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ORIGINAL ARTICLE

Play it safe: renal function after bilateral flexible ureteroscopy for kidney stones

Alexandre Danilovic[1] · Caio Vinicius Suartz[1] · Fabio Cesar Miranda Torricelli[1] · Giovanni Scala Marchini[1] · Carlos Batagello[1] · Fabio Carvalho Vicentini[1] · William C. Nahas[2] · Eduardo Mazzucchi[1]

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Abstract

Purpose We searched for perioperative renal function deterioration risk factors in patients that underwent bilateral flexible ureteroscopy (fURS) for kidney stones.

Methods From August 2016 to February 2020, symptomatic patients > 18 years old with bilateral kidney stones up to 20 mm in each side were prospectively studied. Serum creatinine samples were collected on admission to surgery, immediate post-operative (IPO), on POD 3, 10, and 30. Estimated glomerular filtration rate (eGFR) was calculated using Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) without a race coefficient.

Results Thirty patients underwent bilateral fURS. Comparing to preoperative eGFR, median IPO and POD3 eGFR ($p < 0.001$) were significantly lower, and POD10 ($p = 0.092$) and POD30 ($p = 0.648$) were similar to preoperative eGFR. During follow-up, 22/30 (73.3%), 14/30 (46.7%), and 7/30 (23.3%) of the patients presented a decrease > 10% eGFR, > 20% eGFR, and > 30% eGFR, respectively. Multivariate analysis demonstrated that lower preoperative eGFR is a risk factor for eGFR < 60 mL/min/1.73 m^2, $p = 0.019$ [1.021–1.263; 1.136]; ASA > 1 is a risk factor for decrease of eGFR > 10%, $p = 0.028$ [1.25–51.13; 8.00]; longer operative time is a risk factor for decrease of eGFR > 20%, $p = 0.042$ [1.00–1.05; 1.028]; and operative time ≥ 120 min is a risk factor for decrease of eGFR > 30%, $p = 0.026$ [0.016–0.773; 0.113].

Conclusions Renal function suffers a reversible decrease after bilateral fURS. Our study suggests that adequate selection of patients and maintaining operative time < 120 min are relevant factors in preventing acute renal function deterioration following bilateral fURS.

Keywords Kidney stone · Renal function · Risk factors · Ureteroscopy · Urolithiasis

✉ Alexandre Danilovic
alexandre.danilovic@hc.fm.usp.br

Caio Vinicius Suartz
caio.v_suartz@hotmail.com

Fabio Cesar Miranda Torricelli
fabio.torricelli@hotmail.com

Giovanni Scala Marchini
marchinism@gmail.com

Carlos Batagello
carlosbatagello@hotmail.com

Fabio Carvalho Vicentini
fcvicentini@gmail.com

William C. Nahas
wnahas@uol.com.br

Eduardo Mazzucchi
emazzucchi20@gmail.com

1 Urology, Hospital das Clinicas, Faculdade de Medicina, Universidade de Sao Paulo, Av. Dr. Eneas de Carvalho Aguiar, 255, 7 and. Sala 7175, São Paulo, SP 05403-000, Brazil

2 Urology, Hospital das Clinicas, Faculdade de Medicina, Universidade de Sao Paulo, São Paulo, Brazil

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Introduction

Urolithiasis is increasing worldwide and bilateral disease is reported in up to 11% of the stone formers [1]. Flexible ureteroscopy (fURS) is a popular minimally invasive treatment modality for kidney stones [2]. Bilateral fURS could be done in symptomatic patients but also can be advantageous for asymptomatic patients due to a lower incidence of stone relapse [3]. Bilateral fURS for kidney stones is an efficient procedure to spare resources. It presents a similar stone-free rate (SFR) and length of stay (LoS) with less disposable devices use than unilateral fURS. However, the patient could experience more overall complications and more emergency room (ER) visits than unilateral procedures [4, 5].

High intrarenal pressure during fURS is a concern as it may increase the risk of infection and acute renal function deterioration [6, 7]. High hydrostatic pressure may cause tubular damage and temporarily impair intrarenal blood flow, which can reduce the glomerular filtration rate [8]. Despite all efforts to keep intrarenal pressure as close to the physiological level as possible, fURS may lead to pyelocaliceal pressure increase due to forced saline irrigation [9, 10]. That is even more relevant in bilateral procedures. A previous prospective study comparing unilateral to bilateral fURS demonstrated that bilateral fURS is associated with a more pronounced increase of creatinine levels during early follow-up [5].

