Mitral valve prolapse: role of 3D echocardiography in diagnosis

Ricardo Benenstein and Muhamed Saric

Purpose of review
To review the utility and the latest developments in three-dimensional (3D) echocardiography of mitral valve prolapse.

Recent findings
Although 3D echocardiography has been invented in 1974, it has not gained wide clinical acceptance until the introduction of real-time 3D echocardiography in the first decade of the 21st Century. Driven by improvements in probe technology and increases in computing power, 3D echocardiography now provides unprecedented images of mitral valve prolapse and its associated mitral regurgitation with no or minimal requirements for image post processing.

Summary
3D echocardiography has become the echocardiographic modality of choice for establishing the diagnosis, describing the precise anatomy, and visualization of mitral regurgitant jets in mitral valve prolapse. 3D echocardiography is becoming indispensable in guiding surgical and percutaneous methods of mitral valve repair and replacement.

Keywords
mitral valve prolapse, real-time 3D echocardiography, transesophageal echocardiography, transthoracic echocardiography

INTRODUCTION
The word prolapse (from Latin ‘to slip forward’) has been used since the 17th Century to refer to slipping of a body part (such as the uterus) from its usual position. It appears that the term prolapse was first applied to the mitral valve in 1966 by Criley et al. [1].

Mitra valve prolapse (MVP) may be defined as an abnormal protrusion or bulging of mitral valve leaflet segments into the left atrium past the plane of the mitral annulus during ventricular systole. In typical MVP, the free leaflet edges point toward the left ventricle during systole. In more severe forms of MVP, the free edges of mitral leaflets may lose their chordal support and evert into the left atrium during systole. When that occurs, the mitral valve leaflet is said to be flail.

Mitral valve prolapse is the leading cause of mitral regurgitation and the most frequent reason for mitral valve surgery in the industrialized world. On the basis of two-dimensional (2D) transthoracic imaging, the prevalence of MVP in the Framingham population is calculated at 2.4% [2].

Due to complexity of the mitral valve apparatus, especially the saddle-shaped nature of the mitral annulus, MVP is often difficult to fully characterize by cross-sectional imaging techniques such as 2D echocardiography. Real-time three-dimensional (3D) echocardiography – notably 3D transesophageal echocardiography (3D-TEE) – provides unprecedented views of the mitral valve apparatus including the unique real-time en face view of the mitral valve from the left atrial perspective.

The 3D echocardiographic en face view is equivalent to the way surgeons see the mitral valve. One can usually visualize all the details of MVP from this single 3D en face view – something that can only be accomplished by multiple cross-sectional images and a fair amount of mental Leon H. Charney Division of Cardiology, New York University Langone Medical Center, New York, USA

Correspondence to Muhamed Saric, MD, PhD, Noninvasive Cardiology Laboratory, New York University Langone Medical Center, 560 First Avenue, New York, NY 10016, USA. Tel: +1 212 263 5665; fax: +1 212 263 8461; e-mail: muhamed.saric@nyumc.org

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Three-dimensional (3D) echocardiography is an excellent imaging technique for establishing the diagnosis of MVP, and provides means for detailed description of MVP in preparation for surgical or percutaneous repair.

3D echocardiographic techniques that are useful in MVP include the en face zoomed view of the mitral valve as well as liver 3D, full-volume 3D, and 3D color Doppler techniques.

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The study of MVP originally started in the field of cardiac auscultation and phonocardiography rather than in imaging. Clinicians of the 19th and 20th Century noted that typical mitral regurgitation presents with a holosystolic murmur and is often functional in nature (e.g. due to left-ventricular dilatation). In the 20th Century, with the advent of phonocardiography – electronic recordings and graphical representations of cardiac sounds which allowed precise timing of cardiac events – it became evident that some patients present with murmurs that start in mid-systole and terminate at end-systole and are often preceded by a mid-systolic click.

In 1963, the South African cardiologist John B. Barlow et al. [3] were apparently the first to demonstrate clinically that these mid-systolic onset murmurs – based on their response to amyl nitrite inhalation, Valsalva maneuver, and phenylephrine injection – were due to mitral regurgitation; it was previously thought that they were pericardial or pleural in origin. Subsequently, Barlow and his colleagues performed cine angiograms (ventriculograms) in these patients but erroneously interpreted them as showing ‘subvalvular ventricular aneurysm’ [4].

