Validation of Right and Left Ventricular Conductance and Echocardiography for Cardiac Function Studies

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Background. Continuous estimation of left ventricular volume from instantaneous conductance has compared favorably with "gold standards," is less labor intensive, and provides real-time data. Little information exists, however, correlating right ventricular conductance with such gold standards or examining the effects of an electrical field generated in the opposite ventricle.

Methods. In open-chested sheep, right and left ventricular conductance, two-dimensional echocardiography, and thermodilution cardiac outputs were measured at steady-state conditions. After these measurements, postmortem pressure-volume relations, ventricular mass, and ventricular casting were performed.

Results. The corrected end-diastolic volume measured by conductance correlated well with volumes measured by echocardiography ($r = 0.89$), postmortem pressure-volume relations ($r = 0.84$), and casts ($r = 0.85$). Left ventricular end-diastolic volume measured by conductance did not differ significantly from other standards by analysis of variance. The presence of an electrical field in the opposite ventricle did not affect measured conductance in the studied ventricle.

Conclusions. Conductance is useful for the measurement of right and left ventricular end-diastolic volumes in the beating heart and is not affected by the presence of an electrical field in the opposite ventricle. Hence, conductance is a useful tool in studies involving interventricular dependence and function.

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Continuous estimation of left ventricular volume from instantaneous conductance has facilitated studies of left ventricular contractility [1–4]. Compared with previous methods such as x-ray contrast, radionuclide angiography, computed tomography, and magnetic resonance imaging [5–10], conductance provides data in real time while avoiding the adverse effects of contrast injections and radiation exposure. Compared with echocardiography and sonomicrometry, labor-intensive planimetry methods are avoided, costs are lower, and equipment is less cumbersome.

Despite its recognized limitations, conductance ventriculography is a valuable tool that provides a continuous estimate of left ventricular volume without requiring thoracotomy. In previous studies, left ventricular conductance measurements have correlated linearly with stroke volumes measured with electromagnetic or ultrasonic aortic flow probes and thermodilution cardiac output [1]. Correlation with left ventricular volume measured by sonomicrometry and cineventriculography also has been satisfactory [1, 2, 11–13]. Details of the conductance technique in laboratory and clinical settings have been published [1–3, 11–14].

Although multiple studies have reported the accuracy of conductance for measurement of left ventricular volume, little information is available regarding the accuracy of right ventricular conductance in vivo. In vitro studies have demonstrated that conductance is useful in measuring volume in balloons with geometry similar to that of the right ventricle at end-diastole [15].

This experiment was designed to do the following: (1) assess the potential of conductance for studying right ventricular dimensions, (2) study the interaction between the electrical fields during conductance measurements in the left or right ventricle with simultaneous measurements in the left or right ventricle with simultaneous measurements in the opposite ventricle, and (3) assess the usefulness of conductance and two-dimensional echocardiography for physiologic studies.

Material and Methods

Experimental Protocol

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the Institute of Laboratory Animal Resources and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH publication 86-23, revised 1985).

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Sheep (n = 7) weighing 35 to 40 kg were anesthetized with thiamylal (3 to 5 mg/kg intravenously), acepromazine (0.5 mg/kg intramuscularly), ketamine (20 mg/kg intramuscularly), and atropine (1 to 2 mg intramuscularly). The animals were intubated and mechanically ventilated, maintaining arterial blood gas values within physiologic norms. Anesthesia was maintained with isoflurane (1.75% to 2.25%) and oxygen. While monitoring the electrocardiogram, peripheral arterial blood pressure, and body temperature, we performed a median sternotomy. After a longitudinal pericardiotomy, a pericardial well was created by sewing a plastic sheet to the pericardium and draping the free edges over the opened sternum.

