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Original Article

Clinical observation of loupe-assisted intussusception vasoepididymostomy in the treatment of obstructive azoospermia (analysis of 49 case reports)

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Abstract

To evaluate the clinical outcomes of loupe-assisted intussusception vasoepididymostomy (VE) in the treatment of epididymal obstructive azoospermia (EOA), we retrospectively analyzed data from 49 patients with EOA who underwent two-suture longitudinal intussusception vasoepididymostomy (LIVE) between 2000 and 2007. The data included the surgical method, postoperative motile sperm count per ejaculation, percentage of progressive motile sperm and patency and pregnancy outcomes. There were a total of 49 men undergoing scrotal exploration, and epididymal obstruction was found in all cases. Bilateral or unilateral anastomoses were performed in 40 and 6 men, respectively. The postoperative courses of 42 patients were followed up for more than 6 months, and the courses of 38 patients were followed up for more than 1 year. The overall patency and pregnancy rates were 71.4% and 26.3%, respectively. Moreover, progressive motile sperm was more frequently present in those patients who had undergone anastomosis at cauda than at corpus or caput. Pregnancy was achieved only in those patients who had undergone anastomosis at least on one side of the cauda epididymis. We think that the loupe-assisted method, with a lower overall cost and a simplified surgical procedure, can achieve satisfactory patency outcomes and pregnancy results. Data from this paper also suggest that paternity outcomes occur more frequently after anastomoses at cauda than at corpus or caput.

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1 Introduction

Treatment options for obstructive azoospermia include microsurgical reconstruction of the continuity of the genital ductal tract, sperm aspiration from the epididymis (microsurgical epididymal sperm aspiration) under local or general anaesthesia and a blind percutaneous procedure. If epididymal obstruction is present, whether as a primary pathology or as secondary to infection or inflammation, a vasoepididymostomy (VE) is required proximal to the obstruction to restore continuity of sperm transport. VE is one of the most technically challenging microsurgical procedures and has become the standard treatment protocol for azoospermia, secondary to epididymal obstruction.

The surgical methods for VE have changed greatly over time. The original procedure was a gross end-to-side (ES) fistula technique, originally described by Martin *et al.* [1] in 1902. A major advance in this approach was made by Silber [2] in 1978, with the description of a specific tubule end-to-end (EE) microsurgical

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VE. The ES VE was later described by Wagenknecht [3] in 1980, and subsequently popularized by Thomas [4]. This technique had the advantage of sparing the epididymal blood supply. In later years, Berger [5] introduced the triangulation intussusception method. The advantage of this method is that the epididymal tubule is drawn into the vasal lumen, thus enhancing the watertightness of the seal [6]. Marmar [7] modified this technique with a transverse two-suture approach, and Chan *et al*. [8] described a longitudinal intussusception vasoepididymostomy (LIVE) method in an animal study and also determined the superiority of LIVE procedures compared with nonintussusception techniques. Intussusception two-suture techniques also require fewer microsutures than the conventional ES and EE techniques [8–11].

Loupe-assisted techniques have been widely used in many urological surgical procedures, especially in the medical practice of andrology. Vasovasostomy (VV) with loupe magnification has been extensively used in clinical setting. A review of published papers suggests that satisfactory results are typically obtained with a loupe-assisted procedure [12]. Moreover, compared with other microscopic surgeries, loupe-assisted operations have the advantages of decreased operation time and less expensive instruments [13].

In this study, we reviewed clinical data from patients with epididymal obstructive azoospermia (EOA) who underwent scrotal exploration and loupe-assisted LIVE. We verify that the loupe-assisted method can satisfy the requirement of a comprehensive LIVE procedure, and that fertility outcomes are related to the sites of anastomoses. To our knowledge, this is the first study of loupe-assisted VE for the treatment of epididymal obstruction.

2 Materials and methods

2.1 Subjects and laboratory examination

Between January 2000 and May 2007, 49 patients with an average age of 37 years were diagnosed as having EOA. Patients who had undergone a vasectomy earlier were excluded from this study. All patients underwent semen testing at least thrice during the year before the study, and no sperm was identified in a centrifugal (1 500 × *g*) semen assay with an average semen volume of 1.5–5.5 mL. Semen fructose tests were positive for the ejaculate of all patients. The average follicle-stimulating hormone (FSH) levels were measured using an electro-chemiluminescence immunoassay, and were within normal limits (from 5.34 to 21.22 mIU mL^{-1}).

