Radionuclide Evaluation Pre- and Postextracorporeal Shock Wave Lithotripsy for Renal Calculi

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Forty-two patients were evaluated pre- and postextracorporeal shock wave lithotripsy (ESWL) using [^{99m}Tc]DTPA renography. A quantitative evaluation showed that the relative renal function decreased 2–3 days post-ESWL on the treated side, and the parenchymal transit time index (PTTI) increased 2–3 days post-ESWL ($p < 0.001$) on the treated side and returned to the pretreatment level by 3 wk post-ESWL. The untreated side showed an increase in PTTI 2–3 days post-ESWL ($p < 0.01$), which returned to normal by 3 wk post-ESWL. A significantly greater increase in PTTI was seen in patients who received >1,000 shocks as compared with those who received <1,000 shocks. Five patients developed obstructing uropathy post-ESWL, when stone fragments caused ureteric obstruction.

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Extracorporeal shock wave lithotripsy (ESWL) is a new modality used for treating renal lithiasis (*1,2*). The principle on which ESWL works is based on the fact that shock waves are generated when a mass moves in a certain medium with a velocity higher than that of sound for the same medium. An ultrashort high tension electrical discharge is passed underwater to form an arc between two electrodes. The electrodes are placed at the first focus of a hemi-ellipsoid reflector. The fluid surrounding the arc path vaporizes to produce a rapidly expanding gas bubble. As a result of this rapid expansion a shock wave is created which radiates from the focus in a circular manner and is accurately refocused to produce a high tensile pressure precisely at the small area of the second focus. The calculus is localized at the second focus using biplanar radiography. The patient is anesthetized and catheterized and placed in a water bath in a semi-reclining position, with electrocardiographic electrodes attached. Each shock wave is synchronized with the 'R' wave of the ECG to avoid inducing cardiac arrythmias. Between 500–2,000 shock waves are given over a period of 30–120 min, the shattered stone fragments being flushed out in the urine over the subsequent days or weeks.

The aim of this study was to determine whether there is any effect of extracorporeal shock wave lithotripsy on the renal function and in particular to demonstrate possible evidence for the development of obstructive nephropathy. To this end renal radionuclide studies were performed before, 2 to 3 days after, and 3 wk after ESWL. The following functions were measured. Relative renal function was assessed as the percentage uptake of technetium-99m diethylenetiaminepentaacetic acid ([^{99m}Tc]DTPA) by each kidney. Renal transit time was assessed using the parenchymal transit time index (PTTI) (*3–5*). The effect of furosemide induced diuresis on the renal images and activity/time curves was also determined. Total renal function as glomerular filteration rate was not estimated as it was thought that only unilateral changes in function would occur. A priori it was thought from our experience of the use of renal transit times in the evaluation of obstructive nephropathy (*3,6,7*) that these would be the most sensitive tests in the context of this study.

MATERIALS AND METHODS

Forty-two adult patients were included in the study. Each patient was selected on the basis of clinical history and ultrasonographic and radiological evidence of renal calculi. Before

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each study serum levels for urea, electrolytes, and creatinine were measured. Each patient underwent a radiological and ultrasonographic study pre-ESWL and post-ESWL, and these form the basis of a separate report.

Radionuclide evaluation was carried out pre-ESWL, 2–3 days post-ESWL and 3 wk post-ESWL. Half an hour before each study patients were given 400 ml of water to drink, to ensure adequate hydration. A large field-of-view gamma camera* fitted with a general purpose, parallel hole collimator with an on-line computer (Nodecrest V76) was used. The patient was seated in a modified dental chair with the camera positioned posteriorly angled 20° back from vertical so that the patient reclined against its face. A 21-gauge butterfly needle was placed in an antecubital vein connected to a three-way stopcock. Approximately 10 mCi of [^{99m}Tc]DTPA in a volume of 0.1–0.4 ml was injected through the three-way stopcock and flushed with 20 ml of isotonic saline. Transparent film images were acquired every 30 sec for 3 min and then at 5-min intervals for 30 min. Between 15 to 18 min 40 mg of furosemide was given intravenously. A higher than average activity was used so that statistically adequate data would be obtained to enable deconvolution analysis to be performed on the activity/time curves subsequently. This was accepted by the Administration of Radioactive Substances Advisory Committee (ARSAC) U.K. Informed consent was obtained for each patient.