Fluid-filled pressure catheters were placed in the right and left atria through pursestring sutures in the atrial appendages. A 3.5F pediatric injectate catheter (Baxter Health Care Corp, Irvine, CA) was also placed in the right atrium. A 3.0F thermodilution thermistor probe (Baxter Health Care Corp) was placed in the main pulmonary artery through a pursestring suture in the right ventricular outflow tract. Micromanometer (5F) catheters (Millar Instruments, Houston, TX) were placed in both ventricles through the atrial appendages. A 5F, 10-electrode, single-field conductance catheter (Webster Labs, Baldwin Park, CA) was placed retrograde into the left ventricle, axial to the long axis through the left carotid artery. A second identical conductance catheter was placed retrograde in the right ventricle from the pulmonic valve to the apex through a pursestring suture in the pulmonary artery. The position of each conductance catheter was verified by two-dimensional echocardiography (VingMed CFM 750; VingMed Sound, Inc, Salt Lake City, UT) to ensure that myocardial contact with the electrodes was avoided.

After instrumentation, the pericardial well was filled with gel (Ultraphonic scanning gel; Pharmaceutical Innovations, Inc, Newark, NJ) to provide a stand-off for two-dimensional echocardiography. Data, digitized at 200 Hz with an analog-to-digital converter (MacLab; AD Instruments Inc, Milford, MA) and recorded on a digital computer (Macintosh Quadra 950; Apple Computer, Cupertino, CA), included electrocardiogram, right and left atrial pressures, right and left ventricular pressures, and right and left ventricular conductance. Data were collected in triplicate at steady state with the lungs held at end-expiration. Thermodilution cardiac output was then recorded using injections of 10 mL cold (4°C) normal saline into the right atrium. Echocardiographic images were then obtained using a 5.0-MHz transducer (see later). The echocardiography well was maintained with gel at a constant level (2 to 3 cm above the anterior right ventricular wall) [5] throughout the experiment. Pressure influences from the gel in the pericardial well were measured by placing a fluid-filled pressure catheter into the gel at the midventricular level. In data analysis, the static gel pressure was subtracted from the intracardiac pressures measured during data collection. After completion of data collection, all instruments were removed, and the hearts were arrested for measurement of postmortem pressure-volume curves and glutaraldehyde fixation using methods described previously [5, 16].

Table 1. Calculation of α for Both Right and Left Ventricles

Sheep	SVc	SV(td + e)	α
Right ventricle			
1	. . .	. . .	. . .
2	30	34	0.88
3	32	49	0.64
4	25	46	0.55
5	14	38	0.37
6	17	33	0.51
7	29	38	0.76
Mean ± SEM	24 ± 3	40 ± 3	0.62 ± 0.07
Left ventricle			
1	27	40	0.68
2	26	33	0.79
3	39	49	0.80
4	34	46	0.74
5	25	38	0.66
6	26	33	0.79
7	32	38	0.84
Mean ± SEM	30 ± 2	40 ± 2	0.77 ± 0.03

α = slope constant derived from conductance; SEM = standard error of the mean; SVc = stroke volume from conductance; SV(td + e) = stroke volume averaged from thermodilution and echocardiography.

Conductance

The number of conductance catheter segments used to estimate total ventricular volume was determined prospectively by plotting individual ventricular pressure-volume loops for each segment on a digital oscilloscope (1201BB Oscilloscope; Hewlett Packard, Andover, MA). Segments producing counterclockwise rotation of the pressure-volume loops were included in the measurement of total conductance, whereas segments forming pressure-volume loops in a clockwise fashion were in the great vessels and therefore were excluded.

Before data collection, 6 mL of arterial blood was collected to measure intrinsic blood resistivity, ρ [3], with the rho cuvette using the Leycom Sigma-5 conductance module (Rijnsburg, The Netherlands).

Immediately after data collection, parallel conductance for both the right and left ventricles was measured using standard hypertonic saline techniques [3]. Parallel conductance was determined from changes in raw conductance during hypertonic saline injection.

Alpha (α), the dimensionless calibration factor that converts raw conductance corrected for parallel conductance to an absolute or corrected volume, was derived from the ratio of conductance stroke volume to a "gold standard" stroke volume (averaged from echocardiographic and thermodilution cardiac output) (Table 1).

Corrected conductance volume (mL) was then calculated as follows: $\mathrm{Vol}_{\mathrm{Cor}} = (\mathrm{Vol}_{\mathrm{raw}} - \mathrm{P_c})/\alpha_{\mathrm{LV}}$.