If 1964, Barlow visited the Johns Hopkins Hospital in Baltimore and met John Michael Criley who correctly interpreted the cine angiograms in patients with mid-systolic onset murmurs as showing systolic protrusion of the mitral leaflets into the left atrium. It was Criley who appears to have introduced the term ‘mitral valve prolapse’ to refer to these angiographic findings [1]. Barlow himself preferred the term ‘billowing of the mitral valve’ [4].

Thereafter the eponym ‘Barlow’s disease’ or ‘Barlow’s syndrome’ was introduced into the medical parlance (probably as early as 1974), but its strict definition remains unclear [5]. Some use the term Barlow’s disease to refer to MVP due to diffuse myxomatous degeneration and extensive bileaflet redundancy, billowing, and broad prolapse [6**]. Interestingly, Barlow himself in his initial study described the billowing of the posterior leaflet alone (Barlow and Bosman [7]).

Others (notably the French surgeon Alain Carpentier) use the term Barlow’s disease to refer to primary forms of MVP that are related to myxomatous leaflet degeneration as opposed to fibroelastic deficiency or connective tissue disorders [8].

MVP has a wide spectrum of presentations spanning from single leaflet segment involvement to generalized bileaflet pathology. With respect to its cause, MVP may be either primary or secondary. Primary MVP refers to conditions in which there is primary abnormality of the mitral leaflet anatomy, whereas secondary MVP refers to conditions in which mitral leaflet prolapse is secondary to abnormalities in the subvalvular mitral apparatus (Table 1).

The two leading causes of primary MVP include myxomatous degeneration and fibroelastic deficiency [9]. Myxomatous degeneration is likely a genetic condition in which there is replacement of the normal leaflet and chordal tough fibrous structure with a loose mucopolysaccharide-rich material. The genetics of myxomatous generations are complex and are likely due to multigene,
multichromosomal autosomal dominance with incomplete penetrance [6**].

Myxomatous degeneration typically leads to progressive thickening, redundancy, and billowing of multiple leaflet segments. Frequently significant mitral regurgitation develops by the time patients reach their middle age. Because myxomatous degeneration is the most predominant cause of MVP, the terms myxomatous degeneration and MVP are often (albeit incorrectly) used synonymously. Interestingly, MVP that is macroscopically and histologically similar to myxomatous degeneration in humans also occurs with a very high frequency in certain breeds of dogs, such as Cavalier King Charles Spaniels [10].

In contrast, fibroelastic deficiency typically presents with a single-segment prolapse in an elderly patient. The prolapse segment is thick and redundant. However, the remaining mitral leaflet tissue is thinner than normal and has translucent (pellucid) appearance. The cause of fibroelastic deficiency is unknown but is clearly age-related [11].

Other causes of primary MVP include connective tissue disorders such as Marfan’s disease and Ehlers-Danlos syndrome. In many forms of primary MVP, there is concomitant involvement of the tricuspid valve (as in myxomatous degeneration) or the aortic valve (as in Marfan’s disease). Secondary MVP results when structurally normal mitral valve leaflets lose their chordal and papillary muscle support as it may occur in endocarditis, papillary muscle rupture during acute coronary syndromes or following left-ventricular remodeling and papillary muscle displacement (as in patients with chronic infarction surrounding the posteromedial papillary muscle).

### HISTORY OF THREE-DIMENSIONAL ECHOCARDIOGRAPHY OF MITRAL VALVE PROLAPSE

As early as 1974, a 3D transthoracic echocardiography (3D-TTE) system was developed in the US; it used a long mechanical arm to locate the position of the transducer in space and allow alignment of multiple 2D images and subsequent offline reconstruction of very-low-resolution 3D image of the heart [12]. This system was primarily a proof of concept rather than a clinically useful imaging tool.

