

# Retrograde intrarenal surgery with central neuraxial blockade versus general anesthesia: A systematic review and meta-analysis

## ABSTRACT

**Objective:** The aim of the article is to assess the impact of retrograde intrarenal surgery under central neuraxial blockade in comparison to general anesthesia (GA).

**Material and Methodology:** This systematic review was conducted following the guidelines set out by the preferred reporting items for systematic reviews and meta-analyses. We conducted a comprehensive search across major electronic databases, including various types of studies such as descriptive studies and full-text literature, all of which were incorporated into the current review from 2018 to 2023. We involved those studies, which included the comparative study of spinal anesthesia (SA), epidural anesthesia (EA), and combined spinal epidural anesthesia with GA.

**Result:** In our meta-analysis of 12 studies, it was found that anesthesia technique significantly affected operation time, with neuraxial anesthesia (NA) showing a mean difference of  $-2.28$  (95% confidence interval (CI):  $-3.5$  to  $-1.04$ ,  $P = 0.003$ ) compared to GA. However, there were no significant differences in rates of stone clearance, 24-h pain scores and length of hospital stay among patients administered with NA or GA for retrograde intrarenal surgery (RIRS).

**Conclusion:** On the basis of the outcomes of study, NA can serve as a viable alternative to GA for RIRS. Our analysis reveals no significant differences in rates of stone clearance, operation duration, 24-h pain scores, complication rates, and length of hospital stay between NA in addition to GA in the context of RIRS. This suggests that given the potential economic advantages, NA might be a preferable choice over GA, contingent on patient preferences, baseline characteristics, and stone burden.

**Key words:** General anesthesia, neuraxial anesthesia, retrograde intrarenal surgery

## Introduction

Renal stones are a public health issue with a rising number of cases.<sup>[1]</sup> Within the field of urology, minimally invasive technologies have emerged, including extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy (PCNL) as well as retrograde intrarenal surgery (RIRS), which have become primary

treatment modalities for renal stones. Among these options, RIRS is particularly suggested as a substitute approach for renal stones measuring less than 2 cm, as per the guidelines set forth by the European Association of Urology (EAU).<sup>[2]</sup> Because of its capacity to access renal stones through the normal tract (urethra

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as well as ureter), RIRS results in less injury as compared to PCNL. Due to its high effectiveness as well as reduced complication rates, RIRS is regarded by some urologists as a suitable option for day-care surgery.<sup>[3-7]</sup> As instrumentation and techniques have evolved, RIRS has emerged as an established minimally invasive procedure, characterized by rapid recovery, short hospital stays, and low complication rates.<sup>[8-11]</sup>

Renal function irregularities or perioperative renal dysfunction resulting from anesthesia may manifest in patients who initially exhibit normal renal function. A prior study found that renal dysfunction could develop in patients with normal preoperative renal function.<sup>[12]</sup> The likelihood of these complications is linked to the surgical procedure, baseline renal function, underlying medical conditions, and intraoperative bleeding. Spinal anesthesia (SA) might offer an advantage over general anesthesia (GA) in terms of kidney function by avoiding the potential toxic impact of muscle relaxants, opioids, and inhalational anesthetics.<sup>[13]</sup> Nevertheless, it is worth noting that high-grade complications are still possible,<sup>[14]</sup> often associated with the use of GA. In this perspective, the adoption of SA may offer a pathway to reduce invasiveness, costs, and hospitalization duration.

Moreover, the utilization of GA results in increased expenses due to the use of specific medications and equipment. Recent research has concentrated on examining the viability as well as safety of RIRS under RA and has consistently found that RA offers comparable effectiveness and safety to GA.<sup>[15,16]</sup> Nonetheless, a consensus is yet to be reached on this contentious matter. RIRS could potentially elevate the risk of electrolyte imbalances as a result of the absorption of irrigation fluid as well as GA has boundaries in promptly detecting such electrolyte irregularities. Nevertheless, there is a scarcity of prior research comparing different anesthesia approaches concerning their impact on renal function.<sup>[15,17,18]</sup> Therefore, the present study shed light on the RIRS with central neuraxial blockade versus GA.