Data Analysis

The data are collected in frame mode at 10-sec intervals from the time of injection for 180 frames. The data is displayed in a 64 × 64 matrix on a high quality video monitor. Regions of interest are set over the left ventricle (from an early frame), over the renal areas (using the frames around 2 min, that is before any tracer has left the parenchyma to enter the pelvis), and over the renal background areas identified superior and medial to each kidney avoiding the region of the central vessels. From these renal and background images relative renal function as a percentage left/(left + right) is calculated from the relative quantity of activity in each kidney from 2 min until a time before any activity is lost from a kidney (*4*). The normal range is 50 ± 7%.

The renal transit times were measured for each kidney. The whole kidney mean transit time was obtained, comprised of the mean pelvic transit time and mean parenchymal transit time. The mean parenchymal transit time is calculated by deconvolution analysis, where the activity/time curve from the left ventricle and the chosen renal parenchymal areas are used (*5,8*). The mean parenchymal transit time is given by the sum of a minimum transit time common to all nephrons and a mean residual nephron transit time which is called the parenchymal transit time index (PTTI). In order to measure parenchymal transit times a region of "pure" parenchyma free of any calyceal activity must be chosen. This is obtained using a "mean time" image from analysis of the activity/time curves of each pixel (*5*) where the mean time "t" is given by

$$t = \sum_i t_i N_i / \sum_i N_i,$$

where N_i is the counts recorded between time t_i and the time t_{i+1} and the sampling interval is 10 sec. Since the appearance of activity in the pelvis is delayed by 2.5 min or more as compared with the parenchyme, a gray or color scale display of the mean time image shows calyceal and pelvic regions clearly. Superimposition of this image upon the 2-min renal image allows some part of the parenchyme to be seen separately from the pelvicalyceal region. Since time and not count content is the important variable, this part of the parenchyme may be taken as representative of the whole parenchyme and it is not necessary to attempt to separate all the parenchyme from the entire pelvis; indeed, this is often impossible. The intact nephron hypothesis (*9*) is appropriate in this context, and justifies the determination of the parenchymal transit time from part of the kidney as representative of the whole, for the working nephrons show the same transit time features as other working nephrons.

Since [^{99m}Tc]DTPA is not reabsorbed, its transit time through the nephron depends on the rate of reabsorbtion of water. This is related to salt reabsorbtion in the proximal and distal tubules, and to the osmolality gradient in the medulla in the collecting duct. The rate of salt and water reabsorbtion is governed by active and passive forces, particularly slight differences in the relative pressure in the proximal tubular lumen and the adjacent peritubular capillaries. A relative decrease in peritubular capillary pressure consequent on a fall in perfusion pressure as occurs with ischemia enhances salt and water reabsorbtion, as does a relative increase in tubular luminal pressure as occurs with a resistance to outflow in obstructive nephropathy. This prolongation of the parenchymal transit time of [^{99m}Tc]DTPA would reflect one or both of these processes. However, prolongation of the parenchymal transit time in obstructive nephropathy is associated with pelvic dilatation and retention of tracer due to the presence of the resistance to outflow which does not occur with ischemia. To enhance the sensitivity of the measurement, subtraction of the minimum transit time common to all nephrons (which is thought to reflect mainly the collecting duct transit time common to all nephrons) helps to reduce the effect of variation in urine flow. The mean residual transit time is called the parenchymal transit time index (PTTI) which is very sensitive to the presence of obstructive nephropathy (*3,5,7*). The upper limit for the normal values of PTTI is <156 sec.