In 1989, using a more advanced but conceptually similar 3D transthoracic system, Levine et al. [13,14] at the Massachusetts General Hospital confirmed their seminal discovery of the nonplanar, saddle-shaped nature of the mitral annulus.

The saddle-shaped nature of the mitral annulus had a profound implication on the diagnosis of MVP which, from then on, was defined as systolic bulging of mitral leaflets above the high points of the annulus. These high points are located in the antero-posterior direction and are best seen in parasternal or apical three-chamber TTE views. In contrast, the leaflets may normally protrude past the medio-lateral low points of the annulus which are seen in the apical four-chamber view. The saddle-shaped nature appears to minimize leaflet stress during systole and is evolutionarily conserved (apart from humans, it occurs, for instance, in sheep and baboons) [15].

In these initial 3D echocardiographic attempts, the mitral valve was represented by a low-resolution wire mesh from which one could appreciate the overall shape and size of the mitral annulus, but the details of the leaflet anatomy were lacking.

In the 1990s, a method for volume rendering of the cardiac structures including the mitral valve using standard 2D transesophageal probes was developed. In this system, a series of 2D-TEE images was obtained at regular angle intervals using ECG and respiratory gating. The images were then transferred to a computer work station for often laborious and lengthy offline postprocessing. Despite its limitation, the system was capable of rendering the anatomy of the mitral valve leaflets for the first time [Fig. 1, Supplementary Digital Content (SDC)1 and SDC2, http://links.lww.com/HCO/A7, http://links.lww.com/HCO/A8]. This offline 3D-TEE method was soon applied to the diagnosis of MVP [16–18]. In addition, more precise measurements of the mitral annulus became feasible [19].

All these initial 3D echocardiographic systems – whether transthoracic or transesophageal – relied on standard 2D probes for image acquisition and used off-line computer systems for 3D reconstruction. The field of 3D echocardiography was revolutionized in the first decade of the 21st Century by the introduction of novel matrix array transducers which feature a several-fold increase in the number of imaging elements compared to

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<td>Secondary mitral valve prolapse</td>
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<td>Myxomatous degeneration</td>
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conventional 2D transducers. For instance, a standard 2D-TEE probe has 64 imaging elements, whereas the 3D-TEE probe has approximately 3000 of them [20]. With this new probe technology, real-time (or near real-time) 3D echocardiographic imaging became feasible for the first time.

MODERN THREE-DIMENSIONAL ECHOCARDIOGRAPHIC IMAGING OF MITRAL VALVE

Soon after the release of the matrix array 3D-TTE probe (in 2003) and the matrix array 3D-TEE probe (in 2007), real-time 3D echocardiographic imaging was used to diagnose and characterize MVP. It soon became evident that real-time 3D-TEE imaging [21,22] is superior to real-time 3D-TTE imaging [23–25] of MVP.

As previously noted, the most clinically useful 3D echocardiographic images for the diagnosis of MVP are the en face views of the mitral valve from the left atrial perspective. Since the left atrial side of the mitral valve is in the near-field of 3D-TEE and in the far-field of 3D-TTE, 3D-TEE provides superior imaging of MVP compared to 3D-TTE. In general, modern 3D echocardiographic imaging has three general modalities: volume-rendered; biplane or multiplane; and color Doppler.

**Volume-rendered imaging**

Volume-rendered 3D imaging has three spatial dimensions; two of these (lateral and depth) are the same as in 2D imaging. The third spatial dimension relates to the slice thickness and is referred to as elevation. On the basis of the magnitude of each dimension, volume-rendered 3D imaging is further subdivided into live 3D, 3D zoom, and full-volume modalities.

Live 3D (narrow-angle) imaging provides a fixed pyramid of data with approximately 60° of lateral width, 30° of elevation, and the full depth. It requires no ECG gating and has reasonable temporal resolution (typically around 20 frames per second). It is often useful for demonstrating the anatomy of MVP in the long axis (Fig. 2, panel a and SDC3, http://links.lww.com/HCO/A9). Frequently, the entire mitral valve cannot be captured with one live 3D slice.