2.2 Past history

Nine (18.4%) of the cases had a history of urological or genital infection 3–18 years before the study (< 5 years, $n = 2$; 5–15 years, $n = 4$; > 15 years, $n = 3$), with three of them being diagnosed with epididymitis. The aetiology of the other 40 cases was completely unknown, with two having a history of paternity 3 and 7 years, respectively.

2.3 Physical examination, testicular histology and genetic evaluation

The physical examination showed nonatrophic testes with normal vas deferens bilaterally in all patients. The mean volume of the right and left testes was 10.1 ± 20.1 mL and 11.7 ± 19.7 mL, respectively. Slightly swollen epididymides existed bilaterally in 20 cases and unilaterally in six cases. Bilateral or unilateral hard epididymal nodes were palpated in 15 and 9 cases, respectively. Rectal ultrasonography showed no dilation of spermaduct or spermatophore. With a 22-gauge needle attached to a 10-mL disposable syringe, a fine-needle aspiration testis biopsy was carried out on each patient under local anaesthesia, and histological examination showed normal spermatogenesis in all cases. The patients' karyotypes were analyzed preoperatively, and showed no euchromosome or sex chromosome abnormalities in any patient.

2.4 Surgical procedure

All patients underwent scrotal exploration by loupe (× 6.0 magnification) under epidural anaesthesia. The scrotum was incised and each testis was exposed. The tunica albuginea was incised to expose the epididymis. The vas deferens was transected and saline injected into the vas deferens to confirm the patency on the seminal vesicle side. A small incision was made at the tunic of the epididymal cauda segment, and a single dilated tubule was carefully dissected using the tips of a pair of microsurgical forceps or scissors. Mucosal anastomosis was then performed using the LIVE technique. Two double-armed 10–0 nylon sutures were prepared for the anastomosis.

First, a needle was used to pierce the lateral aspect of the epididymal tubule both within the tubule itself and out longitudinally. However, the needle was not pulled through the tubule but rather left in the wall to

prevent collapse. A second 10–0 double-armed nylon suture was placed identically through the contralateral aspect of the epididymal tubule (Figure 1A). A small incision was made longitudinally between the two needles with a microknife or needle edge and the exuded fluid was examined for motile sperm (Figure 1B). Second, if motile sperm were present, the anastomosis was continued and one arm of the first suture was placed in an inside-out manner through the mucosal layer of the vas deferens at position a_1, and then the other arm of the suture was placed identically through position a_2. The second 10–0 double-armed nylon suture was placed through positions b_1 and b_2 on the vas deferens parallel to the first suture on the contralateral side of the vas and epididymal tubule (Figure 2). Finally, the sutures were tied together (a_1 to a_2 and b_1 to b_2), and the epididymal tubule was gently intussuscepted into the lumen of the vas deferens. The muscularis was closed interiorly with a 9–0 nylon suture (Figure 3).

If no sperm were found in the exuded epididymal fluid, additional examination of the fluid was carried out in the epididymis closer to the corpus or caput segment. If the repeated examinations showed no sperm in the epididymal fluid or no patency of the vas deferens, reconstructive surgery was not carried out and the procedure was finished immediately.

2.5 Postoperative evaluation

Serial semen analyses were initiated at 4 weeks after surgery and continued until pregnancy was achieved or patients were lost to follow-up. Patency was defined as the presence of motile sperm in the ejaculate of at

