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Review Article

Percutaneous nephrolithotomy versus ureteroscopic lithotripsy for ureteral calculi therapy: a meta-analysis

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Abstract: *Background*: The present study aimed to explore the efficacy of percutaneous nephrolithotomy versus ureteroscopic lithotripsy, systematically, in the treatment of ureteral calculi. *Methods*: PubMed, Cochrane, and Embase databases, updated to September 2017, were searched by index words to identify relevant studies, including qualified randomized controlled studies or comparison studies. Studies were also identified by tracking reference lists from papers and internet searches. This meta-analysis was performed using mean difference (MD), odds radio (OR), and 95% confidence interval (95% CI) to analyze main outcomes. *Results*: A total of 12 studies were included in this meta-analysis, with 649 subjects in the PCNL group and 633 subjects in the URSL group. Results indicated that PCNL significantly increased hospital stays (SMD, 2.13; 95% CI 1.46-2.80), stone-free rates (3 days) (OR, 6.70; 95% CI 2.61-17.17), and other stone-free rates (1 month) (OR, 4.59; 95% CI 3.02-6.97), compared to the URSL group. However, there were no significant differences in operation times (WMD, 14.09; 95% CI: -0.76-28.94) and complications (OR, 1.25; 95% CI 0.71-2.20) between the two groups. *Conclusion*: Favorable outcomes regarding stone-free rates of 3 days and 1 month were identified in the PCNL group, compared to the URSL group, but URSL significantly decreased hospital stays. More high quality studies are required to confirm the efficacy of PCNL and URSL in identifying the best therapy for ureteral calculi.

Keywords: Percutaneous nephrolithotomy, ureteroscopic lithotripsy, ureteral calculi, meta-analysis

Introduction

Urolithiasis is the most common urologic disease, with a prevalence rate of 10-15% and recurrence rate of 50% [1]. Large proximal ureteral stones can lead to urinary obstruction, resulting in function injury and life-threatening sepsis. Considering the high recurrence rate and serious complications, timely therapy and removing the stone completely are of vital importance for patients.

Over the past decades, several techniques and multiple methods, including endoscopic stone fragmentation, percutaneous nephrolithotomy (PCNL), shockwave lithotripsy (SWL), and ureteroscopic lithotripsy (URSL), have been implemented. SWL and URSL have been proposed in American Urological Association (AUA) Guidelines as the first-line treatments for proximal ureteral stones [2]. In some special cases, such as patients with larger stones (>10 mm), stones influencing proximal ureteral calculi with dilated renal collecting system, or when the ureter is not suitable for retrograde manipulation, PCNL has been recommended, according to 2016 European Association of Urology (EAU) guidelines [3]. However, controversy remains in determining the most appropriate therapy, but timely intervention to remove the stones completely is still of great importance.

SWL has been a priority therapy for patients with stones smaller than 10 mm. However, if the stones stay for a long time in the same ureteral location, this may lead to local chronic inflammation and even incarcerated ureteral calculi [4, 5]. PCNL has shown a high stone clearance rate in proximal ureteral stones since it was first introduced into routine clinical practice in the 1980s [6, 7]. Despite reliable efficiency, each technique has its own limitations. Migration of stones or fragments is the main reason of failure in rigid URSL. It is required for further auxiliary procedures, including flexible

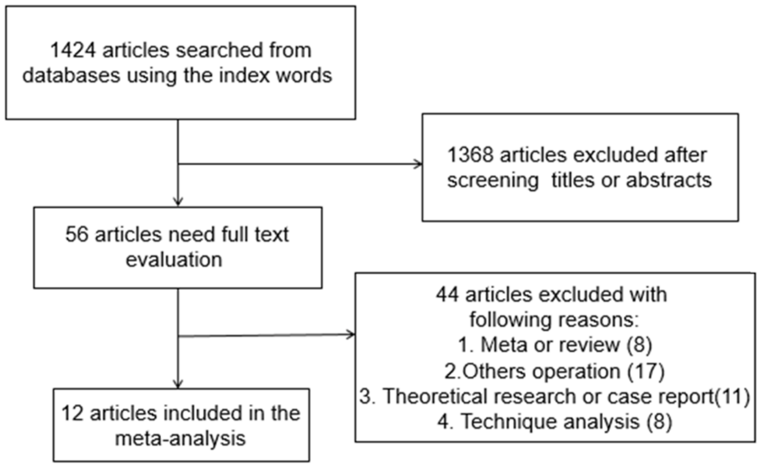

Figure 1. Flow diagram of the literature search and selection process.

