The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 5, 2025

FEASIBILITY AND OUTCOMES OF RETROGRADE INTRARENAL SURGERY AS A DAY CARE PROCEDURE: A SINGLE-CENTER RETROSPECTIVE STUDY

Assad Ur Rehman[1], Nadeem Bin Nusrat[2], Shujah Muhammad[3], Nauman Zafar[4], Asadullah Aslam[5], Sarmad Imtiaz[6], Hafiz Abdul Hanan[7], Ammar Asghar[8], Sharafat Ali[9], Saira Imtiaz [*10]

[1,3]*FCPS Urology, Consultant Urologist*
[2]*FRCS ED (Intercollegiate Specialty Board of Urology), CCST, Consultant Urologist*
[4]*MRCS Urology, Consultant Urologist*
[5]*MBBS, MRCSEd, MMSc, FRCSEd (Urol), FEBU, Consultant Urologist*
[6]*MS Urology, Consultant Urologist*
[7,8,9]*MBBS, Post Graduate Resident*
[*10]*Research Assistant/ Data Analyst, MPhil (Microbiology and Serology)*

[1]assad.rehman@pkli.org.pk, [2]nadeem.nusrat@pkli.org.pk, [3]shujah.muhammad@pkli.org.pk, [4]nauman.zafar@pkli.org.pk, [5]asadullah.aslam@pkli.org.pk, [6]sarmad8074@gmail.com, [7]abdul.hanan@pkli.org.pk, [8]ammar.asghar@pkli.org.pk, [9]sharafat.ali1@pkli.org.pk, [*10]saira.khan@pkli.org.pk

[3]0009-0002-4030-3316, [4]0009-0005-0950-4066, [5]0000-0003-3883-0846, [*10]0000-0003-1197-7565

DOI: https://doi.org/10.5281/zenodo.15597884

Keywords
Retrograde Intrarenal Surgery, Day Care Surgery, Kidney Stones, Feasibility, Stone Clearance, Same-Day Discharge.

Article History
Received on 23 April 2025
Accepted on 23 May 2025
Published on 31 May 2025

Corresponding Author: * Saira Imtiaz

Abstract

Objectives: *To evaluate the feasibility, safety, and effectiveness of retrograde intrarenal surgery (RIRS) as a day care procedure, focusing on perioperative complications, stone clearance rates, and factors influencing same-day discharge.*

Methods: *A retrospective, single-center study conducted from September 2018 to September 2024 included 260 patients aged 18+ who underwent RIRS with planned same-day discharge. The outcomes analyzed included discharge success, perioperative complications, and stone clearance. Demographics, clinical parameters, and surgical details were compared between feasible and non-feasible groups using statistical tests.*

Results: *Day care surgery was feasible in 189 (72.7%) patients, while 71 (27.3%) required extended care. The feasible group had significantly lower BMI (22.00 ± 5.0 vs. 24.00 ± 5.0, $p = 0.018$), smaller stones (1.25 ± 0.6 cm vs. 1.50 ± 1.0 cm, $p = 0.027$), lower pre-operative creatinine (0.90 ± 0.2 vs. 1.00 ± 0.5 mg/dL, $p < 0.001$), and lower hematocrit (35.80 ± 5.10% vs. 38.09 ± 5.87%, $p = 0.002$). Logistic regression identified larger stone size (OR = 2.521, $p = 0.004$), male gender (OR = 2.595, $p = 0.023$), and UTIs as significant predictors of feasibility. Post-operative complications were lower in the feasible group (99.5% vs. 54.9%, $p < 0.001$).*

Conclusion: *RIRS is a feasible and safe day care procedure for selected patients, with high success rates, minimal complications, and effective stone clearance, offering a viable alternative to traditional hospitalization.*

INTRODUCTION

RIRS is an approach to management of renal stone with minimal invasive methods, hence considered in settings where ESWL or PCNL is unsuitable [1,3]. Conventionally, RIRS requires postoperative admission in the hospital due to potential complications and reversal of anesthesia post-procedure [4-7]. However, recent advancements in surgical techniques, anesthesia, and patient management have made it feasible to perform RIRS as a day care procedure, potentially reducing the burden on healthcare resources and allowing patients to return home on the same day [8].

