients instead still elect to manage symptoms when they develop.

SHARED DECISION MAKING

When engaging in shared decision making with a patient with respect to the decision to pursue TAVR as opposed to medical management, it is important to ascertain the patient's goals of care, values, and preferences. Although TAVR will often prolong survival, this outcome may not be the patient's primary goal of treatment, given that many patients prioritize improvement in quality

of life and reduction of symptoms over prolonged survival.

It is also important to ensure that the patient understands the expected progression of disease and what the anticipated trajectory would be with each treatment option, including requirements for additional diagnostic procedures and follow-up appointments, potential complications, and expected recovery time. Although TAVR can be a very effective tool to improve quality of life for a patient with symptoms due to aortic stenosis, it involves both diagnostic and therapeutic procedures that take time and are associated with risks.

Ultimately, we must actively listen to patients, work to understand their values and goals, help them understand the trade-offs and potential consequences of their choices, and then support these decisions as best we can. Patients should not feel abandoned if they choose medical management over invasive interventions. Access to effective palliative care services is critical, since progression of symptoms is expected but can be anticipated and well managed.

FOLLOW-UP

Dr. Simmons: I referred the patient to a cardiologist, and I counseled her that she would be discussing management options for aortic stenosis. I assumed that she would be offered TAVR and expected that she would choose to proceed with that option. The patient met with the cardiologist three times over the course of a year and carefully discussed her options. The patient ultimately decided that she did not wish to undergo the extensive testing that would be required to be considered for aortic-valve replacement. She indicated that when she becomes more symptomatic with aortic stenosis, she would like to enroll in hospice care and cited her husband's positive experience with hospice as one of the reasons she was choosing this path. She has chosen to have no further monitoring of her aortic stenosis.

Approximately 1.5 years after the current presentation, the patient continues to feel well and engages in her usual activities, including dancing, without dyspnea or substantial fatigue. She continues to receive apixaban therapy for stroke prevention. The complete blood count has been

checked every 2 to 3 months, and anemia has not recurred.

PATIENT PERSPECTIVE

The Patient: When I had started feeling short of breath, I didn't expect that it would lead to the discovery of a serious heart-valve problem. I've had atrial fibrillation and a heart murmur for years, but it was still surprising to learn that I had severe aortic stenosis.

At 93 years of age, as I deliberated the option of valve replacement, which would have had risks, I saw the choice as being between treatment and an end-of-life decision. Without valve replacement, my projected life span would be 2 years. The risks of the procedure — like stroke or other complications — just didn't feel worth it to me. I decided to forgo treatment based on my understanding of human life as impermanent, my advanced age, and gratitude for the fullness of life — a loving family; close friends; community; opportunities in education, social justice, and advocacy work; housing in a continuing-life-care community; and excellent health care. Additional factors that entered into my decision making were being a child of immigrant parents and helping them navigate medical systems; the strength, fearlessness, and practical sense of my mother; my studies in Eastern religions; my teaching and practice of Hatha yoga for nearly 30 years; my loving church community; and the influence of Erik Erikson's human developmental theory of eight life stages, including the last one in which creativity, generativity, legacy-building, and social connection are called for.

My cardiologist recommended valve replacement and spoke about it favorably, but she always made sure to remind me that it was my choice. I felt respected and supported throughout. I'm still doing yoga, taking walks, and going to dance class. I don't feel out of breath anymore, and I'm grateful for that. Looking back, I have no regrets. This decision reflects my values, and I'm thankful for the care I've received and for the freedom to make the choice that felt right for me.

On a practical level, I suggest that attention be paid to a patient's ability to hear. At times during my medical visits, I struggled to hear what doctors were saying and didn't fully under-

stand my diagnosis until my son joined me for a visit about my heart condition and could hear the conversation better. To ensure a patient's understanding, I suggest that the physician provide a written summary of the diagnosis and recommendations at the end of the visit. Lastly, another very practical consideration is for the physician to speak slowly and deliberately.

FINAL DIAGNOSIS

Aortic stenosis.

CASE RECORDS EDITORS' NOTE — LESSONS LEARNED

Dr. Simmons: In reflecting on this patient's care, I think about the importance of allowing the proper time for deliberation when decisions are not clinically urgent, as well as the importance of clinicians being open to hearing patients' perspectives on what treatments are right for them. I was certain that this patient would want to proceed with TAVR; after all, she had chosen total knee replacement twice, at the ages of 85 and 88 years. She had been very satisfied with her decisions to have surgery. However, our duty as her physicians went beyond diagnosing the aortic stenosis. In order to make the best recommendation for management, we first had to ascertain the patient's preference. When she told me she did not want to proceed with TAVR, I had to adjust my own expectations about a successful management outcome for her aortic-valve disease. I came to understand her perspective on the burden and the risk of the preparatory testing and procedures that would be required before undergoing TAVR.

The work of coming together with our patients on a shared decision requires training, time, and tools to support both clinicians and patients.¹² I hope this patient's story will serve to promote shared decision making that is individualized for patients across the spectrum of clinical care.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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