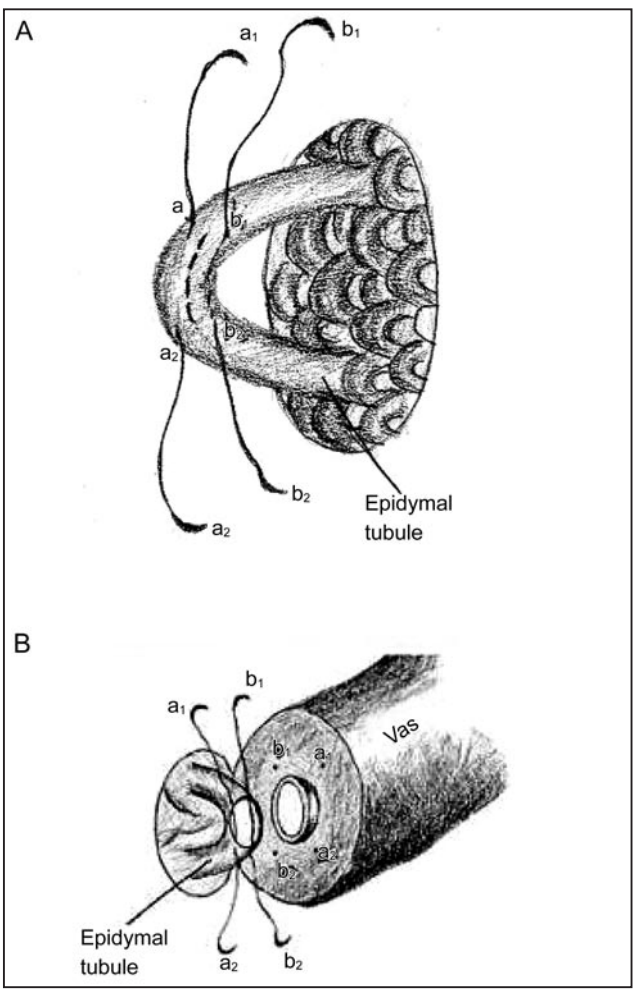

Figure 1. (A): Two double-armed sutures longitudinally through the wall of the epididymal tubule. (B): Epididymal tubule opened longitudinally and examined for motile sperm.

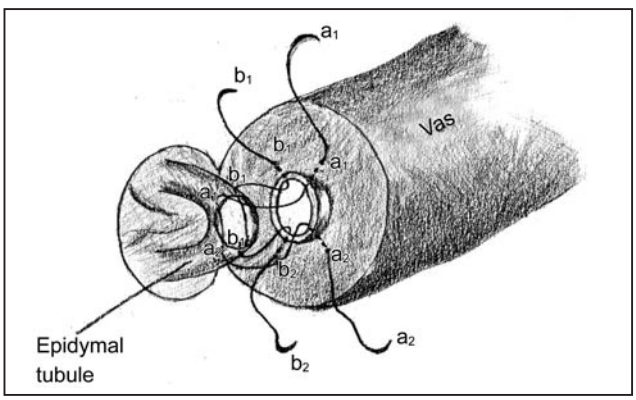

Figure 2. Sutures a and b tied together (a_1 to a_2 and b_1 to b_2).

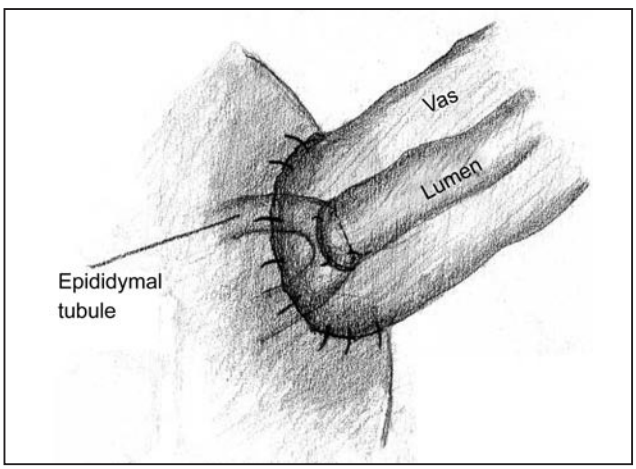

Figure 3. Epididymal tubule intussuscepts into lumen of vas deferens.

least one postoperative semen sample. Pregnancy was defined as unassisted establishment (no assisted reproduction) of a viable pregnancy leading to a live birth. Follow-up information was obtained from clinic visits, telephone contact and in some instances, written letters from the patients. Patients without a postoperative semen analysis or patients who underwent LIVE within 6 months of follow-up were excluded from the patency-rate analysis, unless they had motile sperm present in the semen or were able to achieve pregnancy. For those patients whose partners had yet to conceive, the minimum follow-up time was 6 months. Only naturally conceived pregnancies were included in the calculations, and none of the female partners used assisted reproduction techniques to achieve pregnancy. Patients with less than 12 months of follow-up or no ongoing interest in achieving conception were excluded from the pregnancy rate analysis, unless they had achieved pregnancy.