Day care surgery has been of great interest in urological procedures, promoting earlier discharge, reduced healthcare costs, and higher patient satisfaction. It is particularly attractive in facilities with limited hospital resources or where the length of stay for patients is a concern [9]. To ensure that RIRS can be done as a day care procedure, several factors have to be considered, such as patient selection, feasibility of same-day discharge, and potential perioperative complications [10,11].

Previous work has been done on the safety and efficacy of RIRS in the management of renal stone [12-14], though to our best knowledge, not much published work is available for its use in the day care setting [15]. Factors that influence the success rate of same-day discharge are size of stones, comorbidities, and UTI [15-17]. There are further researches needed to decide on the suitability of candidates with potential probable benefit. Such drawbacks involved may be infections and bleeding or missed stone clearance under overnight monitoring only.

This study aims to assess the feasibility and outcomes of RIRS as a day care procedure at the Pakistan Kidney and Liver Institute and Research Center (PKLI & RC), Lahore. The study evaluates perioperative complications, stone clearance rates, and factors influencing patient selection for day care discharge to contribute valuable insights into the clinical applicability and safety of RIRS as an outpatient procedure.

Methods

Study Design and Setting

This is a retrospective observational study conducted at the Pakistan Kidney and Liver Institute and Research Center, Lahore, Pakistan. Ethical approval has been obtained from the Institutional Review Board [PKLI-IRB/AP/00542024]. Data collection would be from September 2018 to August 2024. Informed consent was waived because the study is of a retrospective type.

Patient Selection

A total of 260 patients who underwent retrograde intrarenal surgery (RIRS) were included in the study.

Inclusion Criteria:

- Patients aged 18 years and above underwent RIRS for renal stones.
- Patients planned for same-day discharge.
- Patients with complete medical records.

Exclusion Criteria:

- Patients requiring extended hospitalization due to complications.
- Patients with incomplete medical records.

Sampling and Data Collection

Convenience sampling was employed based on the availability of medical records. All patients meeting the inclusion criteria and undergoing RIRS during the study period were included. Data were extracted from electronic medical records and surgical logs by trained postgraduate residents (PGRs) and entered into a secure, password-protected database.

Surgical Procedure

RIRS was performed under general anesthesia. A disposable OTU trademark flexible ureteroscope was introduced via a Fr re-access ureteric sheath to navigate the renal collecting system. Laser lithotripsy for stone fragmentation was conducted using a Quanta 30 Watt laser system.

Postoperative Follow-Up

Postoperative follow-up included monitoring complications within 24 hours and assessing stone clearance using follow-up imaging.

Outcomes Measured

The primary outcomes of interest were:

- **Feasibility of RIRS as a daycare procedure:** Measured by the proportion of patients successfully discharged on the same day.
- **Perioperative complication rates:** Incidence of complications within 24 hours post-procedure.
- **Stone clearance rates:** Determined by the absence of residual stones on follow-up imaging.

Surgeon Details

All procedures were performed by surgeons experienced in RIRS.

Statistical Analysis

Data variables included:

- **Demographic data:** Age, gender, body mass index (BMI).
- **Preoperative clinical data:** Stone size, location, and associated comorbidities.
- **Operative data:** Operative time, intraoperative complications.
- **Postoperative data:** Complications, stone clearance rates, discharge timing.

Descriptive statistics summarized patient demographics and clinical characteristics. The feasibility of RIRS as a daycare procedure was evaluated by calculating the proportion of patients discharged on the same day. Perioperative complications and stone clearance rates were analyzed using chi-square tests for categorical variables and t-tests for continuous variables. Multivariate analysis identified factors influencing the feasibility of daycare RIRS. All statistical analyses were performed using SPSS software, version 27. Statistical significance was set at a p-value < 0.05.

Results

Of the 260 patients included in the study, 143 (55.0%) were male and 117 (45.0%) were female. Day-care surgery was deemed feasible in 189 (72.7%) cases, whereas in 71 (27.3%) cases, it was not. Independent T-tests comparing patients feasible and not feasible for day care surgery highlighted differences in clinical parameters. Although the average age was slightly lower in the feasible group (FG), the difference was not statistically significant. Pre-operative hemoglobin levels were also lower in FG but did not reach significance. In contrast, pre-operative hematocrit levels were significantly lower in FG, suggesting its potential impact on day care surgery feasibility. Post-operative hemoglobin differences were not significant. These findings underscore the importance of pre-operative hematocrit in patient selection for day care surgery. Mann-Whitney U tests revealed significant differences in clinical parameters affecting day care surgery feasibility. BMI and stone size distributions differed significantly between feasible and non-feasible groups (NFG), rejecting the null hypothesis. Similarly, higher pre-operative creatinine levels were associated with non-feasibility. In contrast, the number of previous stone episodes and pre-operative WBC counts showed no significant differences, retaining the null hypothesis, suggesting minimal impact on surgery feasibility.