Echocardiographic Analysis

Echocardiography was used to determine right and left ventricular end-diastolic volumes and masses using

Simpson's rule [5, 17]. The sections used were two perpendicular long-axis views of the left ventricle excluding the papillary muscles [18] (apical long-axis [S1A], apical two-chamber [S2A]), the apical four-chamber, and the short-axis cross-section of the left and right ventricles just below the mitral valve leaflets at the largest left ventricular diameter. Videotaped images were analyzed with a light-pen system (Varian V-3000, Salt Lake City, UT). Ventricular dimensions were measured by two independent observers and then averaged.

Left ventricular wall volume was determined as the difference between the left ventricular epicardial and endocardial shells [5, 18]. The right ventricular free wall volume was calculated as the difference between the epicardial and endocardial shells in the apical four-chamber and cross-sectional short-axis views. The wall volumes in cm^3 were multiplied by the specific gravity of the myocardium (1.05 g/cm^3) for determination of the ventricular mass [19, 20] and were compared with the postmortem ventricular weights.

Data Analysis

Data were analyzed using Igor custom software (Wavemetrics, Inc, Lake Oswego, OR). End-diastole was defined as the point on the ventricular pressure tracings coinciding with the R wave of the electrocardiogram. Thermodilution cardiac output was determined from an average of five values within 10% of each other. Stroke volume was calculated by dividing cardiac output by heart rate. Stroke volume from echocardiography was estimated by multiplying the ejection fraction by the end-diastolic volume determined by echocardiography. Conductance stroke volume was determined by calculating the difference between the end-diastolic volume peaks and the end-systolic volume troughs of the conductance tracing. Data were averaged over 10 beats.

Postmortem end-diastolic pressure-volume relations were constructed by calculating an average pressure for each 5-mL volume increment injected into the ventricle during two recorded data runs. Average pressure was plotted versus volume, producing a mean postmortem end-diastolic pressure-volume relation. This curve was compared with the corresponding end-diastolic conductance-pressure relation in vivo.

Statistics

Conductance volume, postmortem volume, volume by echocardiography, and casts were compared by linear regression. In addition, Bland-Altman [21] techniques were used to assess agreement between measurements of volume by conductance and other methods. Volumes were also compared using repeated-measures analysis of variance. Stroke volumes and related slope constants, α, derived from right and left ventricular measurements were compared using paired Student's t test. Mass determinations were compared using paired t test. Corresponding test statistics were considered significant at a level of p less than 0.05.

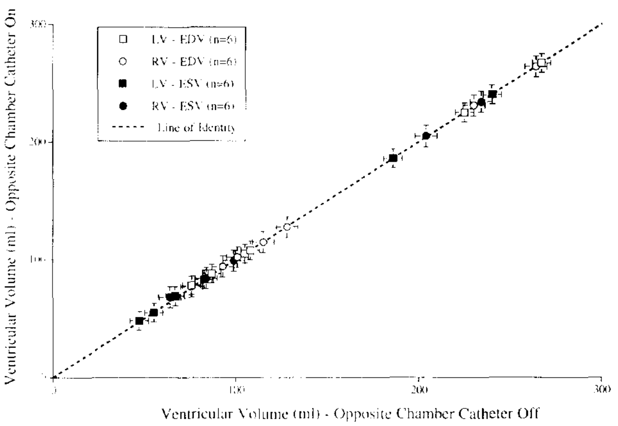

Fig 1. Raw left (LV) and right (RV) ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) by conductance measured while the opposite ventricle's conductance catheter was on and off. Data are coincident with the line of identity.

Results

Figure 1 presents the average raw conductance in each ventricle with and without an electrical field generated by a second conductance catheter in the opposite ventricle. Raw end-diastolic and end-systolic volumes by conductance were not altered significantly by a conductance catheter functioning in the opposite ventricle.