URSL and SWL. Both URSL and PCNL have been widely used as minimally-invasive treatments for large proximal ureteral stones. Rigid URSL is a common-used ureteroscopy technique. It has been reported that its stone-free rate in managing upper ureteral stones ranges from 88% to 100% [8, 9] PCNL, an invasive technique, may generally lead to bleeding in 0-20% patients, with a total of 7% requiring transfusion. Moreover, adjacent organ injury should not be ignored regarding PCNL, despite an incidence of only 0.4%. It has been a tough decision for urologists in choosing the best therapy for patients with large proximal ureteral stones. Since 1999, several studies comparing the efficacy and safety of rigid URSL and PCNL, in the treatment of large proximal ureteral stones, have been carried out.

Therefore, as disagreements have been shown among these studies, a meta-analysis was performed to compare the outcomes of rigid URSL and PCNL. This study assessed existing evidence on the effects of abovementioned therapies. These findings may have important clinical implications.

Materials and methods

Search strategy

The following electronic databases were searched, from their inception to September 2017, for all randomized controlled trials or comparison studies analyzing the efficacy of percutaneous nephrolithotomy and ureteroscopic lithotripsy for treatment of ureteral calculi: Cochrane, PubMed, and Embase databases. Studies were also identified by tracking reference lists from papers and internet searches. Two investigators, independently, extracted data. A third investigator was involved in reaching an agreement.

Study selection

Studies that met the following criteria were included in this review: (1) Randomized controlled trials or comparison studies; (2) Therapies of the two groups were percutaneous nephrolithotomy and ureteroscopic lithotripsy; (3) Outcomes included operation times, hospital stays, stone-free rates, and complications; and (4) Publications available in English.

Studies that met the following criteria were excluded: (1) Repeat publications or shared content and results; (2) Outcomes were not relevant to analyses; and (3) Case reports, theoretical research, conference reports, systematic reviews, meta-analysis, and expert comments.

Data extraction and quality assessment

Two reviewers, independently, extracted data based on predefined criteria. Differences were settled by discussion with a third reviewer. Analyses data were extracted from all included studies and consisted of two parts: basic information and main outcomes. Author name, design, sample size, main age, gender, and stone size were extracted as basic information. Clinical outcomes, including operation times, hospital stays, stone-free rates, and complications were analyzed in the two groups. Studies were performed by two reviewers, independently. Any arising differences were resolved by discussion.

Statistical analysis

All statistical analyses were performed using STATA 10.0 (TX, USA). Chi-squared and I^2 tests were used to assess the statistical heterogeneity of clinical trial results and determine the analysis model (fixed-effects model or random-

Table 1. Basic characteristics description of included studies

Study	Design	No. of patients		Age		Gender		Stone Size	
		PCNL	URL	PCNL	URL	PCNL	URL	PCNL	URL
Shiyong Qi 2014	A prosepective randomized study	52	52	41.1	42.5	30 M	31 M	20.3±3.6	19.8±4.3
Abbas Basiri 2008	Randomized clinical trial	50	50	48	39	32 M	33 M	20.3±3.3	17.8±2.4
Gu Xiao-Jian 2013	Randomized compare study	30	29	42.5	44.22	28 M	17 M	17.27	16.23
Xiaowen Sun 2007	Randomized compare study	44	47	40.4	39.6	30 M	31 M	14.7±2	14.6±1.8
Yuanhua Liu 2013	Compare study	45	45	-	-	-	-	-	-
Ibrahim Halil Bozkurt 2015	Compare study	45	41	44.7	42.1	22 M	27 M	31.4±6.4	26.1±4.7
Hongjian Zhu 2014	A four-year retropective study	30	22	51.9	49.6	18 M	14 M	1.4±0.7	1.2±0.8
Hai Li 2013	Compare study	83	91	44.12	45.35	46 M	44 M	20±4.44	20.61±4.26
Yung-Shun Juan 2008	Compare study	22	31	48.2	48.9	16 M	23 M	20.1±5.4	18.6±6.3
Zhongsheng Yang 2012	Compare study	91	91	45.2	46.4	53 M	54 M	15.8±9.6	13.4±8.3
Henglong Hu 2015	Compare study	104	80	65.5	65.1	56 M	45 M	15.8±3.4	15.8±3.4
Chuangjing Wang 2015	Randomized controlled trial	53	54	58.21	57.52	28 M	25 M	13.47±1.8	13.72±1.56