## Methodology

This systematic review adheres to the guidelines outlined by the preferred reporting items for systematic reviews and meta-analyses. A comprehensive procedure accompanies this review, offering comprehensive insights into the study. We conducted the literature search on electronic databases such as Scopus Google Scholar, Web of Science, PubMed, and the Cochrane Library from 2018 to 2023. The combination of related keywords in the following search terms such as “retrograde intra renal surgery,” “central neuraxial blockade,” “general anesthesia,” and “regional anesthesia” were used with limitation to publications in English. It is important

to notice that the search syntax was customized for each database based on their unique requirements instructions. The initial assessment of the primary search results involved a scrutiny of titles as well as abstracts to recognize citations necessitating full-text study. Subsequently, the full texts of the articles were independently reviewed by two evaluators, guided by predetermined inclusion as well as exclusion criteria. Any discrepancies were resolved by consulting a third reviewer. Additionally, we conducted a reference check of the comprised studies as well as previous reviews pertaining to the subject to uncover any supplementary studies. Several eligibility factors, including inclusion and exclusion criteria, were taken into consideration when doing the study selection.

### Inclusion criteria

1. Comparative study of SA, epidural anesthesia (EA), combined spinal epidural anesthesia (CSEA) with GA.
2. Adults, aged over 18 years, who have been diagnosed with urolithiasis and are undergoing RIRS.
3. Results include rates of being free of stones, operation duration, pain levels, and complications.
4. Studies available in the English language.

### Exclusion criteria

1. Studies that do not report important results.
2. Noncomparing studies.
3. Only abstract published studies.
4. Studies not published in the English language.
5. Insufficient studies.

### Statistical analysis

In this study, risk of bias assessment was conducted using RevMan 5.4.1 in accordance with the Cochrane Review guidelines (Higgins 2011).<sup>[19]</sup> The tool assesses six specific domains, each accompanied by “risk of bias” tables. Each study entry commences with a description of the research events. Subsequently, the tool assigns a judgment of bias risk to the entry: categorizing it as low risk, unclear risk, or high risk.

## Result

The initial search yielded 1,295 articles, which were identified through database searches and registrations. After this preliminary search, we excluded a total of 579 duplicate or triplicate articles. After screening an additional 733 records, we excluded 696 articles due to missing parameters in the articles, incompleteness, and lack of comparativeness. Studies that did not meet the inclusion and exclusion criteria were eliminated. We assessed 37 full articles for the study, and some of these articles contained only abstracts. Additionally, some literature was not available in the English language. Consequently, articles were removed for these

various reasons. Following a thorough analysis of all the available data, we selected 12 studies based on the inclusion criteria, as shown in Figure 1. Consequently, our analysis incorporates a total of 12 studies. The articles ranged in date from 2018 to 2023 [Figure 1, Table 1].

**Short keys:** RCT: randomized control trial; M: male; F: female; CT: computed tomography; USG: ultrasonography; NS: not

stated; R: right L: left; KUB: kidney, ureter, and bladder radiograph; RA: regional anesthesia.

In the analysis of 11 studies focusing on operation time, a statistically significant difference was observed when comparing different anesthesia techniques (mean difference:  $-2.28$ , 95% confidence interval [CI]:  $-3.5$  to  $-1.04$ ,  $I^2 = 51\%$ ,  $P = 0.003$ ) [Figure 2].