Table 1 presents the calculation of α for each ventricle based on the stroke volume as measured by conductance, echocardiography, and thermodilution. Mean α values were not significantly different, but right ventricular stroke volume by conductance differed significantly from left ventricular stroke volume ($p < 0.05$). There was also a poor correlation between the right ventricular stroke volume by conductance and the gold standard ($r = 0.43$), whereas left ventricular stroke volume by conductance correlated well ($r = 0.87$). For these reasons, αLV was used for all subsequent calculations. Table 2 presents the conductance calibration factors and a linear representation of the calculation for corrected conductance. Corrected conductance for both ventricles differed significantly from both raw conductance and conductance corrected for parallel conductance ($p < 0.05$). Figures 2 through 4 and Table 3 demonstrate good agreement between right ventricular end-diastolic volume determined by conductance and that determined by postmortem pressure-volume relations, two-dimensional echocardiography, and ventricular casts, respectively. The mean difference (±2 standard deviations) between conductance and postmortem pressure-volume relations was 0.4 ± 9 mL, between conductance and two-dimensional echocardiography was −0.7 ± 7 mL, and between conductance and casts was 1.4 ± 9 mL. Correlation coefficients were 0.89, 0.84, and 0.85, respectively.

The following correlations were also satisfactory: casts versus the postmortem pressure-volume relations ($r = 0.78$), echocardiography versus the postmortem pressure-volume relations ($r = 0.78$), and echocardiography versus casts ($r = 0.93$).

Table 2. Calculation of Corrected Right and Left Ventricular End-Diastolic Volumes Using Conductance

Sheep	Raw EDC	V_p(HSAL)	EDC(V_p)	α	EDV$_\alpha$
Right ventricle					
1	. . .	. . .	. . .	. . .	. . .
2	264	240	24	0.81	30
3	115	84	31	0.80	39
4	230	191	39	0.74	53
5	107	81	26	0.65	40
6	105	73	32	0.79	41
7	128	90	38	0.83	46
Mean ± SEM	158 ± 29	127 ± 29	32 ± 2	0.77 ± 0.03	41 ± 3[a]
Left ventricle					
1	110	71	39	0.68	57
2	267	217	50	0.81	61
3	226	180	46	0.80	57
4	102	60	42	0.74	57
5	105	70	35	0.65	53
6	84	48	36	0.79	46
7	87	41	46	0.83	55
Mean ± SEM	140 ± 28	98 ± 27	42 ± 2	0.76 ± 0.03	55 ± 2[a]

[a] $p < 0.05$ versus EDC(V_p).

α = slope constant; EDC = end-diastolic conductance (mL); EDC(V_p) = end-diastolic conductance corrected for parallel conductance; EDV$_\alpha$ = corrected end-diastolic volume (mL) using α and V_p; SEM = standard error of the mean; V_p(HSAL) = parallel conductance from hypertonic saline injection (mL).

Figure 5 compares the mean end-diastolic volumes for both the right and left ventricles measured by four methods; the means were not significantly different by analysis of variance.

Figure 6 compares the mean masses of both the left and right ventricles as calculated by echocardiography and postmortem weighing. There was no difference between the methods.

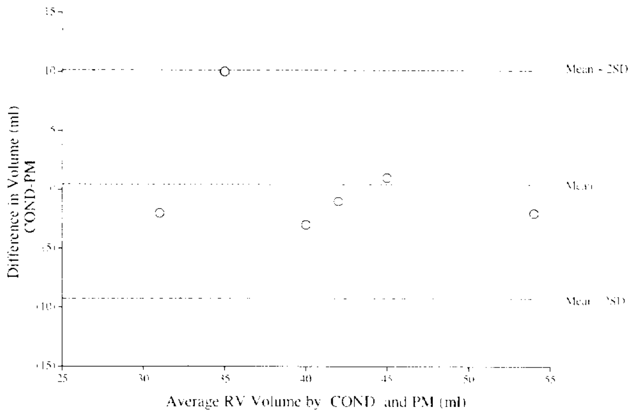

Fig 2. Difference between right ventricular (RV) end-diastolic volume measured by conductance (COND) and postmortem curves (PM) versus the mean of the two measurements in 6 sheep. (SD = standard deviation.)

