The use of endoscopic combined intrarenal surgery in the treatment of nephrolithiasis

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Aim. To summarize the data of the world scientific literature on the treatment of nephrolithiasis by studying a combination of percutaneous nephrolithotripsy and retrograde or antegrade flexible intrarenal surgery based on the evaluation of their effectiveness and safety.

Materials and methods. The literature review was conducted using the databases PubMed, Google Scholar, Web of Science and Scopus for the period 2015–2022. The following keywords were used for the search: surgical treatment of nephrolithiasis, endoscopic combined intrarenal surgery (ECIRS), percutaneous nephrolithotomy, retrograde intrarenal surgery, simultaneous use of flexible ureterorenoscopy and percutaneous nephrolithotomy, simultaneous use of flexible ureterorenoscopy and percutaneous nephrolithotripsy.

Conclusions. The use of ECIRS increases the effectiveness of one-stage treatment of nephrolithiasis with minimal complications and reduces the number of re-operations required. Treatment of complex forms of nephrolithiasis may be a priority for ECIRS. The main disadvantages of ECIRS are the need for simultaneous operation of two operating surgeons and the availability of two sets of endoscopic equipment, which make this procedure expensive.

Urolithiasis is one of the most common urological conditions (30–45 %), peaking in the 4th–6th decades of life. About 50 % of patients have one recurrent episode of nephrolithiasis during their lifetime, and among the operated patients, more than 10–15 % of individuals report recurrences with the need for repeated surgical treatment.

Increasing the incidence of nephrolithiasis worldwide requires the development of new and improvement of existing methods of surgical treatment, which would be characterized by a high level of efficiency and low invasiveness with minimal complications and postoperative rehabilitation. The use of a combination of percutaneous nephrolithotripsy and flexible ureterorenolithotripsy, especially in complex cases of urolithiasis, can increase the safety and improve the treatment of nephrolithiasis by combining the positive qualities of both methods.

Key words: nephrolithiasis, kidney stones, endoscopic combined intrarenal surgery, percutaneous nephrolithotomy, retrograde intrarenal surgery, robotic surgery, endoscopy.

У роботі розглядається використання ендоскопічної комбінованої інтраренальної хірургії в лікуванні нефролітіазу.

Використання ендоскопічної комбінованої інтраренальної хірургії в лікуванні нефролітіазу

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Мета роботи – узагальнити відомості світової наукової літератури, що присвячена лікуванню нефролітіазу, шляхом вивчення комбінації перкутанної нефролітотрипсії та ретроградної або антеградної гнучкої інтраренальної хірургії на основі оцінювання їхньої ефективності та безпеки.

Матеріали та методи. Огляд літератури здійснювали використовуючи дані PubMed, Google Scholar, Web of Science та Scopus за період 2015–2022 рр. Для пошуку застосовували ключові слова: surgical treatment of nephrolithiasis (хірургічне лікування нефролітіазу), endoscopic combined intrarenal surgery (ендоскопічна комбінована інтраренальна хірургія, EKIPX), percutaneous nephrolithotomy (перкутанна нефролітотрипсія, flexible ureterorenoscopy (гнучка уретеронефроскопія), retrograde intrarenal surgery (ретроградна інтраренальна хірургія), simultaneous use of flexible ureterorenoscopy and percutaneous nephrolithotomy (сімультанне використання гнучкої уретеронефроскопії та перкутанної нефролітотрипсії).

Висновки. Використання EKIPX підвищує ефективність одноетапного лікування нефролітіазу при мінімальному рівні ускладнень, зменшує кількість необхідних повторних операцій. Підробним напрямом використання EKIPX може бути лікування складних форм нефролітіазу. Основні недоліки EKIPX полягають у необхідності одночасної роботи двох операційних хірургів і необхідності двох комплектів ендоскопічного обладнання, що робить цю процедуру доволі дорогою.