Full-volume (wide-angle) 3D imaging is essentially a series of live 3D slices acquired over several cardiac cycles using ECG gating and then electronically stitched together (Fig. 2, panel b and SDC4, http://links.lww.com/HCO/A10). This modality provides the largest possible pyramid of data (approximately 100° in both lateral and elevation directions and the full depth). It has the best temporal resolution of all volume-rendered techniques (approximately 30 frames per second) and is thus well suited to demonstrate leaflet movement in MVP. However, full-volume 3D has low spatial resolution and frequently suffers from stitching artifacts (misalignment of individual slices).

Three-dimensional zoom imaging is similar to live 3D imaging except that it trades depth for...
an increase in the lateral and elevation dimensions. This modality is the most useful for 3D imaging of MVP. It provides good spatial resolution (Fig. 2, panel c and SDC5, http://links.lww.com/HCO/A12) but suffers from low frame rate (typically around 10 frames per second).

Biplane or multiplane imaging

In these modalities orthogonal 2D images are automatically extracted from the pyramidal 3D data set by the ultrasound system. Biplane imaging is useful for understanding of MVP anatomy in two orthogonal planes (Fig. 3 and SDC6, http://links.lww.com/HCO/A13). Multiplane reconstruction (MPR) imaging is essentially an extension of biplane images [26]. In addition to two longitudinal axes there is an additional short-axis view (Fig. 4). MPR may improve the accuracy the description of MVP compared to 2D imaging [27].

Three-dimensional color Doppler imaging

At present, the 3D color Doppler imaging is available only in the full-volume mode. It is useful in determining the size, direct, and the shape of the
mitral regurgitant jet. More importantly, it allows quantification of mitral regurgitation through 3D planimetry of the vena contracta as discussed below. In general, 3D color Doppler imaging with present technology of prolonged multibeat acquisition is not truly real-time and is frequently suboptimal due to stitching artifacts [28]. True real-time 3D color imaging (for instance, as an overlay of 3D zoom images) may soon become commercially available.

THREE-DIMENSIONAL ECHOCARDIOGRAPHIC ANATOMY OF MITRAL VALVE

The mitral valve is a complex structure that consists of the mitral annulus, two leaflets, two commissures, and two papillary muscles with associated chordae and the supporting left-ventricular myocardium.

Anatomically, the mitral valve orifice is almost vertical in diastole, rotated at 45° leftward from the sagittal body plane, and its ventricular side faces anterolaterally and slightly inferiorly toward the left-ventricular apex. Although this anatomically (attitudinally) correct plane is obtainable by 3D echocardiography it is not commonly used. Instead the so-called surgical view of the mitral valve is used (Fig. 5).

The surgical view is rotated counter-clockwise by approximately 45° from the anatomically correct view because following left atriotomy the operating table is rotated by that degree at the time of surgery to facilitate direct visualization of the mitral valve by the surgeon [29].

The mitral leaflet anatomy is usually described using the nomenclature developed by the French cardiac surgeon Alain Carpentier (Carpentier et al. [30]). Carlos Duran, a Spanish-American surgeon, has proposed an alternative to the Carpentier...

FIGURE 4. Multiplane reconstruction (MPR) image of mitral valve. MPR is a standard technique used in three-dimensional (3D) echocardiography as well as computer tomography and MRI. It allows precise alignment of a structure of interest (flail P2 scallop in this instance) in two long and one short axis.
nomenclature; however, the Duran terminology is infrequently used [31].

On the basis of the Carpentier nomenclature, the posterior mitral leaflets is typically divided by two small clefts into three scallops named P1, P2, and P3 and numbered from the anterolateral commissure (near the left atrial appendage) toward the posteromedial commissure (near the interatrial septum). The posterior leaflet accounts for 2/3 of the mitral annular circumference but only for 1/3 of the total mitral leaflet area.

The anterior mitral leaflet typically has no visible clefts. It is divided into three segments: A1, A2, and A3, which correspond to the scallops of the posterior mitral leaflets. The anterior mitral leaflet accounts for 1/3 of the mitral annular circumference and 2/3 of the total mitral leaflet area.

It is important to note that there is significant variability in the mitral leaflet anatomy and that variations from the Carpentier system may occur in a substantial number of patients [32].