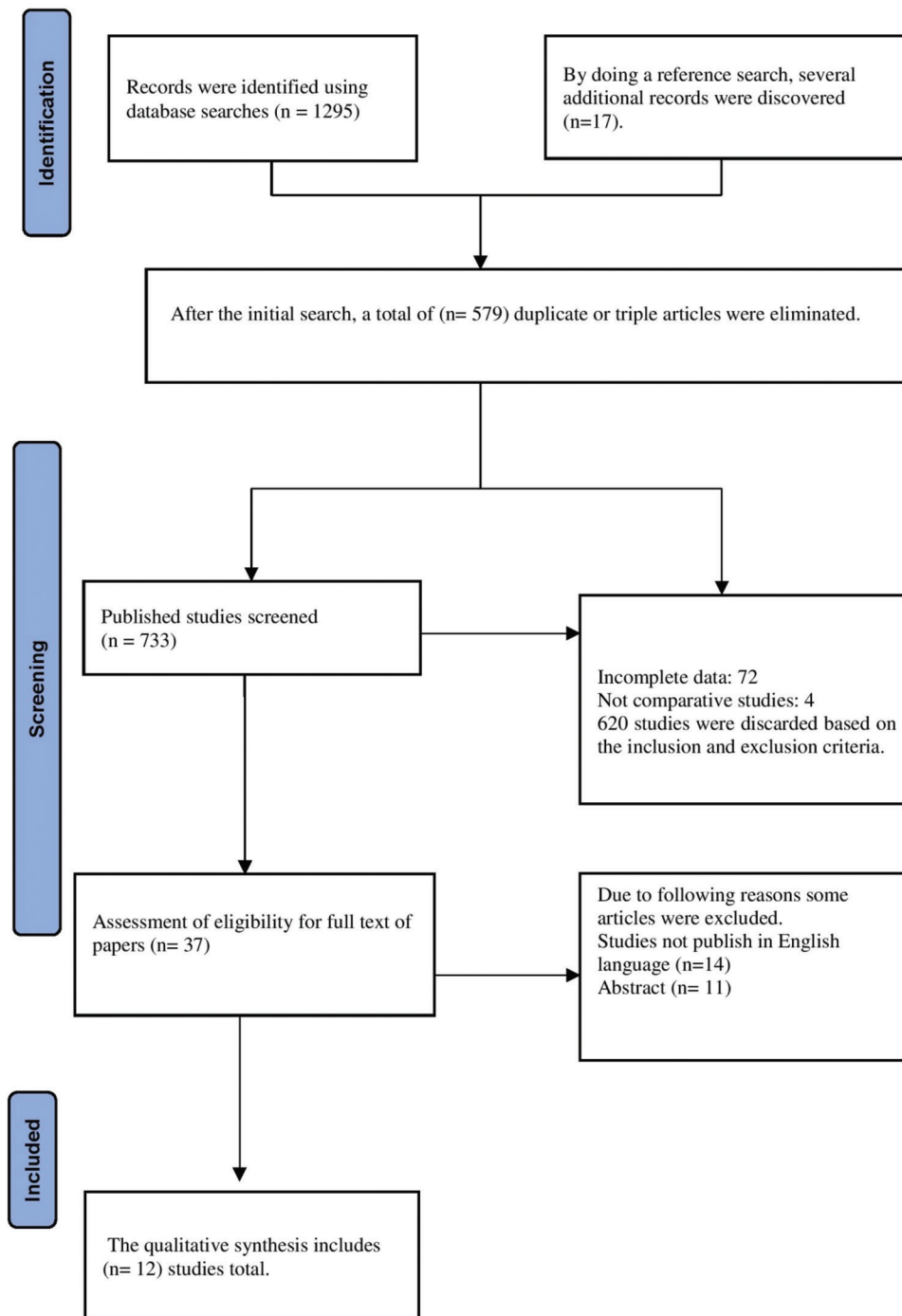


Figure 1: The study assortment criteria for systematic review

**Table 1: Characteristics of the included studies regarding renal surgeries**

| Author/Year                             | Study design | Total patients | Anesthesia groups | Mean age                            | Mean BMI (kg/m <sup>2</sup> )      | Mean stone size (mm)           | Stone density                             | Side of stone (R/L)     | Duration of follow-up (months) | Follow-up in radiograph | Outcomes  |
|---|--------------|----------------|-------------------|-------------------------------------|------------------------------------|--------------------------------|---|-------------------------|--------------------------------|-------------------------|---|
| Karabulut et al. (2018) <sup>[18]</sup> | RCT          | 40             | SA<br>GA          | NS<br>NS                            | NS<br>NS                           | NS<br>NS                       | NS<br>NS                                  | NS<br>NS                | 1                              | KUB, USG, CT            | RIRS performed under spinal anesthesia is as effective as when done under general anesthesia, with the choice dependent on patient-specific factors and preferences   |
| Bosio et al. (2018) <sup>[15]</sup>     | RC           | 139<br>47      | SA<br>GA          | 52±14.8<br>48.7±12.8                | NS<br>NS                           | 14±6<br>14±4.9                 | NS<br>NS                                  | NS<br>NS                | 0.5                            | KUB and USG             | RIRS under SA appears to be a viable and efficient option for treating renal stones in day surgery settings   |
| Baran et al. (2019) <sup>[16]</sup>     | RCT          | 697<br>664     | SA<br>GA          | 47±14.2<br>48.4±14                  | 26.5±4.3<br>27.1±4.5               | 17.6±5.9<br>17.2±6             | 779.9±175.9<br>764±164.9                  | NS<br>NS                | 1                              | CT                      | RIRS can be safely performed under either spinal or general anesthesia, and its success under spinal anesthesia is independent of the surgeon, making it a viable alternative to general anesthesia                   |