Ключові слова: нефролітіаз, сечокам'яна хвороба, гнучка уретеронефроскопія, перкутанна нефролітотрипсія, ретроградна інтраренальна хірургія, відомі методи лікування, гнучка нефролітотрипсія. UDC 616.61-003.7-072.1-089.879.
Urolithiasis is one of the most common urological conditions (30–45%), peaking in the 4th–6th decades of life. The high level of recurrence is burdened with significant socio-economic consequences [1]. About 50% of patients have one recurrent episode of nephrolithiasis, and more than 10–15% of patients report frequent recurrences with the need for second-look surgical treatment [2]. Their probability is 11%, 20%, 31%, and 39% after 2, 5, 10 and 15 years, respectively [3]. The incidence of nephrolithiasis is prevalent throughout the world and varies from 1–5% in Asia, 7–13% in North America, 20.1% in Saudi Arabia [4]. In most countries over the century, there has been a steady increase in the incidence of nephrolithiasis in both adults [5] and children [6], with a reduction in the gender gap [3]. In a study of the general age population of the United States from 1970 to 2000, the ratio of sick men to sick women changed from 3:1 to 1:3.1:1.0, respectively [7]. According to a study conducted in 2010, in the age group from 10 to 29 years, 62–63% of the nephrolithiasis incidence occurred in men [8], and in the sample of up to 50 years there was an equality of 6.3% in men against 6.4% in women [9].

An increase in the number of patients with nephrolithiasis is observed, even in regions with historically constant low incidence. This phenomenon is called a “stone wave”. According to some authors, the main predictors of increasing the number of patients are improved diagnostic capabilities, steady Earth’s population growth, the trend of global warming, changes in diet and the associated increase in obesity [10] and diabetes [11].

The increasing incidence of nephrolithiasis in the world determines the need to develop new safe and effective methods of treatment for urolithiasis. Currently, there are three main types of surgical treatment of renal stones: percutaneous nephrolithotomy (PNL), retrograde intrarenal surgery (RIRS) and extracorporeal shockwave lithotripsy (ESWL). Each of these methods has its own indications for performance, which are obtained by conducting a large number of studies that have been summarized in the European and American urological guidelines [12–14]. Unfortunately, most of them are aimed at competitive comparisons of the efficacy of surgical treatment and they do not highlight the benefits of their combination [15].

Since its introduction in 1976, PNL has been indicated to treat large, including staghorn renal stones with the absence of residual stones (SFR) in 71.0–98.5% [16]. However, in cases with a large stone mass in the kidney, a high rate of complications occurs after PNL. This fact has led to the search for new options for endoscopic treatment of nephrolithiasis and study on the effect of combining existing methods.

Endoscopic combined intrarenal surgery (ECIRS) is a symbiosis of percutaneous nephrolithotomy and retrograde intrarenal surgery, presented as a new method of endoscopic treatment of nephrolithiasis and upper urinary tract (UUT) calculi, aimed at eliminating the disadvantages in their use as a monotherapy [17].

To date, available studies comparing ECIRS and PNL have shown conflicting results. There is still no consensus on the advantage of ECIRS in terms of surgery duration, length of hospital stay, and even the rate of complete removal of a calculus or the complication rate.

**Aim**

To summarize the data of the world scientific literature on the treatment of nephrolithiasis by studying a combination of percutaneous nephrolithotomy and retrograde or antegrade flexible intrarenal surgery based on the evaluation of their efficacy and safety.

**Materials and methods**

The literature review was conducted using the databases PubMed, Google Scholar, Web of Science and Scopus for the period 2015–2022. The following keywords were used for the search: surgical treatment of nephrolithiasis, endoscopic combined intrarenal surgery, percutaneous nephrolithotomy, flexible uretero-renoscopy, retrograde intrarenal surgery, simultaneous use of flexible ureterorenoscopy and percutaneous nephrolithotomy.

**Results**

The idea of combined (percutaneous and retrograde) endoscopic treatment of UUT calculi originated in the 80s of the twentieth century, but the level of technical support at that time made it impossible to develop this area [18]. Only in 2004 Undre et al. described the method of “pass the ball” in the treatment of staghorn calculus of the upper pole of the kidney with simultaneous use of PNL and RIRS methods [19].

Simultaneous performance of retrograde and antegrade (percutaneous) access to the renal collecting system was described in detail by G. Ibarluzea et al. in 2007 [20]. Although their first experience in a combination of these methods dates back to 1992 [21].