Comparison of clinical and operative parameters between patients feasible and not feasible for day-care retrograde intrarenal surgery (RIRS), highlighting differences in BMI, stone size, pre-operative creatinine, and hematocrit shown in **Table 1.**

Table 1: Baseline Clinical and Operative Parameters of Patients Undergoing Day-Care RIRS

Clinical Parameters	Feasible as Day Care Mean ± SD	Not Feasible as Day Care Mean ± SD	P Value
Patient Age	44.75 ± 14.71	45.23 ± 16.70	0.822*
Body Mass Index	22.00 (5)	24.00 (5)	0.018**
Stone Episodes Experienced	1.00 (1)	1.00 (1)	0.642**
Size of Stone in Centimeters	1.25 (0.6)	1.50 (1.0)	0.027**
Pre-operative WBC	8.00 (2.5)	8.50 (2.7)	0.064**
Pre-operative Creatinine	0.90 (0.2)	1.00 (0.5)	< 0.001**
Pre-operative Hemoglobin	12.03 ± 1.76	12.39 ± 1.81	0.148*
Pre-operative Hematocrit	35.80 ± 5.10	38.09 ± 5.87	0.002*
Post-operative Hemoglobin	11.68 ± 2.02	12.08 ± 2.08	0.165*

T-tests: Mean ± SD *
Mann-Whitney U tests: (Median (IQR)) **

For operative time, the FG had a shorter median duration of 75 minutes (IQR = 45), compared to 90 minutes (IQR = 55) in the NFG. Similarly, laser time was reduced in the FG, with a median of 55 minutes (IQR = 41) versus 70 minutes (IQR = 55) in the NFG. Post-operative hematocrit levels were lower in the FG, with a median of 34% (IQR = 6.0) compared to 37% (IQR = 8.0) in the NFG. Post-operative creatinine levels also differed, with a median of 0.9 mg/dL (IQR = 0.2) in the FG, slightly lower than the 1.0 mg/dL (IQR = 0.5) in the NFG. It had lower postoperative WBC counts, with a median of 8.3 x10^3/uL (IQR = 2.2) versus 12 x10^3/uL (IQR = 7.0) in the NFG. Postoperative stay was also significantly shorter in the FG with a median of 24 hours (IQR = 4) as compared to 33 hours (IQR = 21) in the NFG. The residual fragment size was also smaller in the FG, at a median of 0 mm (IQR = 3) compared with the NFG, at a median of 0 mm (IQR = 6). DJ stent and Foley's catheter sizes did not differ between groups, with a median size of 6 Fr for DJ stent and 16 Fr for Foley's catheter. The pain analogue score was also equivalent between groups with a median of 2, IQR = 1. Timing for DJ stent removal was shorter in the FG at a median of 17 days, IQR = 16 compared to 28 days, IQR = 12 in the NFG.

Additionally, Foley's catheter removal occurred on day 0 (IQR = 1) in the FG, while it was removed on day 1 (IQR = 1) in the NFG.

The analysis of various factors influencing the feasibility of day care surgery revealed notable differences between the feasible and NFG. Gender distribution showed a higher proportion of males (72.7%) in the FG compared to females (27.3%), with a p-value of 0.052, indicating a trend towards significance. Body Mass Index (BMI) categories significantly impacted feasibility, with 72.7% of patients in the FG categorized as having healthy BMI compared to those in the NFG, which demonstrated a strong association (p = 0.001).