| Çakici et al. (2019) <sup>[20]</sup>    | RCT          | 45<br>50       | CSEA<br>GA        | 46.7±14.6<br>42.8±11.4              | 26.8±3.8<br>25.4±3.2               | 16.1±5.3<br>13.9±7             | 764±164.9<br>835.6±189.1                  | 23/22<br>27/23          | 1-3                            | CT                      | The utilization of combined spinal-epidural anesthesia, known for its positive intraoperative and postoperative results, is poised to emerge as a viable alternative to general anesthesia                            |
| Kwon (2019) <sup>[21]</sup>             | RCT          | 31<br>39       | SA<br>GA          | 54.7±14<br>54.1±14.5                | 25±3.7<br>24.7±2.7                 | 12±3.4<br>11.3±3.3             | 961.1±354.4<br>937±294.2                  | 15/16<br>15/24          | 2-3                            | KUB or CT               | RIRS with spinal anesthesia improves renal function at 3 months, reduces pain on the first morning. Operator performance initially weaker but enhances with sedation. Lower pain score on the first postoperative day |
| Oztekin et al. (2020) <sup>[22]</sup>   | RCT          | 35<br>35<br>35 | EA<br>SA<br>GA    | 47.3±14.8<br>45.8±15.4<br>44.9±14.6 | 23.3±7.1<br>37.4±61.5<br>33.4±22.9 | 11.8±2.9<br>12.7±3.6<br>13±3.8 | 854.6±384.2<br>1035.8±371.8<br>1116±294.9 | 17/18<br>20/15<br>20/15 | 1                              | CT                      | GA may be advisable to reduce manipulations for successful initial ureteral access and to expedite the stone retrieval process, provided there are no contraindications   |
| Pelit et al. (2020) <sup>[23]</sup>     | RCT          | 50<br>50       | SA<br>GA          | 45.1±14.9<br>48.9±15.9              | NS<br>NS                           | 18.1±5.3<br>17.3±4.1           | NS<br>NS                                  | 19/31<br>22/28          | 3                              | KUB, USG or CT          | RIRS conducted with SA demonstrates comparable stone clearance and complication rates to those under GA, establishing its safety and effectiveness in kidney stone treatment  |
| Sahan et al. (2020) <sup>[24]</sup>     | RCT          | 45<br>61       | CSEA<br>GA        | 44.1±12.6<br>46±16.3                | NS<br>NS                           | 15.7±7.3<br>17.2±7.7           | NS<br>NS                                  | 25/20<br>30/31          | 1                              | CT                      | Both GA and RA are equally effective and safe for f-URS procedures  |

Contd...

Table 1: Contd...