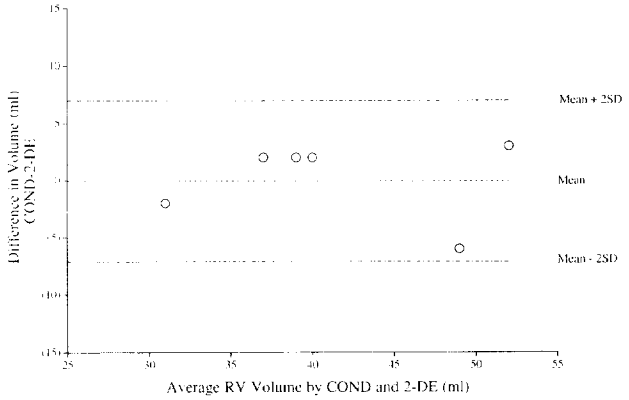

Fig 3. Difference between right ventricular (RV) end-diastolic volume measured by conductance (COND) and echocardiography (2-DE) versus the mean of the two measurements in 6 sheep. (SD = standard deviation.)

Comment

The results of this study support the use of both conductance and quantitative two-dimensional echocardiography for studies of right and left ventricular function. In addition, the results indicate that conductance measured in one ventricle is not affected by an electrical field generated by a conductance catheter in the opposite ventricle. Therefore, conductance can be used for simultaneous measurements in studies involving interventricular dependence and mechanics.

Right ventricular end-diastolic conductance corrected for parallel conductance and left ventricular slope constant correlated well with right ventricular end-diastolic volume measured by the postmortem pressure-volume relations, echocardiography, and casts. Though our results demonstrated good estimation of end-diastolic volume using conductance, current techniques for measuring parallel conductance must be explored further for feasibility in the clinical setting. Factors such as the rate

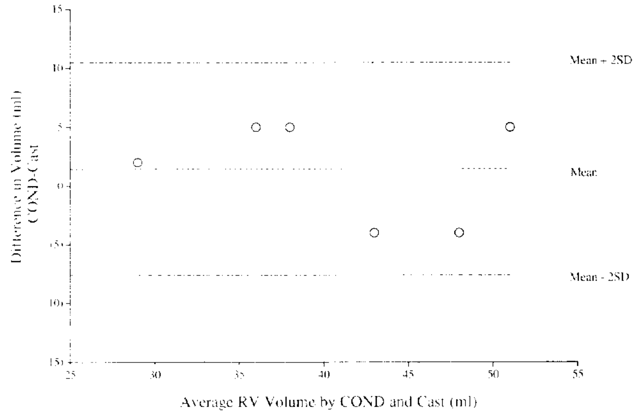

Fig 4. Difference between right ventricular (RV) end-diastolic volume measured by conductance (COND) and ventricular casts (Cast) versus the mean of the two measurements in 6 sheep. (SD = standard deviation.)

Table 3. End-Diastolic Volumes Measured by Different Methods for Both Right and Left Ventricles

Sheep	EDV_{COND}	EDVpm	EDVe	EDVcst
Right ventricle				
1	. . .	. . .	. . .	. . .
2	30	32	32	28
3	38	41	36	33
4	53	55	50	48
5	40	30	38	35
6	41	42	40	45
7	46	45	52	50
Mean ± SEM	41 ± 3	41 ± 4	41 ± 3	40 ± 4
Left ventricle				
1	58	52	53	59
2	61	50	52	58
3	57	47	57	45
4	57	60	66	55
5	53	42	55	50
6	46	53	53	52
7	55	50	58	53
Mean ± SEM	55 ± 2	51 ± 2	56 ± 2	53 ± 2

EDV = end-diastolic volume (mL); EDV_{COND} = corrected EDV from conductance (mL); EDVcst = EDV from cast (mL); EDVe = EDV from two-dimensional echocardiography (mL); EDVpm = EDV from postmortem pressure-volume relation (mL); SEM = standard error of the mean.

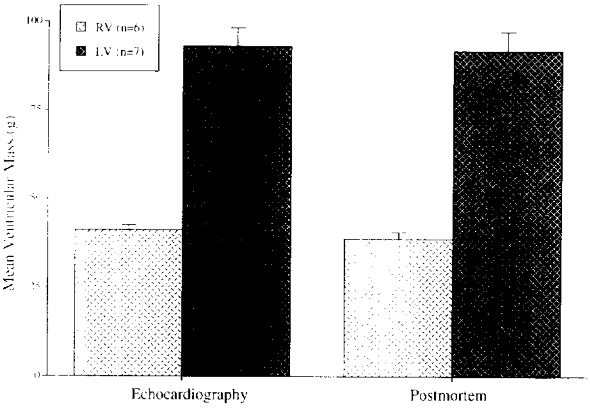

Fig 6. Mean left ventricular (LV) and right ventricular (RV) mass measured by echocardiography and postmortem weights.