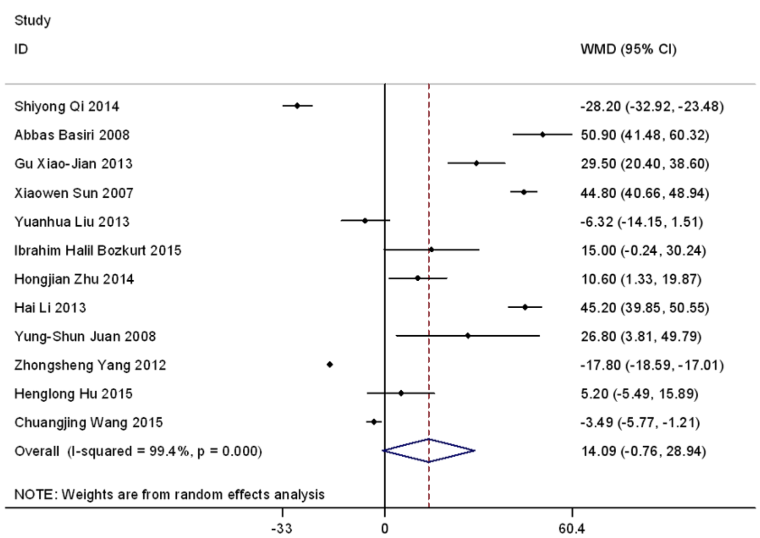

Figure 2. Forest plot showing operation times.

effects model). Heterogeneity was acceptable when the Chi-squared test *P*-value was less than 0.05 and the value of I^2 was greater than 50%, assessed by a random-effects model. It was defined as homogeneous data when Chi-squared test *P*-values were more than 0.05 and the value of I^2 was less than 50%, assessed by a fixed-effects model. Continuous variables are expressed as mean ± standard deviation and were analyzed by mean difference (MD). Categorical data were calculated as percentages and were analyzed by relative risk (RR) or odds ratio (OR). Operation times and hospital stays were analyzed by MD and 95% CI. Stone-free rates and complications were analyzed by OR and 95% CI.

Results

Characteristics of included studies

A total of 1,424 articles were searched. A total of 1,368 articles were excluded during the preliminary screening of title or abstract, leaving 56 articles for further selection. After full-text screening, 44 articles were excluded due to the following criteria: meta or review (8), other operations (17), theoretical research or case report (11), and technique analysis (8). Finally, 12 studies [10-21] were selected for the meta-analysis, with 649 subjects in the PCNL group and 633 subjects in the URSL group. The selection process is presented in **Figure 1**. Main characteristics of included studies are summarized in **Table 1**. Basic information included the design, age, gender, and stone size. Five studies were randomized control trials, six were comparison studies, and one was a retrospective study.

Operation times

Twelve studies with 1,282 subjects (PCNL group = 649, URSL group = 633) reported operation times. Based on Chi-squared test *P*-values (P = 0.000) and I^2 tests-values (I^2 = 99.4%), a random effects model was chosen to analyze results. Pooled results showed that operation