As previously noted, the mitral annulus has a saddle shape with two high points (near the aortic valve at the base of the A2 segment and posteriorly at the base of the P2 scallop) and two low points (near the mitral valve commissures). Using specialized 3D-TEE software, one can appreciate this saddle shape nature of the mitral annulus (Fig. 6 and SDC7, http://links.lww.com/HCO/A14).

The posterior leaflet is anchored to the fibrous skeleton of the mitral annulus. In contrast, the anterior leaflet is contiguous with the aorto-mitral curtain (intervalvular fibrosa) which is located between the two trigones.

UTILITY OF THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN DIAGNOSIS OF MITRAL VALVE PROLAPSE

Three-dimensional echocardiography allows establishment of the precise diagnosis of MVP, advanced quantification of leaflet and annular anatomy, and quantification of mitral regurgitation due to MVP.

General diagnosis of mitral valve prolapse

Three-dimensional TEE has been shown to be more accurate in describing the details of MVP anatomy than 2D-TEE when compared to intraoperative findings. For instance, in a study of 204 patients, 3D-TEE had an accuracy rate of 92% compared to the 78% of accuracy rate of 2D-TEE imaging [33]. This is not surprising since 2D imaging depends on memorization of location of leaflet segments in each 2D view and a creation of a complex mental image of MVP [34,35].

In contrast, the en face images of MVP on 3D echocardiography are practically self-evident. The number of prolapsing segments, their location, and their extent and the presence of absence of flail segments can easily be visualized by 3D-TEE (Fig. 7). It is important to evaluate the en face view of the mitral valve not only in the surgical view but...
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**FIGURE 6.** Reconstruction of the mitral annulus and the mitral leaflets. Using specialized software the mitral annulus and the mitral leaflets can be reconstructed in such a way to allow a variety of measurements such as the annular size and the prolapse volume. Images were obtained from a patient with prolapse of the P2 scallop of the posterior mitral leaflet. A, anterior; AL, anterolateral; P, posterior; PM, posteromedial. SDC7 (HTTP://LINKS.LWW.COM/HCO/A14) corresponds to this figure.

also from other perspectives after rotating the *en face* view along the so-called Z-axis (the axis that is perpendicular to the plane of the imaging monitor) [36*].

**Advanced diagnostic parameters of leaflet anatomy**

Specialized software packages for advanced MVP calculations are commercially available, and their

**FIGURE 7.** Three-dimensional (3D) echocardiographic appearance of prolapsed and flail mitral segments. Images were obtained from different patients using the 3D zoom technique. All panels show the *en face* view of the mitral valve from the left perspective. Panela: Prolapse of the A1 segment of the anterior mitral leaflet. Panel b: Prolapse of the A2 segment of the anterior mitral leaflet. Panel c: Prolapse of the A3 segment of the anterior mitral leaflet. Panel d: Prolapse of the P1 scallop of the posterior mitral leaflet. Panel e: Flail P2 scallop of the posterior mitral leaflet. Panel f: Flail A3 scallop of the posterior mitral leaflet.
clinical utility is being investigated. These software packages allow both leaflet and annular quantifications (Fig. 6 and SDC7, http://links.lww.com/HCO/A14). Quantifiable leaflet parameters include anterior and posterior leaflet area, as well as the billowing height and billowing volume of each prolapsing segment [37]. Annular quantifications include the antero-posterior annular diameter, intertrigonal and intercommissural distances, and annular circumference [38].

These advance quantification techniques allow discrimination between Barlow’s disease, fibroelastic deficiency, and the controls. In Barlow’s disease there is a marked increase in the overall leaflet area, leaflet billowing (as judged by billowing height and volume), and annular size (as measured by the annular circumference and the diameters), as well as in an overall flattening of the annular saddle. These changes are much less pronounced in fibroelastic deficiency [39,40].

Quantification of mitral regurgitation

On the basis of 2D echocardiographic imaging it is usually said that single-leaflet prolapse typically produces a jet that is directed contralaterally (i.e. isolated posterior leaflet prolapse leads to an anteriorly directed jet and vice versa) [41]. The jets are typically eccentric and crawl along the left atrial wall or the left atrial side of the contralateral mitral leaflet. With the advent of 3D color imaging it became evident that MVP-related regurgitant jets are more complex and feature a variety of shapes (e.g. spoon-shaped and tongue-shaped jets) [42].