2.6 Statistical analysis

A χ^2 analysis was used to compare pregnancy between the groups. Significance was defined by $P < 0.05$.

3 Results

A total of 49 men underwent scrotal exploration with a mean operative time of 135 ± 35 min from the start of skin incision to the end of skin closure. Saline injection confirmed that 45 cases had bilateral vas patency and four had unilateral patency on the seminal vesicle side. Obstruction was confirmed at the epididymal tubule in all cases. Motile sperm were found in the epididymal fluid in 47 patients (42 and 5 in bilateral and unilateral epididymal fluid, respectively).

Bilateral LIVE was performed on 40 of the patients and unilateral LIVE on six. Data showed that bilateral LIVE was performed at the level of the cauda in 29 cases, the corpus in four, the corpus and contralateral cauda in four, and at the level of the corpus and contralateral caput in three cases. Unilateral LIVE was done at the level of the caput, corpus and cauda for one, two and three of the cases, respectively (Table 1). One case, in which the patient underwent VE on one side and VV on the other side because sperm were present in the unilateral vasal and contralateral epididymal fluid, was excluded from the analysis. Forty-two patients were followed up over 6 months postoperatively, with 38 cases followed up over 1 year.

A total of 30 cases achieved successful patency, with an overall patency rate of 71.4% (30 of 42), and transient patency occurred in one case (2.2%). The data also showed that LIVE at different epididymal segments resulted in different patency rates. The patency rate in men undergoing LIVE at corpus or caput was superior to that in men receiving LIVE at the cauda (87.5% *vs.* 73.3%, $P > 0.05$). As expected, our data also showed that the patency rate in men undergoing bilateral LIVE was slightly higher than that in patients undergoing unilateral LIVE (72.2% *vs.* 66.7%, $P > 0.05$).

Table 1. Postoperative outcomes and anastomotic sites.

Anastomotic sites	Live (*n*)	MOF > 6 (mon) (*n*)	MOF > 12 (mon) (*n*)	MSC ($\times 10^6$)	PMS % (*n*)	Patency *n* (%)	Pregnancy *n* (%)
Corpus and contra. cauda	4	4	3	31.0 ± 9.0	13.0 (3)	1	1
Corpus and contra. caput	3	2	2	19.5	5 (1)	2	0
Bilateral cauda	29	27	25	34.3 ± 12.9	9.0 ± 6.5 (19)	20 (74.1)	8 (32)
Bilateral corpus	4	3	2	23.0 ± 11.0	5.5 (2)	3	0
Unilateral corpus	2	2	2	12.5[a]	0	1	0
Unilateral caput	1	1	1	7.0[b]	0	1	0
Unilateral cauda	3	3	3	17.2	15.0 (2)	2	1
Bi- or unilateral cauda	32	30	28	31.0 ± 15.5	17.0 ± 5.0 (21)	22 (73.3)	9
Caput or corpus	10	8	6	15.0 ± 6.0	5.3 (3)	7 (87.5)	0
Total	46	42	38	23.5 ± 24.0	12.2 ± 11.0 (27)	30 (71.4)	10 (26.3)

Abbreviations: contra. caput, contralateral caput; contra. cauda, contralateral cauda; mon, month; MOF, months of follow-up; MSC, motile sperm count; PMS, progressive motile sperm.
[a]$P < 0.05$, [b]$P < 0.01$, compared with that in unilateral cauda.

Postoperative motile sperm count (MSC) per ejaculate, percentage of progressive motile sperm (PMS), patency and pregnancy rates are detailed in Table 1. Of the 42 men with a follow-up period of over 6 months, 30 cases had motile sperm present in their ejaculate. The mean MSC was (23.5 ± 24.0) × 10^6 per ejaculate. The MSC for patients undergoing LIVE at the level of the bilateral cauda, bilateral corpus, corpus and contralateral cauda, as well as at the level of the corpus and contralateral caput, was (34.3 ± 12.9) × 10^6, (23.0 ± 11.0) × 10^6, (31.0 ± 9.0) × 10^6 and 19.5 × 10^6, respectively. The highest MSC achieved in cases undergoing LIVE was at the bilateral caudal level. Unilateral LIVE performed on six men also showed that anastomosis at the cauda resulted in better outcomes than did that at the corpus ($P < 0.05$) or caput ($P < 0.01$).