There is limited data on renal function during the perioperative time of bilateral fURS for kidney stones. Better selection of the patients would increase the safety of the procedure. We searched for perioperative renal function deterioration risk factors following bilateral fURS for kidney stones.

Materials and methods

From August 2016 to February 2020, symptomatic patients > 18 years with bilateral kidney stones up to 20 mm on each side were prospectively studied. We excluded from this study patients previously submitted to invasive urinary tract procedures, patients with kidney malformations or hydronephrosis, and patients pre-stented with double-J or with untreated urinary tract infection. The institutional ethics committee approved the study protocol (IRB No. 11851) and written informed consent was obtained from all patients according to the Declaration of Helsinki Ethical Principles for Medical Research involving Human Subjects.

Patients were classified according to the American Society of Anesthesiologists physical status classification system (ASA) and adjusted-age Charlson score preoperatively [11, 12]. Preoperative computed tomography (CT) exams were obtained of all patients. A senior radiologist evaluated all CT exams in the magnified (400%) bone window (width, 1600 UH/ level, 500 UH) in the three axes [13]. Stone size was considered the sum of the longest diameter of each stone in the renal unit. Stone volume was calculated using the sum of the volume of each stone in the renal unit using the ellipsoid formula as length × width × depth × π × 0.167. Stone density was measured by free hand region of interest (ROI) determination coincident with the stone borders.

Table 1 Clinical features of 30 patients who underwent bilateral fURS

Feature	Bilateral fURS
Gender, female *N* (%)	13 (43.3)
Age (mean ± SD), years	45.6 ± 12.6
BMI (mean ± SD), Kg/m^2	27.2 ± 4.5
ASA, *N* (%)	
I	12 (40.0)
II	12 (40.0)
III	6 (20.0)
CCI, *N* (%)	
0	12 (40.0)
1	2 (6.7)
2	3 (10.0)
3	5 (16.7)
4	5 (16.7)
5	1 (3.3)
6	0 (0.0)
7	1 (3.3)
8	0 (0.0)
9	1 (3.3)
10	0 (0.0)
Preop creatinine (mean ± SD), mg/dL	1.0 ± 0.6
Preop eGFR (median [interquartile range]), mL/min/1.73 m^2	93.3, 82.6–105.2
Stone size (mean ± SD), mm	30.9 ± 12.7
Stone volume (mean ± SD), mm^3	669.9 ± 510.8
Stone density (mean ± SD), HU	1062.0 ± 374.5
Stone composition	
Calcium oxalate monohydrate, *N* (%)	13 (43.3)
Calcium oxalate dihydrate, *N* (%)	11 (36.7)
Calcium phosphate, *N* (%)	4 (13.3)
Struvite, *N* (%)	2 (6.7)

N Number; % percentage; *SD* standard deviation; *Kg* kilograms; *m* meter; *mg* miligrams; *dL* deciliter; *mL* mililiters; *min* minutes; *mm* milimeters; *HU* Hounsfield unit; *ASA* American Society of Anesthesiology; *BMI* body mass index; *Preop* preoperative; *eGFR* estimated glomerular filtration rate; *CCI* Charlson comorbidity index