| Author/Year                            | Study design                       | Total patients | Anesthesia groups | Mean age  | Mean BMI (kg/m <sup>2</sup> ) | Mean stone size (mm)      | Stone density | Side of stone (R/L) | Duration of follow-up (months) | Follow-up in radiograph | Outcomes   |
|--|------------------------------------|----------------|-------------------|-----------|-------------------------------|---------------------------|---------------|---------------------|--------------------------------|-------------------------|--|
| Topaktaş et al. (2020) <sup>[25]</sup> | RCT                                | 40             | SA                | 41.9±12.3 | NS                            | 10.1±2.2                  | 991.7±404     | NS                  | 1                              | CT                      | Ureterorenoscopy for proximal ureter stone treatment in adults is a reliable procedure feasible under both SA and GA. SA provides the benefit of lower postoperative pain compared to GA |
|  |                                    |                | GA                | 40.3±13.3 | NS                            | 11.1±2.1                  | 1093.4±489    | NS                  |                                |                         |  |
| Olivero et al. (2021) <sup>[26]</sup>  | PC                                 | 40             | SA                | 55.8±13.9 | 25.4±2.9                      | 12.3±5.4                  | NS            | NS                  | 1                              | KUB or USG              | RIRS performed under both SA and GA yielded similar surgical outcomes and complication rates   |
|  |                                    |                | GA                | 54.9±16.9 | 25±2.6                        | 12.3±4.1                  | NS            | NS                  |                                |                         |  |
| Cai et al. (2021) <sup>[27]</sup>      | RC                                 | 116            | EA                | 47.8±11.3 | 25.9±3.1                      | 10.9±1.9                  | NS            | 61/55               | 1                              | CT                      | This study recommends using GA for flexible ureterorenoscopy when there are no contraindications   |
|  |                                    |                | SA                | 45±11.8   | 25.5±2                        | 11.1±2.9                  | NS            | 69/62               |                                |                         |  |
| Yoldas et al. (2022) <sup>[28]</sup>   | Retrospective, observational study | 250            | GA                | 39.8±8.4  | 25.2±1.9                      | 11.5±3.5                  | NS            | 71/74               |                                |                         | RIRS under both SA and GA yielded comparable surgical outcomes and complication rates  |
|  |                                    |                | SA                | 46.16±3.8 | NS                            | 12.43±2.8 cm <sup>2</sup> | NS            | 128/122             | 3                              | CT                      |  |
|  |                                    | 252            | GA                | 47.31±3.5 | NS                            | 13.57±2.6 cm <sup>2</sup> | NS            | 124/128             |                                |                         |  |

Stone size data from the same studies also revealed a significant difference in operation time between anesthesia techniques (mean difference: 0.60, 95% CI: -0.60-1.80,  $I^2 = 85\%$ ,  $Z^2 = 0.98$ ,  $P = 0.33$ ) [Figure 3].

Regarding pain outcomes, the studies displayed significant variation. Only five studies reported 24-h pain scores on the visual analog scale (VAS), and the meta-analysis indicated no significant difference in pain scores between patients undergoing surgery under SA or GA (mean difference: -0.50, 95% CI: -1.20-0.20,  $I^2 = 95\%$ ,  $P = 0.16$ ) [Figure 4].

All the studies comprised in the analysis provided information on the rate of stone clearance status. The meta-analysis demonstrated that there was no statistically significant difference in the rates of stone clearance among patients who received NA or GA (odds ratio: 0.66, 95% CI: 0.36-1.21,  $I^2 = 95\%$ ,  $P = 0.16$ ) [Figure 5].

Lastly, data from eight studies on length of stay showed no significant difference among the two groups (mean difference: 0.10, 95% CI: -0.07-0.27,  $I^2 = 95\%$ ,  $P = 0.25$ ) [Figure 6].

### Discussion

RIRS is the preferred minimally invasive method for upper urinary tract stone resolution. While the EAU guidelines recommend GA for most procedures, local or SA is also used.<sup>[29]</sup> However, the extensive use of GA can compromise the minimally invasive aspect of the procedure. Although GA can provide better intraoperative management, it is associated with risks such as anaphylaxis due to multiple-drug use and increased endotracheal tube-related complications.<sup>[30]</sup> Particularly in patients with reduced physiological compensatory capacity.

This review provides a comprehensive comparison of outcomes between RIRS implemented under NA and GA by synthesizing data from 11 studies, offering significantly more up-to-date evidence than previous reviews, some of which included only six studies. Our primary outcome analysis, based on data from 2,903 patients, discovered no significant difference in rates of stone clearance status among surgeries accomplished above NA or GA. Altogether studies stated data on rates of stone clearance status. Meta-analysis showed no statistically significant difference in the rate of stone clearance status between patients receiving NA or GA (OR: 0.66, 95% CI: 0.36, -1.21,  $I^2 = 95\%$ ,  $P = 0.16$ ). Similar outcomes were observed in a study conducted by Duan et al.<sup>[31]</sup> where they compared the results of RIRS accomplished under NA or GA by pooling data from