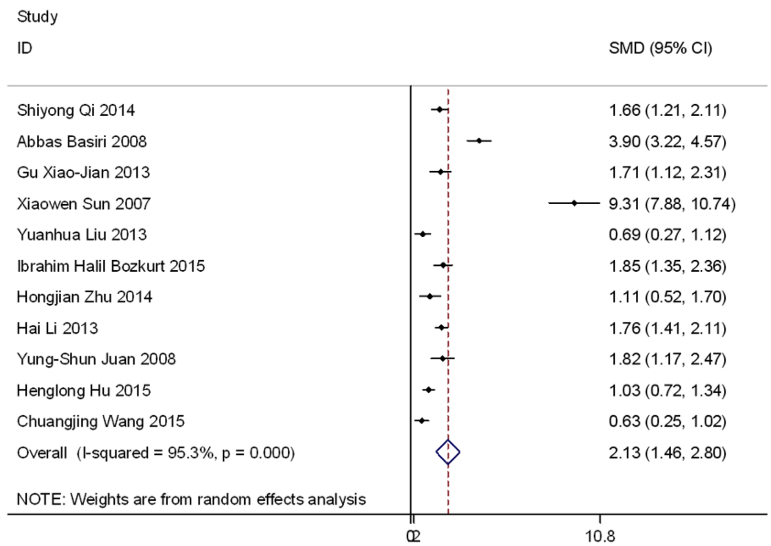

Figure 3. Forest plot showing hospital stays.

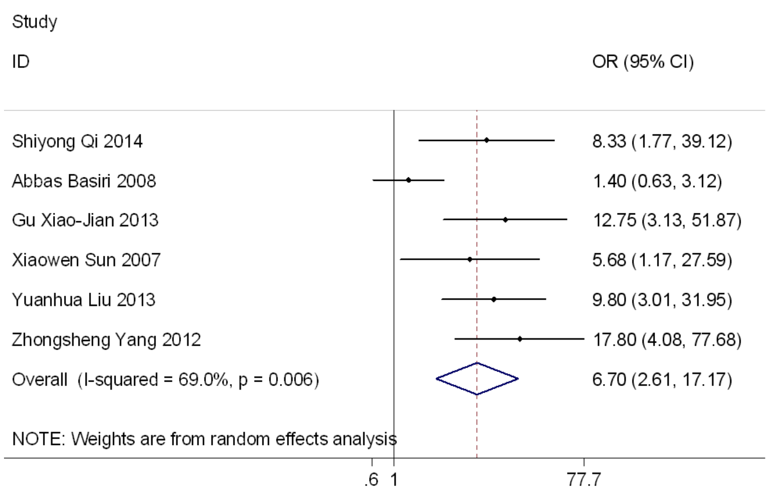

Figure 4. Forest plot showing stone-free rates (3 days).

times were higher in PCNL group than that in URSL group (WMD, 14.09; 95% CI-0.76-28.94, **Figure 2**), without significant differences.

Hospital stays

Eleven studies with 1,100 subjects (PCNL group = 558, URSL group = 542) reported hospital stays. Based on Chi-squared test *P*-values (P = 0.000) and I^2 tests-values (I^2 = 95.3%), a random effects model was chosen to analyze results. Pooled results showed that hospital stays were significantly longer in PCNL group than that in URSL group (SMD, 2.13; 95% CI 1.46-2.80, **Figure 3**).

Stone-free rates

Six studies with 626 subjects (PCNL group = 312, URSL group = 314) reported stone-free rates (3 days). Based on Chi-squared test *P*-values (P = 0.006) and I^2 tests-values (I^2 = 69.0%), a random effects model was chosen to analyze results. Pooled results showed that stone-free rates (3 days) were significantly higher in PCNL group than that in URSL group (OR, 6.70; 95% CI 2.61-17.17, **Figure 4**).

Eleven studies with 1,175 subjects (PCNL group = 596, URSL group = 579) reported stone-free rates (1 month). Based on Chi-squared test *P*-values (P = 0.286) and I^2 tests-values (I^2 = 16.6%), a fixed effects model was chosen to analyze results. Pooled results showed that stone-free rates (1 month) were significantly higher in PCNL group than that in URSL group (OR, 4.59; 95% CI 3.02-6.97, **Figure 5**).

Complications

Five studies with 841 subjects (PCNL group = 428, URSL group = 413) reported complications. Based on Chi-squared test *P*-values (P = 0.044) and I^2 tests-values (I^2 = 56.2%), a random effects model was chosen to analyze results. Pooled results showed no significant differences in complications (OR, 1.25; 95% CI 0.71-2.20, **Figure 6**) between the two groups.