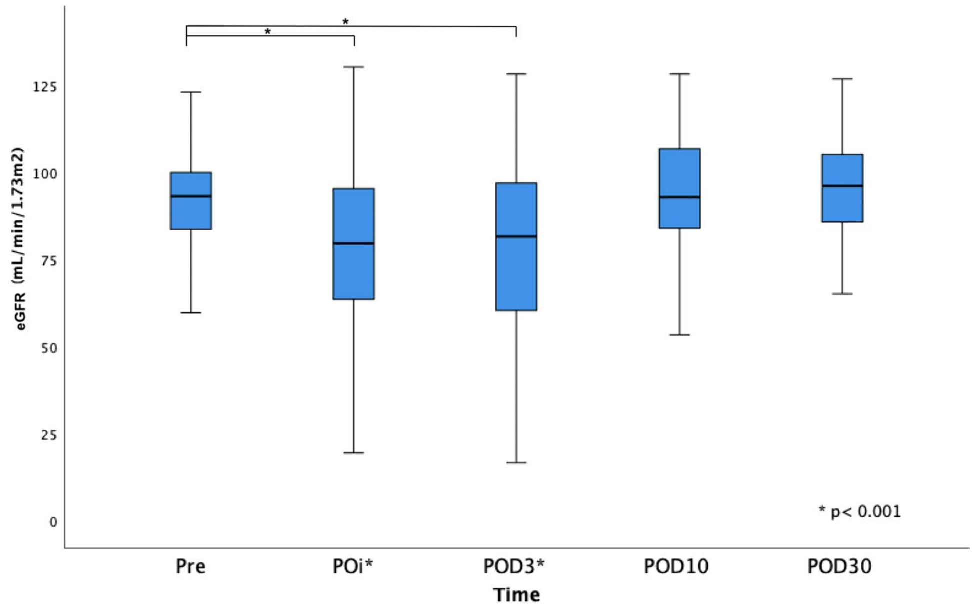

Fig. 1 Median of preoperative, IPO, POD3, POD10 and POD30 eGFR of 30 patients that underwent to bilateral flexible ureteroscopy for kidney stones

Bilateral fURS were performed according to a standardized protocol [14]. In brief, patients were operated on lithotomy position and 15° Trendelemburg, under general anesthesia. Cefazoline was administered during the induction of anesthesia in all patients. The most symptomatic side was operated on first. A safety nitinol guide wire was passed up to the renal pelvis. A 7.5F semi-rigid ureteroscope was passed into the ureter through a PTFE wire. Then, a ureteral access sheath (UAS) 10/12F × 35 cm was passed through the PTFE wire. A reusable flexible ureteroscope URF-P5 (Olympus—JN) was used and irrigation was obtained by a bag of 1 L of saline hung 40 cm above the patient plus flushes of saline with a 20 mL syringe when needed. A 30W laser (Dornier–USA) was used to treat the stones in a combined technique of dusting, set at 15 Hz and 400 mJ, and fragmentation, set at 10 Hz and 1000 mJ, with a 270 micron Holmium laser fiber (Dornier, USA). Stone fragments > 2 mm were removed using a tipless basket. UAS was removed under the endoscopic vision and ureteral lesions were described according to the Post-Ureteroscopic Lesion Scale (PULS) to each ureter [15]. A double J stent 6F was inserted in all renal units. Procedures were accomplished using the less fluoroscopy possible with a low radiation dose [16]. Operative time was recorded from cystoscopy till the end of double J insertion for each renal unit. Patients were discharged on the same day and maintained with standardized oral analgesics and antibiotics until the removal of the double J stent on postoperative day (POD) 10.

Serum creatinine samples were collected on admission to surgery, immediate postoperative (IPO), on POD 3, 10, and 30. The estimated glomerular filtration rate (eGFR) was calculated using the chronic kidney disease epidemiology collaboration equation (CKD–EPI) without a race coefficient [17]. Changes in eGFR levels between preoperative and postoperative values were given as the percentage of change. Renal function deterioration was defined as 10%, 20% and 30% eGFR variation between preoperative and postoperative values on IPO, POD3, POD10 and POD30.

All patients were submitted to a POD 90 non-contrast CT scan for stone status evaluation by a senior radiologist. SFR was considered zero residual fragments on both kidneys on the CT scan. Complications were recorded using the Clavien–Dindo classification during follow-up [18].

Categorical data were reported as frequency and percentage and continuous data as mean and standard deviation. Statistical analysis was performed with Statistical Package for the Social Sciences SPSS®, version 23.0 (IBM Corp©, USA). Wilcoxon test was used to compare preoperative eGFR to postoperative values reported as median and interquartile range. Univariate and multivariate logistic regression was used to identify independent factors of renal function deterioration up to the follow-up of POD 30 after bilateral fURS. Mann Whitney test was used to identify preoperative CT stone features predictors for operative time ≥ 120 min. Statistical significance was considered as $p < 0.05$.