In 2008, C. Scoffone et al. introduced the term “endoscopic combined intrarenal surgery” and published the results of 127 endoscopic surgeries with a combination of RIRS and PNL for management of UUT calculi. Their data showed the safety and efficacy of the method with a combination of positive qualities from both types of surgeries [22]. Later, in 2018, C. Scoffone et al. presented the results obtained after 310 ECIRS, where the stone free rate (SFR) was close to 90% with a duration of surgeries of 88±35 minutes [23]. The authors noted complications (according to the Clavien-Dindo classification) in only 7.4% of cases and only in 1.6% they were higher than the second grade. Ureteral injury was not observed in any surgery. Taking into consideration that the resulting rate of ECIRS complications was lower than when performing PNL in mono-mode, they made an assumption on increasing the safety and efficacy in the treatment of multiple and “complex” stones of UUT by combining endoscopic percutaneous and retrograde accesses.

Since then, scientists around the world have increasingly begun to implement a combination of PNL with flexible nephroscopy, both antegrade and retrogradely. Thus, A. Gücük et al., in 2013, recommended to introduce routine antegrade examination of the kidney and upper 1/3 of the ureter after PNL using a flexible pyeloscope, especially in X-ray low-contrast calculi [24]. However, data from a study by M. I. Gökoe et al., in 2019, represented better SFR in retrograde pyelogram of the kidney using a flexible
ureterorenoscope compared to its antegrade manner. Thus, analyzing treatment of 137 patients who underwent ECIRS with antegrade and retrograde flexible nephroscopy, the authors noted that through percutaneous access, flexible instruments managed to get only 73.7 % of the calyx and 94.9 % through retrograde access. Residual calculi after interventions in order to completely remove stones from the kidney. Despite the high rate of complications and the need for second-look procedures in the upper groups of the renal calyces is associated with a higher rate of complications due to their anatomical position. Thus, about 80 % of the upper pole calyces of the right and 85 % of the left kidney are above the 12th rib and the puncture of these calyces is associated with a high risk of injury to the pleura and lungs. According to the literature data, when performing access above the 12th rib, the frequency of thoracic complications ranges from 2.8 % to 12.0 %, and the formation of the tract above the 11th rib 16 times increases the level of complications [38].

According to the data presented by A. Tefekli et al., obtained in the analysis of 4494 patients operated by PNL method, percutaneous access to renal calyx-pelvic system through the upper pole was followed by a higher rate.
of complications compared to access through the lower pole. The overall rate of perioperative complications was 23.5 % versus 16.1 %. Pulmonary complications occurred in 5.8 % vs. 1.5 %, blood transfusion rate was in 7.3 % vs. 4.0 %, respectively [39]. From their side, K. Blum et al. in the analysis of PNL treatment of 76 patients with staghorn nephrolithiasis, emphasized a more significant difference in the rate of complications between access through the upper and lower groups of renal calyces: 23.5 % vs. 3.4 %, respectively [40].

Based on the above, the use of ECIRS is especially important when calculi are located in the upper groups of calyces, mainly in the complex anatomy of the renal collecting system (Samaio A2, B1) or in the calyceal diverticulum, where a surgeon must perform percutaneous access "to the stone" in the 11th and sometimes in the 10th intercostal space. In such cases, ECIRS is more of a priority, as percutaneous access to the kidney can be performed through a more conveniently located and safe calyx with subsequent movement of the flexible nephroscope to the calculus or its fragments from the calyces which are hard-to-reach through the percutaneous access to the place of direct access [38,41].

The first systematic review and meta-analysis of the treatment of nephrolithiasis complex forms by means of ECIRS and PNL was performed by Y. H. Liu et al. in 2022. It included 7 studies (1 randomized controlled study and 6 retrospective cohort studies) with a total of 919 patients. According to the obtained data, in the ECIRS groups compared to PNL in mono-mode, there was a better result of primary and final SFR, fewer complications and the need for blood transfusion. In the analysis of these methods in the «mini-version», there was an additional reduction in the length of hospital stay in the group mini-ECIRS in comparison with the mini-PNL in mono-mode [42].