The response to furosemide is conventionally interpreted as indicating: obstructing uropathy when there is no change in the rising activity/time curve; absence of obstructing uropathy when there is a rapid fall in the whole kidney activity time curve (*10,11*); and in addition there is a gray area of partial responses. Difficulties in interpretation arise when renal function is reduced. Since the measured change in activity with time is the basis of determining the response to furosemide, then this response is also crucially dependent on the amount of activity taken up by the kidney and the rate of uptake. Therefore, the rate of fall of the kidney's activity/time curve in response to furosemide is dependent on its previous rate of rise. Whether the rate of fall is appropriate for a given rate of rise must be determined. A moderately poorly functioning kidney would have a moderately impaired rate of rise and a moderately impaired but appropriate rate of fall in response to furosemide in the absence of an obstructing uropathy. An inappropriately slow rate of fall in response to furosemide would then support the diagnosis of obstructing uropathy. In our evaluation, a good response is taken as an appropriate rate of fall for a given uptake rate; a poor response

TABLE 1
Radionuclide Data Pre- and Post-ESWL*

	Treated side			Untreated side		
	Pre-ESWL	48–72 hr Post-ESWL†	3/52 Post-ESWL	Pre-ESWL	48–72 hr Post-ESWL	3/52 Post-ESWL
% Function	52 ± 2	48 ± 3	49 ± 2	51 ± 1	54 ± 2	53 ± 2
		($p < 0.01$)	($p > 0.05$)		($p > 0.05$)	($p > 0.05$)
PTTI‡	87 ± 8	126 ± 10	95 ± 7	73 ± 6	89 ± 9	71 ± 6
		($p < 0.001$)	($p < 0.001$)		($p < 0.01$)	($p < 0.05$)

* Values expressed as (mean ± s.e.e.) for 42 patients.
† ESWL: Extracorporeal shock wave lithotripsy.
‡ PTTI: Parenchymal transit time index.

TABLE 2
Percent Change of Function Pre- and Post-ESWL Treated Side

No. of patients	48–72 hr Post-ESWL*	3/52 Post-ESWL
27	No change	No change
5	No change	Decreased by 10–16% (mean 12.6%)
1	Increased by 10%	No change
9	Decreased by 18–21% (mean 16.2%)	4 no change 5 decreased by 8–13% (mean 10.4%)

* ESWL: Extracorporeal shock wave lithotripsy.

is taken as an inappropriate rate of fall for a given uptake rate and together with a nil response indicates obstructing uropathy. A slightly less than appropriate response was taken as indecisive.

STATISTICAL ANALYSIS

Analysis was performed using Student's paired t-test. A p value of <0.05 was taken as significant. Fishers F-distribution test was performed to compare the changes in PTTI of patients receiving >1,000 shocks and those receiving <1,000 shocks, two of 42 patients whose results were outlying the otherwise normally distributed data were excluded from analysis by F-distribution test.

RESULTS

In all cases 2–3 days post-ESWL the treated kidney gave a visual appearance of increased intensity on the 15–25-min images compared with the other kidney (Fig. 1). This pattern resolved 3 wk post-ESWL.

Percent Change in Relative Renal Function

The 42 patients showed a variety of responses, but on average their relative renal function decreased significantly 2–3 days post-ESWL ($p < 0.01$); there was no significant change 3 wk post-ESWL (Table 1). No correlation was found between the number of shocks and the percentage change of function of the treated kidney.

Of these 42 patients, 27 patients showed no change in function post-ESWL (Table 2). Of these 27 patients, five showed no change on the 2–3 days post-ESWL study, but there was a significant decrease at 3 wk ranging from 10–16% (mean 12.6%) where two of the patients were clinically obstructed. One of these two patients had large retained fragments from a staghorn calculus and required ancillary surgical procedures. At 10 wk the patient's function had returned to pre-ESWL level. The other patient had an obstructing ureteric fragment that he passed 10 wk post-ESWL with his function returning to the pre-ESWL level. The third of the five patients had an obstructed calyx on his 3-wk ultrasound study, which may have resulted in decreased function. He required further ESWL. The fourth patient had four large calculi following previous open surgery for staghorn calculus and, in fact, had 2,100 shocks. The fifth patient, however, had a small calyceal stone treated with only 1,200 shocks.

Nine of these 42 patients showed a transient fall in function of 8–21% (mean 16.2%) 2–3 days post-ESWL. Four of these nine patients had returned to pre-ESWL level by 3 wk post-treatment. The other five were improving but still had a decrease in function despite a clinically uneventful course. Interestingly, one of the 42 patients showed a transient rise of 10% in the relative renal function 2–3 days post-ESWL.