Results

Thirty patients underwent bilateral fURS and were included in our study. 18/30 (60.0%) and 3/30 (10.0%) of the patients presented preoperative eGFR > 90 mL/min/1.73 m^2 and eGFR < 60 mL/min/1.73 m^2, respectively. Clinical features of the patients that underwent bilateral fURS are shown in Table 1.

Table 2 Outcomes of bilateral fURS

Feature	Bilateral fURS (N = 30)
Operative time (mean ± SD), min	94.7 ± 40.0
Operative time ≥ 120 min, N (%)	7 (23.3)
Lasering time (mean ± SD), sec	530.0 ± 1114.2
Laser energy (mean ± SD), mJ	3924.0 ± 8068.9
Length of stay (mean ± SD), h	16.00 ± 15.9
Creatinine (mean ± SD), mg/dL	
IPO	1.2 ± 0.7
POD3	1.3 ± 0.8
POD10	1.1 ± 0.6
POD30	1.0 ± 0.5
eGFR (median [interquartile range]), mL/min/1.73 m^2	
IPO	79.6 [62.7–95.3]
POD3	81.6 [59.8–97.2]
POD10	91.8 [77.3–105.2]
POD30	96.1 [85.1–105.1]
Stone free rate, N (%)	
0 mm	16 (53.3)
0–2 mm	6 (20.0)
> 2 mm	8 (26.7)
PULS	
0	50 (83.3)
1	4 (6.7)
2	1 (1.7)
3	0 (0.00)
Clavien–Dindo	
0	18 (60.0)
I	9 (30.0)
II	1 (3.3)
IIIb	1 (3.3)
IVa	1 (3.3)
ER visits, N (%)	8 (26.7)

N Number; % percentage; *SD* standard deviation; *h* hours; *IPO* immediate postoperative; *POD* postoperative day; *PULS* post-ureteroscopic lesion scale; *ER* emergency room; *Kg* kilograms; *m* meter; *mg* miligrams; *dL* deciliter; *mL* mililiters; *min* minutes; *mm* milimeters; *eGFR* estimated glomerular filtration rate; *sec* seconds; *mJ* mili Joules

Compared to preoperative eGFR, patients presented the lowest eGFR at POD3. Immediate PO and POD3 eGFR were significantly lower than preoperative eGFR, whereas POD10 and POD30 were similar to preoperative eGFR. Median [interquartile range] preoperative eGFR 93.30 [82.6–105.2] mL/min/1.73 m^2 vs. IPO eGFR 79.6 [62.7–95.3] mL/min/1.73 m^2, $p < 0.001$; vs. POD3 eGFR 81.6 [59.8–97.2] mL/min/1.73 m^2, $p < 0.001$; vs. POD10 eGFR 91.8 [77.3–105.2] mL/min/1.73 m^2, $p = 0.092$; vs. POD30 eGFR 96.1 [85.1–105.1] mL/min/1.73 m^2, $p = 0.648$) are shown in Fig. 1. During follow-up, 22/30 (73.3%), 14/30 (46.7%), and 7/30 (23.3%) of the patients presented a decrease of > 10% eGFR, > 20% eGFR, and > 30% eGFR, respectively. According to postoperative day, at IPO, 17/30 (56.7%), 11/30 (36.7%) and 6/30 (20.0%) of the patients presented a decrease of > 10% eGFR, > 20% eGFR, and > 30% eGFR, respectively. At POD3, 21/30 (70.0%), 8/30 (26.7%) and 6/30 (20.0%) of the patients presented a decrease of > 10% eGFR, > 20% eGFR, and > 30% eGFR, respectively. At POD10, 9/30 (30.0%), 1/30 (3.3%) and 0/30 (0.0%) of the patients presented a decrease of > 10% eGFR, > 20% eGFR, and > 30% eGFR, respectively. At POD30, 2/30 (6.7%), 0/30 (0.0%) and 0/30 (0.0%) of the patients presented a decrease of > 10% eGFR, > 20% eGFR, and > 30% eGFR, respectively. Four patients (4/27, 14.8%) presented eGFR < 60 mL/min/1.73 m^2 at some moment during follow-up. SFR for combined right and left kidney was 53.3% and residual stone fragments ≤ 2 mm was 73.3%.