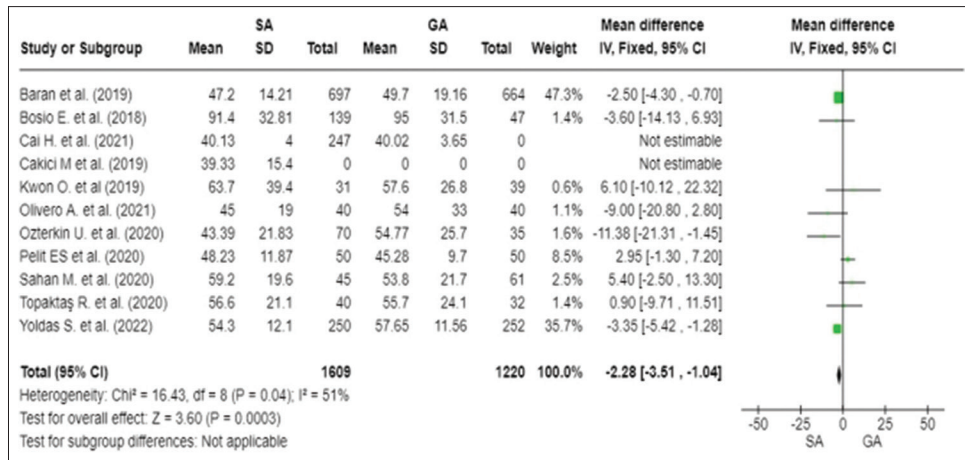


Figure 2: Meta-analysis comparing operative time between SA and GA in retrograde intrarenal surgery (RIRS)

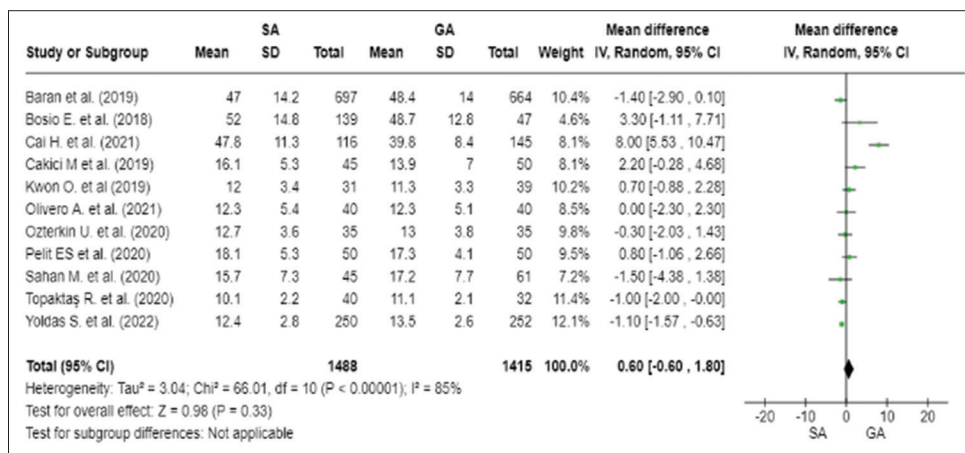


Figure 3: Meta-analysis comparing mean stone size among SA and GA in retrograde intrarenal surgery (RIRS)

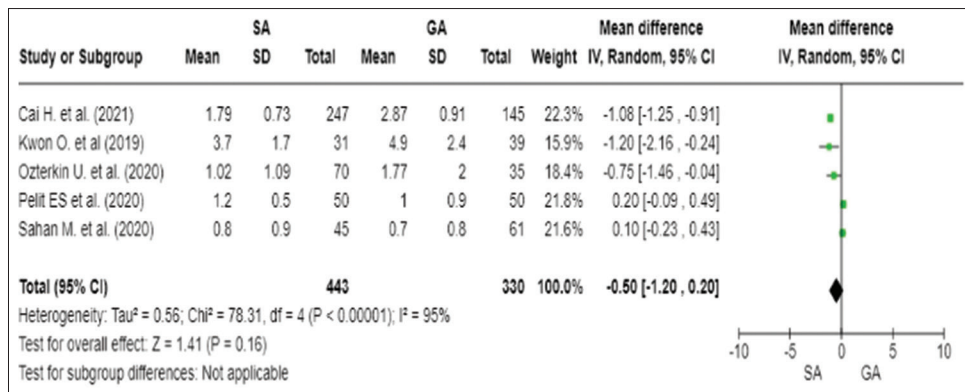


Figure 4: Meta-analysis comparing pain scores among SA and GA in retrograde intrarenal surgery (RIRS)