Changes in Parenchymal Transit Time Index

The PTTI of the treated kidneys (expressed as mean ± s.e.m.) was prolonged from 87 ± 8 sec pre-ESWL to 126 ± 10 sec ($p < 0.001$) 2–3 days post-ESWL (Table 1). By 3 wk post-ESWL the PTTI had decreased to 95 ± 7 sec ($p < 0.001$). PTTI was also prolonged on the untreated side from 73 ± 6 sec to 89 ± 9 sec ($p < 0.01$) 2–3 days post-ESWL and had decreased by 3 wk post-ESWL from 89 ± sec to 71 ± 6 sec ($p < 0.05$).

TABLE 3
PTTI Pre- and Post-ESWL

	Treated side			Untreated side		
	Pre-ESWL*	48–72 hr Post-ESWL	3/52 Post-ESWL	Pre-ESWL	48–72 hr Post-ESWL	3/52 Post-ESWL
PTTI† <156 sec	37/42	27/42	38/42	39/42	39/42	39/42
PTTI >156 sec	5/42	15/42	4/42	1/42	1/42	1/42
Obstructing uropathy	—	4/42	2/42	—	—	—

* ESWL: Extracorporeal shock wave lithotripsy.
† PTTI: Parenchymal transit time index.

Pre-ESWL, 37 of the 42 patients had a normal renal study and five had prolonged PTTI with a good response to furosemide on the treated side (Table 3). On the untreated side two patients had a nephrectomy prior to the study, 39 patients had a normal renal study and one had prolonged transit times with a good response to furosemide which persisted 3 wk post-ESWL.

Two to three days post-ESWL 15 patients had a PTTI >156 sec 2–3 days post-ESWL, 11 of whom had a good response to furosemide. The other four patients had inappropriately poor responses to furosemide showing an obstructing uropathy as well as an obstructive nephropathy. Three of these four patients passed stone fragments in the following 3 wk and the 3-wk post-ESWL study in these patients was within normal range. One patient still had a large ureteric calculus causing obstructing uropathy at 3 wk, but he passed the calculus spontaneously at 10 wk and his radionuclide study returned to pre-ESWL level.

Three weeks post-ESWL, 38 patients had a normal PTTI 3 wk post-ESWL and four had PTTI >156 sec. Two of these four patients had obstructing uropathy determined by a poor response to furosemide. One had the obstructing ureteric calculus referred to above. The second had a prolonged PTTI 2–3 days post-ESWL combined with a good response to furosemide and went on to develop obstructing uropathy 3 wk post-ESWL. He required ancillary surgical procedures and by 10 wk post-ESWL his radionuclide study returned to pre-ESWL level. Of the other two patients one had an obstructed calyx on ultrasound and the other is unexplained.

PTTI <156 sec was recorded in 27 patients throughout all three studies. Interestingly, most of these patients showed a transient rise in PTTI 2–3 days post-ESWL as compared with pre-ESWL level.

There was a significant increase in PTTI 2–3 days post-ESWL in patients who received > 1,000 shocks compared with those who received < 1,000 shocks. Two of the 42 patients were excluded from this comparison (Table 4). Both these patients had < 1,000 shocks but had very prolonged PTTI 2–3 days post-ESWL, and their parenchymal transit times fell well outside the normally distributed range of the other 40 patients. No specific reason could be identified for this prolongation in both cases.

Almost all patients developed macroscopic hematuria during treatment which settled spontaneously within a few hours. 13 patients developed low grade pyrexia in the immediate post-ESWL period which subsided by 2 days on antibiotic treatment. Nine patients developed a prolonged ileus post-ESWL, four of which required intravenous fluids for 2–3 days. The other five recovered on conservative treatment. Fragmented stones were visualized by x-ray or ultrasound in all patients 2–3 days post-ESWL. In nine patients there were still residual fragments 3 mo post-ESWL. Serum urea, electrolytes, and creatinine levels did not change significantly pre- and post-ESWL.

DISCUSSION

The response of the kidneys to ESWL may be manifested in different ways. Schulthess et al. (*12*) have shown, using nuclear magnetic resonance imaging, that the treated kidneys are enlarged and edematous with edema in the surrounding perirenal fat post-ESWL.