Complications were reported in 40.0% of the patients. Clavien–Dindo I and II were reported in 33.3% of the patients. Eight patients visited the ER during follow-up. Major complications occurred in only 6.6% (2/30) of the patients. The outcomes of bilateral fURS are shown in Table 2.

Univariate analysis of risk factors for acute renal function deterioration after bilateral fURS is depicted in Table 3. Multivariate analysis demonstrated that lower preoperative eGFR was a risk factor for eGFR < 60 mL/min/1.73 m^2, $p = 0.019$ [1.021–1.263; 1.136]; ASA > 1 was a risk factor for a decrease of eGFR > 10%, $p = 0.028$ [1.25–51.13; 8.00]; longer operative time was a risk factor for a decrease of eGFR > 20%, $p = 0.042$ [1.00–1.05; 1.028]; and operative time ≥ 120 min was a risk factor for a decrease of eGFR > 30%, $p = 0.026$ [0.016–0.773; 0.113]. We looked for preoperative CT stone features that could predict an operative time ≥ 120 min. The median stone size was the only predictor for operative time ≥ 120 min (40.1 [29.2–50.8] mm vs. 30.2 [21.8–38.2] mm, $p = 0.031$, while number of stones ($p = 0.179$), stone density ($p = 0.147$) and stone volume ($p = 0.159$) were not significant.

Discussion

This prospective study addressed perioperative renal function following bilateral fURS for kidney stones in patients with no previous urinary tract instrumentation. We demonstrated that renal function after bilateral fURS suffers a reversible decrease mainly on POD3. During follow-up, 46.7% and 23.3% of the patients experienced a decrease of > 20% of the eGFR and > 30% of the eGFR, respectively. More importantly, we found that lower preoperative eGFR, higher ASA classification, and longer operative time, particularly ≥ 120 min, are independent risk factors for an acute

Table 3 Univariate analysis of risk factors for acute eGFR decrease after bilateral fURS

Risk factor	eGFR < 60 mL/min/1.73 m^2	Decrease of eGFR > 10%; *p* value [95% CI; HR]	Decrease of eGFR > 20%; *p* value [95% CI; HR]	Decrease of eGFR > 30%; *p* value [95% CI; HR]
Age	0.502	0.238	0.361	0.840
Gender	0.368	0.201	0.431	0.368
BMI	0.235	0.545	0.279	0.529
BMI ≥ 30 kg/m^2	0.096	0.896	0.050 [0.013–1.243; 0.128]	0.096
ASA > 1	0.014 [1.364–3.204; 2.091]	0.018	0.232	0.481
CCI > 1	0.481	0.129	0.654	0.860
Preop eGFR	< 0.001 [1.021–1.263; 1.136]	0.049 [0.09–40.56; 2.75]	0.308	0.706
Stone volume	0.564	0.910	0.941	0.892
Stone density	0.145	0.653	0.276	0.419
OT	0.029 [0.948–1.1001; 0.974]	0.064	0.024 [1.00–1.06; 1.00]	0.088
OT ≥ 120 min	0.016 [0.016–0.773; 0.113]	0.068	0.001 [1.185–3.377; 2.00]	0.016 [0.985–1.055; 1.02]
Laser time	0.315	0.743	0.506	0.980
Laser Energy	0.339	0.725	0.467	0.922
LoS	0.063	0.839	0.528	0.130
ER visit	0.015 [0.172–7.469; 1.133]	0.276	0.976	0.483
SFR	0.526	0.825	0.732	0.818
Clavien–Dindo	0.418	0.604	0.523	0.119

N Number; % percentage; *SD* standard deviation; *Kg* kilograms; *m* meter; *mg* miligrams; *dL* deciliter; *mL* mililiters; *min* minutes; *mm* milimeters; *HU* Hounsfield unit; *ASA* American Society of Anesthesiology; *BMI* body mass index; *Preop* preoperative; *eGFR* estimated glomerular filtration rate; *CCI* Charlson comorbidity index; *OT* operative time; *LoS* length of stay; *ER* emergency room; *SFR* stone-free rate

decrease of renal function following bilateral fURS for kidney stones.