Additionally, the presence of urinary tract infections was a significant factor, with 88.4% of the FG reporting no infections, compared to only 63.4% in the NFG (p < 0.001). Regarding stone clearance, 83.1% of patients in the FG achieved complete clearance, whereas the NFG had 73.2% achieving this outcome, although this did not reach statistical significance (p = 0.075). Finally, complications were significantly lower in the FG, with 99.5% reporting no complications immediately following the procedure compared to 54.9% in the NFG (p < 0.001). These findings suggest that gender, BMI, urinary tract infections, and complications are critical factors affecting the feasibility of day care surgery. Analysis of categorical variables such as gender, BMI categories, urinary tract infections, stone clearance rates, and post-operative complications among feasible and not feasible for day-care RIRS presented in Table 2.

Table 2: Distribution of Key Factors Affecting Feasibility of Day-Care RIRS

Variable	Feasible as Day Care N (%)	Not Feasible as Day Care N (%)	p-value
Gender	189 (72.7%)	71 (27.3%)	0.052
BMI Categories	189 (72.7%)	71 (27.3%)	0.001
Urinary Tract Infections	167 (88.4%)	45 (63.4%)	<0.001
Stone Clearance	157 (83.1%)	52 (73.2%)	0.075
Complications	188 (99.5%)	39 (54.9%)	<0.001

The logistic regression analysis evaluated factors influencing the feasibility of day-care surgery for patients undergoing stone removal. The final model exhibited a strong predictive capability, with an overall accuracy of 84.2%. The presence of UTIs significantly reduced the odds of feasibility (B = -1.445, p = 0.001, Exp(B) = 0.236, 95% CI: 0.106 – 0.524), suggesting that patients without UTIs were more likely to undergo day-care surgery successfully. A larger stone size positively correlated with infeasibility, with each additional centimeter of stone size increasing the odds of infeasibility (B = 0.925, p = 0.004, Exp(B) = 2.521, 95% CI: 1.345 – 4.725).Male patients demonstrated higher odds of feasibility compared to female patients (B = 0.954, p = 0.023, Exp(B) = 2.595, 95% CI: 1.143 – 5.894), indicating

that gender may play a role in the likelihood of successful day-care surgery. These findings highlight that the presence of UTIs significantly hinder the feasibility of day-care surgery. Stone sizes also showed a meaningful association, which may reflect technical challenges related to the procedure. Gender (male) appears to positively influence feasibility, potentially due to anatomical or physiological factors. These predictors call for these to be considered when assessing patients' suitability for day-care surgery and emphasize management of pre-existing UTIs. Evaluation of factors including urinary tract infection, stone size, gender, and BMI category, and respective odds ratios of predicting the feasibility of day-care retrograde intrarenal surgery shown in Table 3.

Table 3: Logistic Regression Analyses on Feasibility of Day-Care RIRS Predictors

Predictor	Odds Ratio (Exp(B))	p-value
Urinary Tract Infections	0.236	0.001
Stone Size (cm)	2.521	0.004
Gender (Male)	2.595	0.023
BMI Category	1.982	0.056

Discussion

The results of our study demonstrate that retrograde intrarenal surgery (RIRS) is a viable and efficient approach for managing renal stones in a day-care setting. A significant finding is the notably shorter post-operative stay in the feasible group (FG), with a median of 24 hours, compared to 33 hours in the non-feasible group (NFG). This is in agreement with Resorlu et al., who pointed out that in the RIRS group, hospital stay was the shortest, 1.3 ± 0.5 days, which in fact was shorter than any of the other patient groups (Resorlu et al., 2013) [16]. Sari et al. reported that hospital stay time in the RIRS group was also significantly short, and thus this might be indeed a minimally invasive and efficient procedure in the management of renal stones (Sari et al., 2017) [17]. Reduced recovery time in the FG implies that RIRS may help to decrease patient burden and health costs and hence, this makes it appropriate for day-care surgery.

In terms of operative efficiency, our results are in agreement with Sari et al., who reported that the mean operative and fluoroscopy times were significantly longer in the PNL group compared to the RIRS group (Sari et al., 2017) [17]. This is further enhanced by Cakiroglu et al., who noted that the mean duration of hospitalization was 1.27 ± 0.5 days in their study of RIRS for calyceal diverticula stones, thus showing short procedural and recovery times associated with RIRS (Cakiroglu et al., 2024) [18]. These findings show that RIRS not only reduces the hospital stay but also decreases the procedural time; therefore, it is a more efficient option compared to PNL, especially for patients who need quick recovery.