TABLE 4
Effect of Shock Waves on PTTI*

		Treated side†		
	Patients	Pre-ESWL‡	48–72 hr Post-ESWL	3/52 Post-ESWL
Shocks <1,000	27/40	78 ± 8	98 ± 10 (p > 0.05)	82 ± 6 (p > 0.05)
Shocks >1,000	13/40	106 ± 15	167 ± 15 (p < 0.005)	126 ± 12 (p < 0.02)

* PTTI: Parenchymal transit time index.
† Values expressed as (mean ± s.e.e.).
‡ ESWL: Extracorporeal shock wave lithotripsy.

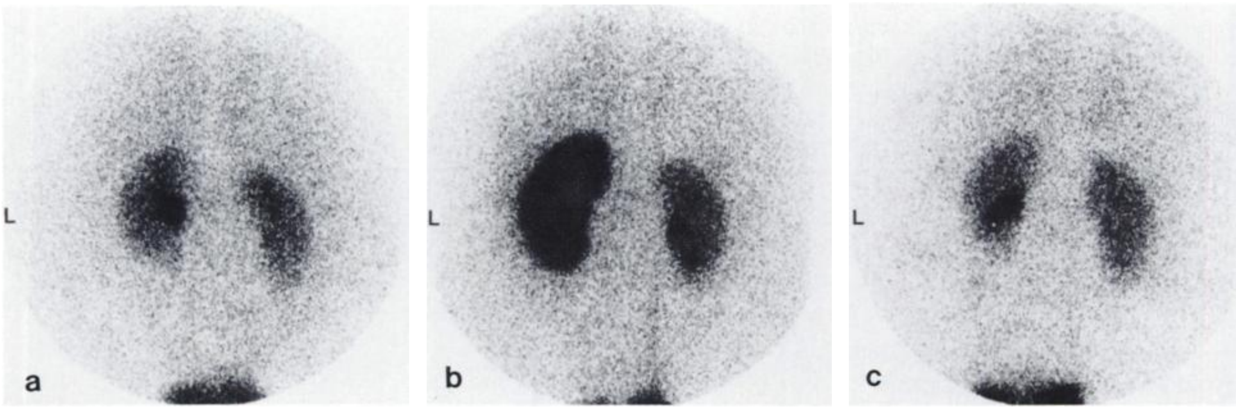
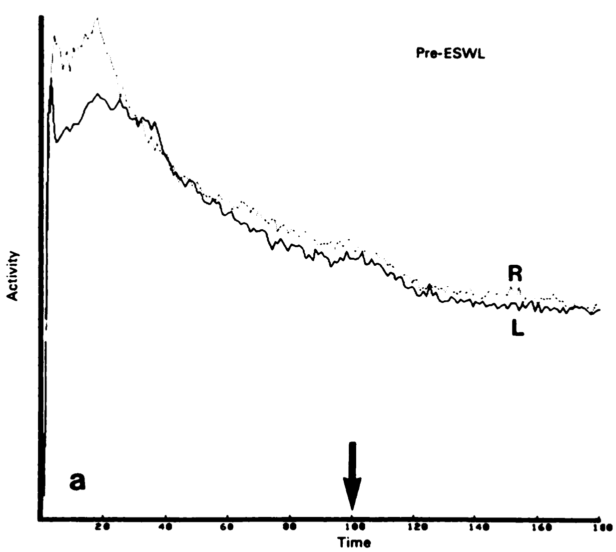
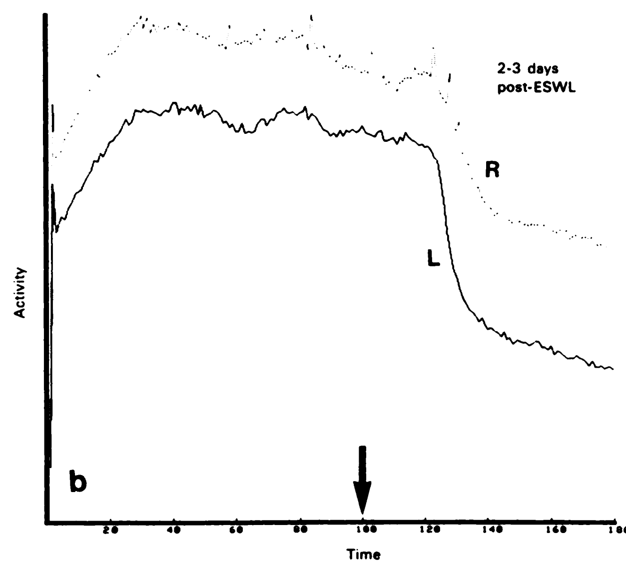


FIGURE 1
Static images 15 min postinjection. (L) Left kidney (treated). A: Pre-ESWL B: 2–3 days post-ESWL C: 3 wk post-ESWL.