13 studies, providing more current evidence than previous reviews, which often included only six studies.<sup>[32,33]</sup> In their study of primary outcome analysis, involving data from 2,912 patients, they found no significant difference in rates of stone clearance status afterward surgery under NA or GA. The success rates in the NA and GA groups were 80.2% and 82.9%, correspondingly.

In contrast, the study conducted by Wang *et al.*<sup>[33]</sup> (OR: 1.07, 95% CI: 0.82, 1.38) in addition to Luo *et al.*<sup>[32]</sup> (OR: 0.96, 95% CI: 0.91, 1.02), which involved a total sample of 1,747 and 580 patients, correspondingly, stated parallel findings. Investigators have indicated that the effectiveness of RIRS hinges on various issues, including urinary tract anatomy, operator practice as well as intraoperative breathing control.

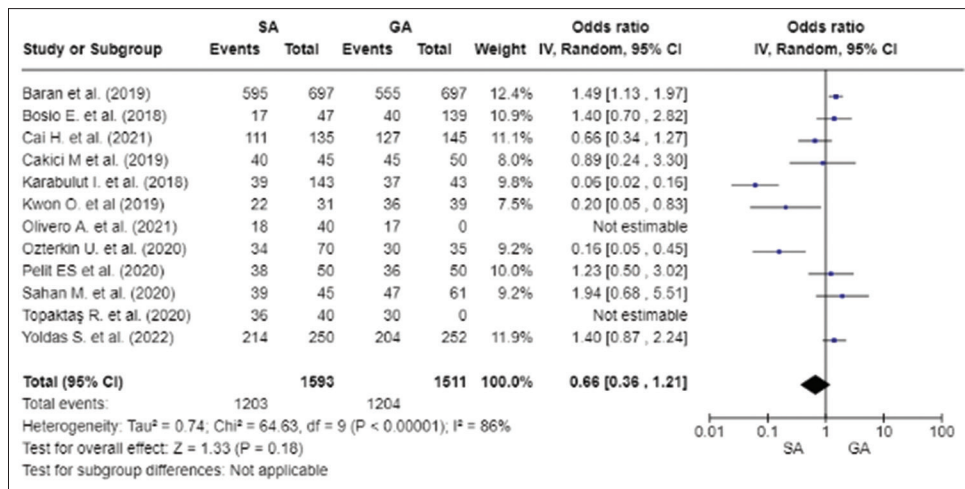


Figure 5: Meta-analysis comparing rates of stone clearance between SA and GA in RIRS

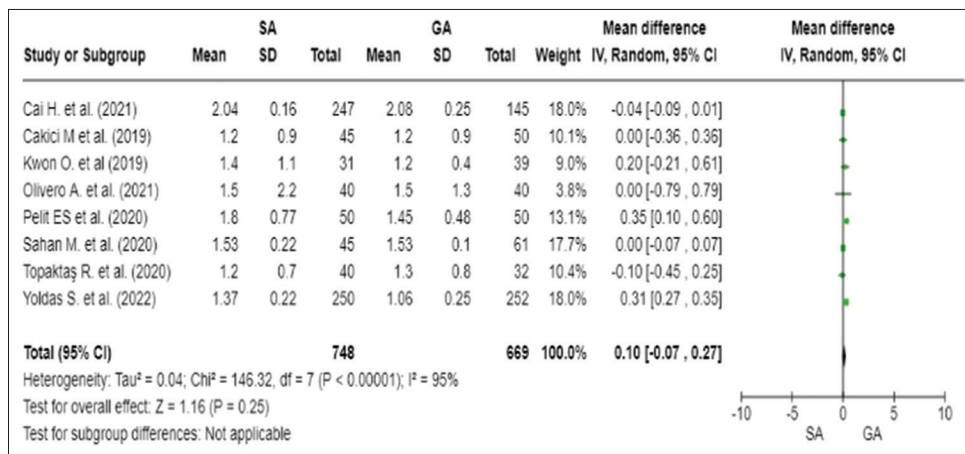


Figure 6: Meta-analysis comparing length of hospital stay (LOS) among SA as well as GA in RIRS