Our study also corresponds to the clinical outcomes of Resorlu et al. and Sari et al., demonstrating a higher stone-free rate and a lower complication rate in the RIRS group in comparison with the other groups. Resorlu et al. reported that the need for ancillary procedures was lower in RIRS group 8.7% compared with PNL 5.7%, and complication rate for RIRS was 10.9%, which was significantly lower compared to PNL 22.1% [16]. Furthermore, according to Sari et al., the stone-free rate after the first procedure was less in the RIRS group at 73.5% as compared with the PNL group at 93.3%. However, the complication rate in the RIRS group was nearly nil, and the percentage of major complications, such as Clavien III-V, was nil (Sari et al., 2017) [17].

However, it should be noted that our study has several limitations. Being a retrospective analysis, it is prone to selection bias because patients were not randomized to treatment groups. In addition, the variations in surgical techniques between different surgeons may have influenced the outcomes, despite all surgeons being experienced in performing RIRS. These limitations are in line with those identified in the study by Pokrzywa et al., which underscored the need for preoperative management, such as the diagnosis and treatment of UTIs, which may impact postoperative complications and outcomes (Pokrzywa et al., 2016) [19]. Future prospective, multicenter studies with standardized protocols are needed to confirm these findings and refine the patient selection criteria for day-care RIRS.

RIRS is a feasible and safe day care procedure for selected patients, with high success rates, minimal complications, and effective stone clearance, offering a viable alternative to traditional hospitalization.

Disclosure

- **Conflict of Interest:** No conflict of interest was declared by the authors.

- **Approval of the Research Protocol:** The present study protocol was reviewed and approved by the Institutional Review Board of Pakistan Kidney and Liver Institute and Research Center – Lahore – Pakistan, approval number: [PKLI-IRB/AP/00542024].
- **Informed Consent:** Not applicable (Informed consent was waived due to the retrospective nature of the study).
- **Registry and Registration Number:** Not applicable.
- **Animal Studies:** Not applicable.
- **Ethical Statement**

This study was approved by the institutional review board (IRB) of Pakistan Kidney and Liver Institute & Research Center, Lahore, Pakistan. As a retrospective study, patient consent was not required; however, confidentiality and privacy of patient data were strictly maintained throughout the study.

Author Contributions

Conceptualization, study design, supervision of data collection, and critical review of the final draft	AUR, NBN, SM, NZ, AA, SI
Literature review, coordination of data collection and management, and critical revisions to the manuscript	AA, SA, AH
Statistical analysis, interpretation of results, critical revisions, and finalization of the manuscript	SI

REFERENCES

1. Gauhar V, Chew BH, Traxer O, Tailly T, Emiliani E, Inoue T, et al. Indications, preferences, global practice patterns and outcomes in retrograde intrarenal surgery (RIRS) for renal stones in adults: results from a multicenter database of 6669 patients of the global FLEXible ureteroscopy Outcomes Registry (FLEXOR). World J Urol. 2023 Feb;41(2):567-574. doi: 10.1007/s00345-022-04257-z. Epub 2022 Dec 19. PMID: 36536170.
2. Ong WLK, Somani BK, Fong KY, Teoh JY, Sarica K, Chai CA, et al. Retrograde intrarenal surgery for asymptomatic incidental renal stones: a retrospective, real-world data analysis. BJU Int. 2024 Aug;134(2):201-206. doi: 10.1111/bju.16292. Epub 2024 Feb 11. PMID: 38343138.
3. Jayaprakash SP, Thangarasu M, Jain N, Bafna S, Paul R. In situ management of large upper ureteric calculus by mini-percutaneous nephrolithotomy in the era of retrograde intrarenal surgery. Res Rep Urol. 2020 Dec 10;12:633-638. doi: 10.2147/RRU.S280454. PMID: 33330143; PMCID: PMC7735938.
4. Rajinder Y, Anurag P, Pravesh G. Role of retrograde intrarenal surgery in management of renal stones: 3 years experience. Ann Urol Nephrol. 2019;1(3):1-5. doi: 10.33552/AUN.2020.01.000514.
5. Gauhar V, Chew BH, Traxer O, Tailly T, Emiliani E, Inoue T, et al. Indications, preferences, global practice patterns and outcomes in retrograde intrarenal surgery (RIRS) for renal stones in adults: results from a multicenter database of 6669 patients of the global FLEXible ureteroscopy Outcomes Registry (FLEXOR). World J Urol. 2023 Feb;41(2):567-74. doi: 10.1007/s00345-022-04257-z.
6. Inoue T, Okada S, Hamamoto S, Fujisawa M. Retrograde intrarenal surgery: past, present, and future. Investig Clin Urol. 2021;62(2):121-135. doi: 10.4111/icu.20200526.