With present commercially available 3D echocardiographic techniques it is still not possible to quantify the size of the regurgitant jet per se. However, the severity of mitral regurgitation can be quantified by measuring the 3D-rendered vena contracta, the narrowest portion of the regurgitant jet at or just distant to the physical regurgitant orifice [43]. 3D echocardiography...
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appears to be able to measure the vena contracta more precisely and without any geometric assumptions made by 2D echocardiography.

On 2D echocardiography, the cross-sectional area of vena contracta – the functional measure of the regurgitant orifice size – is deduced either from measuring the vena contracta diameter or through the use of the proximal isovelocity surface area (PISA) method to calculate the effective orifice area (ERO) [44]. The 2D PISA method assumes a planar ERO and a hemispheric nature of the PISA flow. 3D echocardiography has demonstrated that these assumptions are often incorrect as ERO frequently has elliptical or irregular shape, more so in functional than in MVP-related mitral regurgitation [45].

Using the multiplanar reconstruction techniques (MPRs; Fig. 8), one first aligns the vena contracta in two long axes and then planimeters its area in the third plane showing vena contracta in its short axis [46]. Alternatively, one can use systematic cropping of a 3D color volume set to locate the true short axis of vena contracta and then perform planimetry [47,48]. These 3D echocardiographic techniques have the potential to become the gold standard in Doppler evaluation of the severity of mitral regurgitation.

UTILITY OF THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN POST-SURGICAL REPAIR OF MITRAL VALVE PROLAPSE

There is no effective medical therapy for altering the course of MVP. When severe mitral regurgitation develops and the established clinical criteria are met, MVP becomes a surgical disease. Surgical options include cardiac surgery and percutaneous implantation of a mitral clip. With respect to cardiac surgery, mitral valve repair is preferred over mitral

![FIGURE 9. Three-dimensional (3D) echocardiography of mitral valve surgical and percutaneous techniques used to repair mitral valve prolapse. All images show the en face view of the mitral valve from the left atrial perspective using the 3D zoom technique. Panel a: Mitral annuloplasty band or open ring (arrows). Panel b: Mitral annuloplasty ring (arrows). Panel c: Mitral bioprosthesis with a paravalvular leak (arrow) adjacent to the left atrial appendage. Panel d: Percutaneously placed mitral valve clip (arrows) between A2 and P2 segments of the mitral valve.](image-url)
valve replacement [49]. 3D echocardiography, in general, and 3D-TEE, in particular, is well suited for assessing the results of the repair [50] and for visualizing possible complications of mitral valve surgery including paravalvar and para-annular leaks (Fig. 9).

Three-dimensional TEE is also the preferred echocardiographic technique for guiding the percutaneous repair of the mitral valve using a mitral clip (Perk et al. [51]). This percutaneous procedure was inspired by the surgical technique originally developed by Alfieri et al. [52] and was shown to be noninferior to surgery in the treatment of mitral regurgitation in suitable candidates [53].

**CONCLUSION**

The review summarizes the latest developments in 3D echocardiography of MVP. 3D is superior to 2D echocardiography in visualizing the mitral valve. The intuitive en face views of the mitral valve on 3D echocardiography simplify the diagnosis of MVP, and 3D color Doppler techniques allow more precise quantification of the severity of mitral regurgitation. 3D echocardiography is becoming indispensable in guiding surgical and percutaneous procedures of mitral valve repair and replacement.

**Acknowledgement**

None.

**Conflicts of interest**

No conflict of interest for either of the two authors.

**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:
- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).


This excellent reference summarizes the latest developments in the understanding of MVP cause, pathology, imaging, and treatment.


In this reference, the authors demonstrate that 3D-TEE is better than 3D-TEE in localizing segmental mitral valve lesions including those of mitral valve prolapse.


In this reference, there is a very nice comparison between intraoperative and 3D-TEE findings in patients with MVP.


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