The movement of the kidney, as well as ureters through RIRS, can lead to oscillations that may disrupt the precision necessary for laser stone disintegration.<sup>[16]</sup>

Nevertheless, both our findings and previous reviews<sup>[31,32]</sup> consistently suggest that visceral movements have minimal effect on rates of stone clearance. During NA patients can be instructed to hold their breath, aiding stone disintegration.<sup>[18]</sup> However, it is important to note that the definition of rates of stone clearance status diverse among the included studies, with suitable remnant stone sizes ranging from 1 to 4 mm. Additionally, differences existed in postoperative imaging methods as well as follow-up durations. Given these variations, more studies with standardized definitions are necessary to establish stronger evidence.<sup>[33]</sup>

Our review shows that regarding pain outcomes, the studies displayed significant variation. Only five studies reported 24-h pain scores on the VAS and analysis indicated no significant difference in pain ratings between patients

undergoing surgery under SA or GA (mean difference: -0.50, 95% CI: -1.20 to 0.20, I<sup>2</sup> = 95%, P = 0.16). Similar findings in the study piloted by Tyriztis *et al.*<sup>[34]</sup> demonstrated that SA provides superior pain control during the initial 2-h postsurgery, while GA proves more effective in later phases for patients experiencing transurethral techniques. A study comparing RA with GA for patients undergoing PCNL has demonstrated that RA is associated with reduced pain scores and decreased analgesic needs.<sup>[35]</sup>

In this review, 11 studies focusing on operation time, a statistically significant difference was observed when comparing different anesthesia techniques (mean difference: -2.28, 95% CI: -3.5 to -1.04, I<sup>2</sup> = 51%, P = 0.003) [Table 1]. Similar to rates of stone clearance rates, Duan *et al.*<sup>[31]</sup> found no significant difference between NA and GA in terms of operation time. This contrasts with Wang *et al.*'s review<sup>[33]</sup> which stated shorter operating times with NA but aligns with the outcomes of Luo *et al.*<sup>[32]</sup> which indicated no such difference. Operation time in RIRS can be influenced by

a multitude of variables. For instance, Katafigiotis *et al.*<sup>[36]</sup> demonstrated that factors such as stone number, size, density, instrument type, surgeon experience, operating room setup, and prior nephrostomy tube use can independently affect operating time in RIRS. Given the diverse array of factors influencing this parameter, the observed high heterogeneity in the study, which continued even after subgroup studies, is not surprising.

There are some limitations in this analysis, which are as follows:

- The overall quality of the included studies, whether randomized controlled trials (RCTs) or non-RCTs, was not high. RCTs showed a “moderate” certainty of evidence for most outcomes. The absence of blinding in outcome valuation across all studies could have impacted the outcomes.
- Variation in anesthesia and postoperative analgesia protocols among different study centers was a potential source of heterogeneity. Surgeon experience also played a crucial role, with some centers having only experienced surgeons while others involved a mix of novice and experienced surgeons. Surgeon expertise significantly influences the success rates of RIRS, and inexperienced operators may be at a higher risk of complications due to breathing movements.
- The limited data available from the studies included in this analysis hindered a comprehensive comparison of specific complications, including but not limited to nausea/vomiting, headaches, and urinary retention. This highlights the necessity for further research in this particular domain.

## Conclusion

Based on the outcomes of the study recommended that NA could be a feasible substitute to GA for RIRS. No statistically significant differences were seen between NA and GA in terms of RIRS for stone clearance rates, operation length, 24-h pain ratings, difficulty rates, or the duration of hospital stay. This suggests that given the potential economic advantages, NA might be a preferable choice over GA, contingent on patient preferences, baseline characteristics, and stone burden.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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