Although the clinical repercussion of a mild and temporary decrease in eGFR is debatable, it is important to recognize which patients are at risk for acute renal failure to avoid bilateral fURS or to do a careful monitorization of renal function on early postoperative period. Transitory renal function decrease may cause severe electrolyte imbalance leading to arrhythmias and central nervous system impairment. Göger et al. studied 827 patients that underwent unilateral fURS and found that 13.3% had acute kidney injury during postoperative period [7]. They demonstrated that stone size, operative time, postoperative urinary tract infection and diabetes mellitus are significant predictors of acute kidney injury following fURS [7]. Other authors also suggested that a reduction of operative time could prevent acute renal function decrease after fURS [19]. We found similar risk factors for acute decrease of renal function after bilateral fURS: lower preoperative eGFR, higher ASA classification and longer operative time. Moreover, stone size was a predictor for operative time ≥ 120 min. Therefore, those patients are not the best candidates for bilateral fURS.

Retrospective studies of bilateral fURS suggested that it is a safe procedure [20–28]. However, these studies did not collect serum creatinine samples of several days in the postoperative period but rather collected a single sample of creatinine weeks after bilateral fURS suggesting that renal function was unchanged in a long follow-up [22–26]. Some of the patients in these studies were prestented, which could reduce intrapelvic pressure and reduce the risk of acute renal function decrease [28]. None of the patients in our study was prestented and possibly they were more prone to suffer a decrease in postoperative eGFR. There is one other prospective study comparing preoperative to POD1 creatinine after bilateral fURS. The authors concluded that the level of creatinine did not change significantly [29]. However, we already demonstrated that the most significant rise in creatinine occurs at POD3, not on POD1 [5].

The overall complication rate of the present study is higher than other authors reported for unilateral procedures. A multicentre study showed that unilateral fURS has a complication rate of 15% [30]. The overall complication rate of bilateral fURS of the present study was 40.0%, including 30.0% Clavien grade I, 3.3% Clavien grade II, 3.3% Clavien grade IIIb, and 3.3% Clavien IVa. Major complications were reported on two out of 30 patients of our study. One patient presented at the ER on the POD13 with unilateral pain due to ureteral edema, underwent a double J insertion under general anesthesia and was categorized as Clavien–Dindo IIIb. Other patient who had struvite stones developed urosepsis caused by *Klebsiella sp* after bilateral fURS, was successfully treated in the intensive care unit with intravenous antibiotics and was categorized as Clavien–Dindo IVa. We were unaware of the struvite composition of the stone and the patient had a negative preoperative urine culture before the procedure. The higher complication rate of bilateral fURS should serve as a warning for a careful selection of patients.

This study has some limitations such as the small number of patients from a single center. However, this is a prospective study of symptomatic patients with bilateral kidney stones up to 20 mm on each side with no previous urinary tract instrumentation. Less experienced urologist should be alert to risk factors for acute renal function decrease after bilateral fURS in these particular patients. Our results should be confirmed by other prospective studies with a larger number of participants from different centers.

Conclusion

Renal function suffers a reversible decrease following bilateral fURS. Our study suggests that the adequate selection of patients and maintaining operative time < 120 min are relevant factors in preventing acute renal function deterioration after bilateral fURS.

Author contributions Alexandre Danilovic: protocol/project development; data collection; data analysis; manuscript writing. Caio Vinicius Suartz: data analysis; manuscript writing; Fabio Cesar Miranda Torricelli: data analysis; manuscript editing. Giovanni Scala Marchini: data analysis; manuscript editing. Carlos Batagello: Data analysis; manuscript editing. Fabio Carvalho Vicentini: data analysis; manuscript editing. William C. Nahas: protocol development; data analysis; manuscript editing. Eduardo Mazzucchi: protocol development; data analysis; manuscript editing.

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Data availability Supplementary data is available.

Declarations

Conflict of interest Alexandre Danilovic, Caio Vinicius Suartz, Fabio Cesar Miranda Torricelli, Giovanni Scala Marchini, Carlos Batagello, Fabio Carvalho Vicentini, William C. Nahas, Eduardo Mazzucchi: nothing to disclosure;

Ethical approval The institutional ethics committee approved the study protocol (IRB No. 11851) and written informed consent was obtained from all patients according to the 1964 Declaration of Helsinki Ethical Principles for Medical Research involving Human Subjects and its later amendments.

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