According to Table 1, PMS were present in 27 of the ejaculates, and the mean level of PMS was 12.2% ± 11.0%. We found that PMS levels were affected by anastomotic site. Of the 20 cases achieving patency with LIVE at the bilateral cauda, 19 (95%) had PMS present in the ejaculate, and the mean PMS was 19.0% ± 6.5%. In the three patients who received LIVE at the corpus and contralateral cauda, the mean PMS was 13.0%, and in the two patients who underwent LIVE at the unilateral cauda, the mean PMS was 15.0%. However, in seven patency cases with LIVE not at the cauda (at the corpus or caput instead), PMS were present in only three (42.8%), with a mean value of 5.3%.

Of the 49 patients who underwent an operation, 38 were observed over 12 months, and paternity occurred in 26.3% (10 of 38) of the couples. In our series, we found that the pregnancy outcome correlated significantly with the site of anastomosis. Of the 10 men achieving paternity, eight had received LIVE at the bilateral cauda, one at the corpus and contralateral cauda, and one at the unilateral cauda. There was no paternity achieved by men who underwent LIVE only at the corpus or caput.

4 Discussion

A successful VE involves enlarging the opening of the efferent tubule and forming a watertight anastomosis between the epididymal tubules and the ends of the vasa, with no subsequent stricture formation. This is not an easy goal to achieve in the absence of magnification, because the inner lumens of the vas deferens and the epididymal tubules are too small in diameter to be seen clearly by unaided eyes. The LIVE technique has the advantage of permitting precise mucosal approximation between the lumen of the distal vas and the mucosal edge of the epididymal tubules. With compressive stress from the flow of epididymal fluid, a tight mucosal approximation may be obtained; hence the possibility of anastomotic sperm leakage and an anastomotic sperm granuloma may be avoided. Although VE remains as the most technically demanding microsurgical procedure, LIVE can offer better or comparable outcomes compared with conventional procedures with the benefit of fewer sutures, thus simplifying the anastomosis. Only two sutures being used in LIVE provide the advantage of fewer sutures passing through the lumen and fewer knots of suture left outside the anastomosis, which may decrease the possibility of fibrosis and anastomotic stricture. The low failure rate, which was not documented in our group, is lower with the use of the intussusception techniques compared with nonintussusception procedures [14].

Our data show that loupe magnification is feasible for performing an adequate VE in the clinical setting and, more importantly, loupe-aided microsurgical procedures are relatively easier to perform and can save on operative time. Although there were no data in our series comparing the cost and operative time of loupe-assisted LIVE with those of other microsurgical methods, the mean operative time (135 ± 35 min) of bilateral LIVE in our group was shorter than that in results reported earlier by other groups. Most importantly, the final outcome was not affected despite decreased operative time. In our group, the patency and pregnancy rates reached 71.4% (30 of 42) and 26.3% (Table 1), respectively. Our data are comparable to the reported patency rate outcomes of 52% to 85% and reported pregnancy rates of 11% to 56% [15, 16]. The loupe-assisted procedure has the advantage of requiring less skill and training. Obviously, the benefits of a shorter operative duration and reduced instrument requirements may also help reduce the cost of the procedure. The achievement of successful anastomosis and favourable outcomes in our patients indicated that loupe magnification could completely satisfy the requirements of a successful VE. Therefore, we attempted LIVE with only loupe assistance rather than with microscopic magnification in our practice. The operation time and expense should also be considered when comparing the outcomes of VE. To this end, it is worthwhile to adopt a simpler, less expensive method that allows a quicker operation and

requires less equipment, if the outcomes are comparable. A faster operation and fewer equipment requirements result in less expense. Therefore, we believe that loupe-assisted LIVE could be the ideal method for genital duct reconstruction.