Quality assessment and potential bias

Based on previously mentioned criteria, 12 articles were included in this meta-analysis. Quality assessment and potential bias were accessed by funnel plots, Begg's and Mazumdar's rank test, and Egger's test. The funnel plot for log WMD in operation times of included studies was notably dissymmetrical,

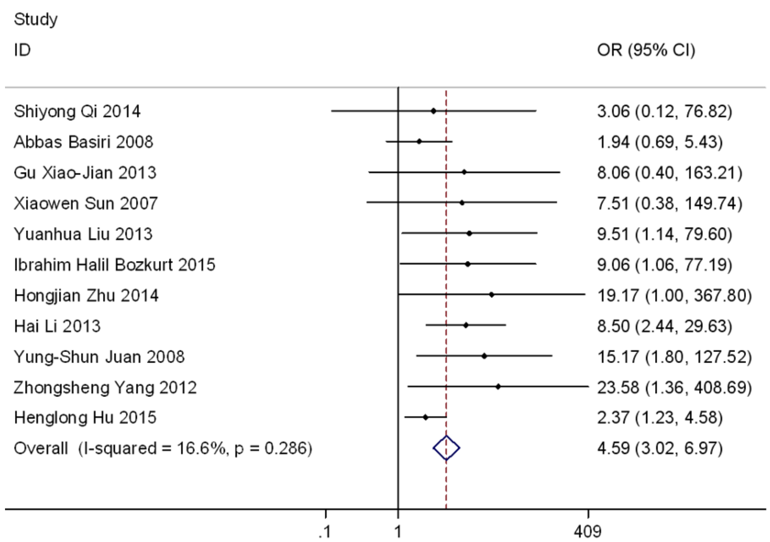

Figure 5. Forest plot showing stone-free rates (1 month).

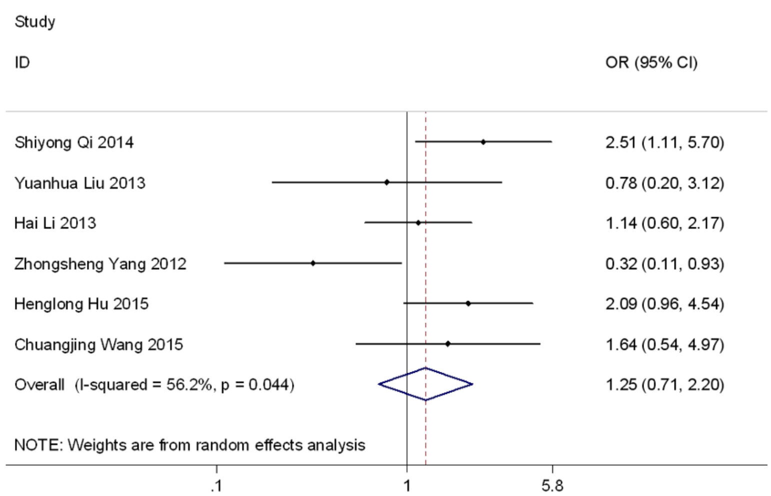

Figure 6. Forest plot showing complications.

suggesting significant publication bias (**Figure 7**). Moreover, significant dissymmetry was detected by Begg's and Mazumdar's rank test (Z = -0.07, P = 1.00). However, Egger's test results showed significant publication bias (P = 0.021).

Discussion

Several similar meta-analyses have been performed. Qing Wang et al. [22] found that patients undergoing rigid URSL were associated with shorter operation times (WMD, -23.66 min; 95% CI -45.00 to -2.32; P = 0.03), shorter hospital stays (WMD, -2.76 d; 95% CI -3.51 to -2.02; P<0.00001), lower 3rd-day (RR, 0.73; 95% CI 0.66 to 0.82; P<0.00001) and 1st-month (RR, 0.82; 95% CI 0.77 to 0.87; P<0.00001) stone-free rates, higher risk of conversion to other surgical procedures (RR, 4.28; 95% CI 1.93 to 9.46; P = 0.0003), higher incidence of migration (RR, 28.49; 95% CI 9.12 to 89.00; P<0.00001) and ureteral perforation (RR, 6.06; 95% CI 1.80 to 20.44; P = 0.004), as well as lower risk of fevers (RR, 0.64; 95% CI 0.42 to 0.97; P = 0.04), transfusions (RR, 0.19; 95% CI 0.04 to 0.85; P = 0.03), and hematuria (RR, 0.38; 95% CI, 0.25 to 0.57; P<0.0001). No significant differences were observed in terms of incidence of embolization, pain, and ureterostenosis. Yang Nianlong et al. [23] found that 15 eligible trials evaluating LSS versus PCNL were identified, including 6 prospective and 9 retrospective studies with 473 patients undergoing LSS and 523 patients undergoing PCNL. Although LSS led to longer operation times (P = 0.01) and higher open conversion rates (P = 0.02), patients had fewer complications (P = 0.03), including decreased bleeding rates (P = 0.02) and blood transfusion rates (P = 0.01), with more stable hemoglobin levels (P<0.001). Stone-free rates were also increased in LSS compared with PCNL (P<0.001), with less secondary/complementary procedures (P = 0.006). There were no significant differences in other demographic parameters between the two groups.