7. Giulioni C, Fuligni D, Brocca C, Ragoori D, Chew BH, Emiliani E, et al. Evaluating the safety of retrograde intrarenal surgery (RIRS): intra-and early postoperative complications in patients enrolled in the global multicentre flexible ureteroscopy outcome registry (FLEXOR). Int Braz J Urol. 2024 Aug 2;50:459-69. doi: 10.1590/S1677-5538.IBJU.2024.0055.
8. Yildiz AK, Bayraktar A, Kacan T, et al. A new protocol for renal collecting system sterilization with antibiotic irrigation during lithotripsy in retrograde intrarenal surgery: a prospective, comparative study. World J Urol. 2024;42:229. doi: 10.1007/s00345-024-04903-8.
9. Ojo EO. Day case surgery and developing countries—a review. Niger J Clin Pract. 2010;13(4). Available from: https://www.ajol.info/index.php/njcp/article/view/64172.
10. Aboutorabi A, Ghiasipour M, Rezapour A, Azar F, Yousefzadeh N, Shokuh M, et al. A cost-minimization analysis of day-care versus in-patient surgery for five most common general surgical procedures. J Health Policy Sustain Health. 2014;1:33-36.
11. Vaishnani B, Khokhar R, Chauhan M. A prospective study of 100 cases of day care surgery in inguinal hernia. Int Surg J. 2021;8(9):2685-9. doi: 10.18203/2349-2902.isj20213596.
12. Giulioni C, Castellani D, Somani BK, et al. The efficacy of retrograde intra-renal surgery (RIRS) for lower pole stones: results from 2946 patients. World J Urol. 2023;41(5):1407-13. doi: 10.1007/s00345-023-04363-6.
13. Akgül M, Çakır H, Çinar Ö. The efficacy and safety of retrograde intrarenal surgery: a multi-center experience of the RIRSearch Group Study. J Urol Surg. 2023;10(2):119-28. doi: 10.4274/jus.galenos.2023.2022.0039.
14. Zhang Z, Zhou L, Cheng Z, Zhang X. Enhancing lithotripsy efficiency in retrograde intrarenal surgery via a flexible kidney-fixed position: findings from a prospective cohort study. Urolithiasis. 2025 Dec;53(1):1-6. doi: 10.1007/s00240-024-01690-0.
15. Park J, Kang M, Jeong CW, Oh S, Lee JW, Lee SB, et al. External validation and evaluation of reliability and validity of the modified Seoul National University Renal Stone Complexity Scoring System to predict stone-free status after retrograde intrarenal surgery. J Endourol. 2015 Aug;29(8):888-93. doi: 10.1089/end.2014.0901.
16. Resorlu B, Unsal A, Ziypak T, Diri A, Atis G, Guven S, et al. Comparison of retrograde intrarenal surgery, shockwave lithotripsy, and percutaneous nephrolithotomy for treatment of medium-sized radiolucent renal stones. World J Urol. 2013 Dec;31(6):1581-6. doi: 10.1007/s00345-012-0991-1.
17. Sari S, Ozok HU, Cakici MC, Ozdemir H, Bas O, Karakoyunlu N, Sagnak L, Senturk AB, Ersoy H. A comparison of retrograde intrarenal surgery and percutaneous nephrolithotomy for management of renal stones ≥2 cm. Urol J. 2017 Jan 18;14(1):2949-2954. PMID: 28116738.
18. Cakiroglu B, Tas T, Aksoy SH, Arda E. Could retrograde intrarenal surgery be used as an efficient technique in the treatment of calyceal diverticula stones? J Coll Physicians Surg Pak. 2024;34(12):623. doi:10.29271/jcpsp.2022.05.623.
19. Pokrzywa CJ, Papageorge CM, Kennedy GD. Preoperative urinary tract infection increases postoperative morbidity. J Surg Res. 2016 Sep;205(1):213-20. doi: 10.1016/j.jss.2016.06.025. Epub 2016 Jun 16. PMID: 27621022; PMCID: PMC6475898.