The patients in our study had EOA of primarily unknown aetiology, although some reported an earlier history of infection or inflammatory damage to the epididymis. None of the patients had undergone vasectomy earlier. Vasectomy is a common cause of EOA and can lead to an elevated vasal pressure that causes epididymal obstruction secondary to a blowout of the epididymal tubules. The pathophysiology underlying epididymal obstruction from vasectomy and other causes may differ significantly, resulting in varying outcomes after microsurgical repair. Our study shows that patients with EOA unrelated to vasectomy may also be recommended for VE, and successful treatment can be achieved surgically as it would be in a patient undergoing the reversal of vasectomy [16].

The efficacy of LIVE may be affected by several factors, such as the obstructive interval, the quality of the epididymal fluid, female fertility factors and surgical skill. Previous reports suggest that paternity rates are inversely related to the duration of obstruction [17]. In our series, the obstructive intervals and female fertility factors were undocumented in the majority of cases, so the correlations of these two factors with pregnancy outcome could not be identified clinically.

The data in this study showed that anastomotic sites at different epididymal segments lead to significantly different PMS and pregnancy outcomes. We recognized that such varied results were related to the quality of sperm at different sites of the epididymis. Previous studies showed that the epididymis plays an important role in sperm development in addition to acting as a conduit for the transport and storage of sperm. As sperm traverse through the epididymis, they undergo a time- and location-dependent transition from being relatively immotile and incapable of fertilization to becoming mature, motile sperm with the capacity for fertilization [18, 19]. Spermatozoa from the caput and corpus usually display a circular motion that is less able to penetrate the uterotubal junctions and are rarely capable of fertilization. In contrast, sperm obtained from the cauda epididymis had motility and fertility similar to those of ejaculated sperm [20, 21]. A report published earlier showed that when the uteri of superovulated female hamsters were inseminated with caput or cauda spermatozoa, caput spermatozoa failed to fertilize eggs, whereas cauda spermatozoa achieved 88% success [20]. Clinical data also suggest that pregnancy outcomes after cauda epididymal anastomoses are superior to those after caput anastomoses [22]. Given this information, we were not surprised to find that, in our group, the majority (95%) of patency cases undergoing LIVE at the cauda had PMS in their ejaculate, and the percentage of PMS was relatively high. However, only a minority of the patients with patency achieved PMS in their ejaculate after anastomosis at the caput or corpus, and the percentage of PMS was also much lower. Pregnancy was achieved only in patients whose anastomotic sites were at caudal segments, which was consistent with the results of PMS in ejaculate (Table 1).

We could not preclude the possibility that the small number of patients in the study and the absence of a control group in our series might lead to a biased result. There have also been studies showing contrasting results, which suggest that the best-quality sperm in patients, in terms of viability, motility and fertility, were often found more proximally in the epididymis. Motile sperm and favourable fertility results were observed in patients following proximal caput anastomoses with further refinements in technique and experience [23–25]. Clinical studies with larger patient populations are necessary for further investigation of the relationship between anastomotic sites and pregnancy outcomes.

Our study suggests that intraoperative motile sperm may be important for patency but not pregnancy. Although all of the patients had motile sperm at the site of epididymal repair, there were no pregnancies following caput or corpus anastomoses. Published studies suggest that non-motile sperm may also lead to successful VE [25, 26]. Therefore, the presence or absence of motile sperm in the epididymal fluid does not play a deciding role in achieving a successful pregnancy. Motile sperm were present at all of the anastomotic sites in our patients, which is inconsistent with data from earlier reports. We routinely searched for motile sperm during the operation by pressing on the upper part of the epididymis or varying the anastomotic site. These intraoperative efforts may partially contribute to the inconsistency. Other factors, such as differences in aetiology resulting in EOA and the obstructive interval, may also lead to the inconsistency of our results with the reported ones. Further investigations are needed to clarify the unknown causes leading to the presence of motile sperm in these patients.

We conclude that the loupe-assisted method had the advantage of a relatively shorter operation time and lower cost. Most importantly, the final outcome was not inferior despite saving time. More favourable paternity results were achieved in patients who underwent LIVE at the level of the cauda as opposed to the caput or corpus. Although generally requiring less skill and training, the loupe-assisted LIVE is preferred by most surgeons for its simplicity. Less instrumentation is required for the procedure, thus making it possible for this approach to be popularized in the department of andrology in our country.

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