The present study found that less time was needed to perform rigid URSL than PCNL. Operation times were not defined clearly in most studies and were calculated using different criteria. This was likely the most important reason for high heterogeneity [24, 25]. Moreover, operation times mainly depend on

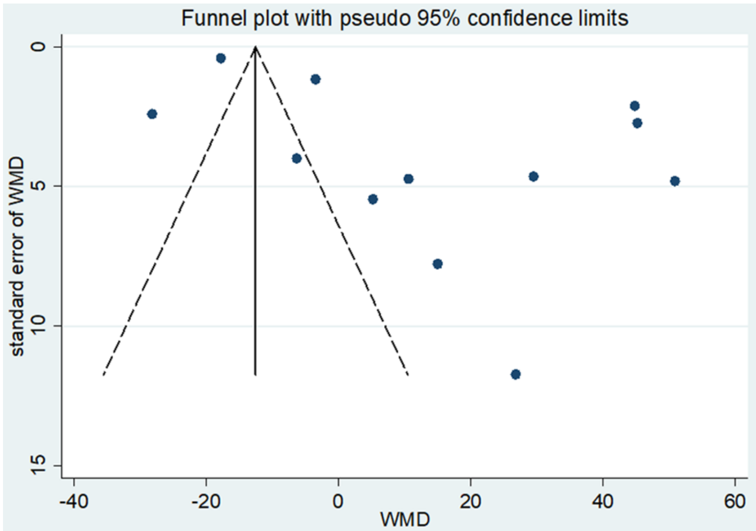

Figure 7. Funnel plot of studies included in the meta-analysis.

patient characteristics and surgeon experience. The shortest and longest operation times for rigid URSL in included studies were 30.6±7.8 minutes [15] and 92.0±32.5 minutes [17], respectively, with 38.5±8.2 minutes [12] and 115.4±49.5 minutes [20] in PCNL, showing significant differences. Rigid URSL yielded significantly shorter hospital stays than PCNL. Recent data has shown that patients undergoing surgery expect to return to work and daily activities as soon as possible. However, invasive techniques often require more time to make sure that no severe postoperative complications happen. After PCNL, patients are therefore required to lie in bed and limit their activities for several days to reduce the risk of bleeding.

In addition, results showed that PCNL was associated with higher risk of transfusions and hematuria, compared to rigid URSL. This is consistent with the fact that bleeding is generally common in PCNL and patients may need transfusions. Actually, one systematic review reported that the overall transfusion rate is about 7%, indicating a low transfusion rate for PCNL [10]. If conservative measures fail, selective embolization is required in 0-1.5% cases [11]. The present meta-analysis showed no significant statistical differences in embolization between the two groups, ensuring the safety of PCNL.

In conclusion, no significant statistical differences were found regarding pain, despite the fact that PCNL is a more invasive procedure. Ureteral perforation generally happened in rigid URSL, according to present analysis, but most of these perforations were minor and could be managed by ureteral stents. Thus, this might be the reason for no significant differences in ureterostenosis. However, only two studies [16, 19] were associated with ureterostenosis and the follow-up times were not the same. Therefore, more high-quality studies are necessary to confirm the current findings.

Admittedly, there were a few limitations to the present study, as follows: (1) RCT or comparison studies were included; (2) Differences in inclusion criteria and exclusion criteria for subjects; (3) Different stone sizes and stone position; (4) All included studies were English publications, suggesting bias; (5) Operation techniques in different studies were inconsistent; and (6) Pooled data were used for analysis and individual patient data was unavailable, limiting comprehensive analyses.

Disclosure of conflict of interest

None.

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