This corresponds to the radionuclide finding of increased visual intensity on the 15–25-min images 2–3 days post-ESWL (Fig. 1). This would suggest that the tracer movement is slowed, which in this study is manifested by a prolongation of the parenchymal transit times.

PTTI prolongation may be due either to renal ischemia or to obstruction. In the context of renal ischemia





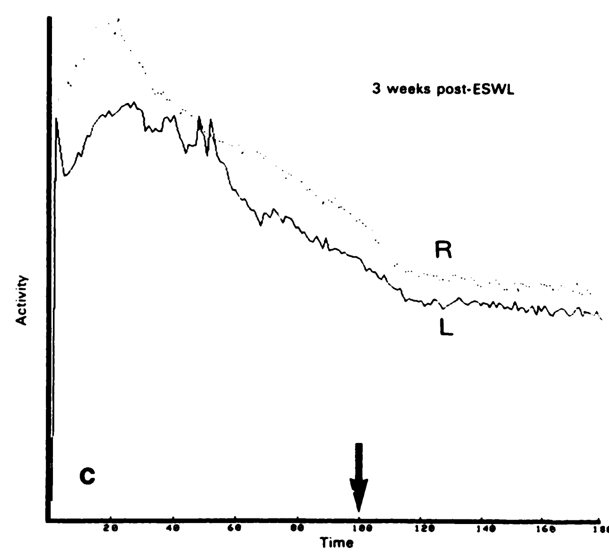


FIGURE 2
Activity/time curves from 0–30 min (0–180 frames at 10-sec intervals). The effect of furosemide given at 16 min (arrow) is seen. A: Pre-ESWL. B: 2–3 days post-ESWL. C: 3 wk post-ESWL. (L) Left kidney (treated side). (R) Right kidney.

this prolongation is due to increased salt and water reabsorbtion by the proximal tubules related to a small relative reduction in peritubular capillary pressure as compared with the proximal tubular intraluminal pressure. In the case of obstruction, PTTI prolongation is due to a rise in intrapelvic pressure as a consequence of increased resistance to flow. Because of this there is a change in pressure gradient from the glomerulus to the site of resistance, resulting in a slight rise of intratubular luminal pressure in the nephron relative to the peritubular capillary pressure and causing an increase in salt and water reabsorbtion.

The distinction may be made by comparing the whole kidney mean transit time with the mean parenchymal transit time. The difference between them gives the pelvic transit time provided the study has been continued long enough to accommodate the whole kidney transit time. Pelvic transit time is normal in ischemia but prolonged in obstructive nephropathy. Additionally the furosemide response is appropriate in ischemia but inappropriate in obstructing uropathy. In this study the parenchymal transit time index was shown to be a more sensitive indicator of disturbed renal function than the relative percentage uptake function.

An interesting phenomenon noted was the transient; but significant prolongation of the PTTI 2–3 days post-ESWL on the untreated side that returned to normal 3 wk post-ESWL, however, with normal pelvic transit times. This phenomenon is illustrated by an example whose activity/time curve is shown in (Fig. 2). A possible explanation could be a reflex autonomic response to renal pelvic stimulation occurring with the fragmentation of the stone by the shock waves. This may cause a transient increase in sympathetic activity that would lead to vasoconstriction of the renal vessels, causing a prolongation of the PTTI. The hypothesis of autonomic reflex is further supported by the findings of ileus in the immediate post-ESWL time period.

Thus, following ESWL prolongation of PTTI during the early 2–3 days post-ESWL period, there may well be a composite effect signifying not only obstructive nephropathy due to residual stone fragments, but also the effect of recent trauma due to the shock waves.

In conclusion, radionuclide studies demonstrate some of the functional changes manifested by the kidneys on both the treated and untreated sides following extracorporeal shock wave lithotripsy.

NOTES

* (GE 400 AT) General Electric, Milwaukee, WI.

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