of flow, portal of entry, and concentration of hypertonic saline injection need further investigation. Kass and associates [4] have reported the use of 8 N saline solution for measurements of parallel conductance in awake patients; there were no side effects, but concerns still exist about its usage. The use of conductance during cardiopulmonary bypass or during volume changes induced by caval occlusions would involve difficulties and was not assessed in this study [11]. We recently demonstrated that changes in right ventricular volume can alter left ventricular conductance by as much as 10% [22]. Furthermore, parallel conductance and blood resistivity may be altered by many factors during cardiopulmonary bypass, and parallel conductance cannot be assessed by hypertonic saline injection in the absence of an ejecting ventricle. Accordingly, alternative methods for calibrating the conductance catheter during bypass, possibly based on echocardiography, are under development in our laboratory [23].

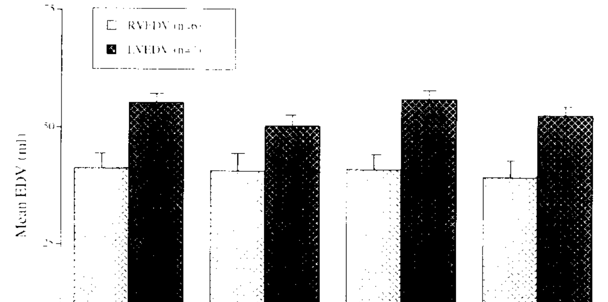

Fig 5. Mean end-diastolic volumes (EDV) for both right ventricle (RVEDV) and left ventricle (LVEDV) measured by conductance, postmortem pressure-volume relation, echocardiography, and ventricular casts.

The slope constant traditionally has been described as a "gain correction" calculated from the slope of the relation between measurements of stroke volume by conductance and by an independent method (thermodilution, flow probe, echocardiography, or angiography). Based on our findings, the slope constant was not affected by an electrical field generated by a conductance catheter in the opposite ventricle. The average value of the slope constant reported in the literature is 0.8 (range, 0.54 to 1.18) [1–4, 11], and variability in its measurement has been attributed to variations in left ventricular geometry [14]. In this study, the range of the calculated slope constant was narrower in the left ventricle (0.65 to 0.80) than in the right ventricle (0.37 to 0.88) and compared more favorably with previously reported values. We find that in both ventricles, end-diastolic volumes corrected for parallel conductance and left ventricular slope constant are significantly different from volumes corrected for parallel conductance alone. Therefore, the left ventricular slope constant adds dimensional accuracy to volume measurements in both ventricles.

Right ventricular stroke volume measured by conductance did not correlate well with stroke volumes obtained from echocardiography and thermodilution cardiac output, whereas stroke volume calculated from left ventricular conductance did correlate well. This implies that measurements of end-systolic volume and hence stroke volume are not as accurate in the right ventricle as in the left ventricle. Thus, calculations of the slope constant, α, using right ventricular conductance are less accurate. This difference can best be explained by the following: (1) right ventricular geometry causing excessive curvature of the conductance catheter, (2) contact between the conductance catheter and the right ventricular endocardium at end-systole, and (3) exaggerated right ventricular asymmetry during systole. Additional studies during cardiopulmonary bypass, when stroke volume can be controlled, may improve methods for accurately measuring α.

The echocardiography gel allowed superior imaging while avoiding external pressure on the heart by separating the transducer from the epicardial surface. The increase in end-diastolic pressure due to gel on the heart was negligible, and ventricular conductance did not change after pouring the gel on the heart [22]. Our results confirm the accuracy of echocardiography for measurement of right and left ventricular masses in sheep.

In conclusion, this study demonstrates the utility of conductance and two-dimensional echocardiography for measurements of right and left ventricular end-diastolic volumes in sheep. Furthermore, echocardiography is an acceptable method for measuring right and left ventricular masses in this species. These techniques may allow improved methods of assessing ventricular function in patients and provide information essential for further validation during cardiopulmonary bypass.

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