Complex forms of urolithiasis also include bilateral nephrolithiasis, which requires a careful choice of both the method of surgical treatment and the stages of its implementation. For decades, simultaneous surgical treatment of bilateral renal stones has been considered a risk factor for acute renal failure and a higher incidence of complications, in order to reduce complications, requires control over the method effectiveness. Depending on a diameter of the nephrostomy tube, ECIRS is divided into standard ECIRS from 24 Fr and mini-ECIRS from 14 Fr to 22 Fr. According to a retrospective study by K. Usui et al. from 2020 which included 144 patients (77 standard ECIRS and 77 mini-ECIRS), SFR was maintained without increasing perioperative complications with a concomitant reduction of postoperative pain and a decrease in hemoglobin in the mini-ECIRS group. According to the study results, the authors concluded that the use of mini-ECIRS was more of a priority than standard ECIRS [34].

These data were confirmed in a previous retrospective study by S. Hamamoto et al. from 2014, where the authors analyzed the results of endoscopic treatment of 161 patients with a complex form of nephrolithiasis. Patients were divided into groups: mini-ECIR – 60 patients, mini-PNL – 19 patients and standard PNL – 82 patients. The average calculus size was 39.2 mm, 38.4 mm, and 34.6 mm, respectively. Comparing the duration of surgery (120.5 min, 181.9 min, 134.1 min, respectively), a decrease in hemoglobin (1.06 ± 0.15 g/dL, 1.10 ± 0.13 g/dL, 1.64 ± 0.19 g/dL, respectively), complication rate (10.0 %, 15.8 %, 30.5 %, respectively) and primary SFR (81.7 %, 38.9 %, 45.1 %, respectively), the authors noted a lower rate of complications in the group using mini-instruments, and a significant advantage in all indicators after the simultaneous combination of retrograde and percutaneous accesses to UUT with mini-instruments [48].

From their side, S. Biligere et al. reported the successful experience of a combination of micro-PNL (nephroscope tube size 7–11 Fr) and RIRS. In this combination, percutaneous and retrograde endoscopic accesses to the renal collecting system were also performed, but the evacuation of calculus fragments, in contrast to the mini-PNL, was performed through a retrograde ureteral introducer [49].

Speaking about ECIRS, it is necessary to note the peculiarities of a patient’s position on the operating table, which is extremely important in the implementation of endoscopic access to UUT. In most cases, ECIRS is performed in a
modified supine patient position (Galdakao-Valdivia), but according to the data provided by S. Hamamoto et al., placing a patient in the prone position with legs spread apart may be an alternative for maintaining a high advantage of SFR (82.0 %) and the competitive rate of complications (Grade I according to the Clavien-Dindo classification – 8.3 %, Grade II – 1.7 % and Grade III–V – 0.0 %). The study included 60 patients with complex forms of nephrolithiasis. The average stone size was 39.2 ± 2.6 mm, and the average surgery duration was 120.5 ± 6.7 minutes. Unfortunately, the prone patient position lacked a number of benefits, but at the same time, it simplified percutaneous access to the renal collecting system, which was a priority for novice endourologists [50].

Creating a percutaneous tract to the renal cavity system, which is generally considered to be the “key to success” in PNL, remains a difficult task, primarily due to the peculiarities of its formation. Performing the technique of percutaneous puncture of the calyx-pelvic system under radiography or ultrasound guidance requires highly professional training of a surgeon. Therefore, nowadays, ancillary mechanisms and virtual simulators are being actively developed to study and improve operational skills in the formation of percutaneous access to the kidney when performing ECIRS.

Recently, a number of works have appeared that offer to perform percutaneous access to the kidney under the visual guidance of a flexible ureterorenoscope, inserted into the target calyx. Thus, K. Taguchi et al. [51] compared the results of percutaneous access to the kidney during ECIRS between two groups of patients: Group 1 (n = 126) – percutaneous access under ultrasound guidance with ureterorenoscopic imaging from the middle of the renal cavity system and Group 2 (n = 187) – traditional percutaneous access only under ultrasound guidance. In their work, the authors showed that puncture of the calyx-pelvic system (CPS) under combined ultrasound and ureterorenoscopic guidance was associated with a lower risk of additional surgery (OR = 0.31; P = 0.011), reducing the number of postoperative infectious complications (OR = 0.34; P = 0.003), the total duration of the procedure (less by 11 minutes; P = 0.011), radiography (less by 3 minutes; P = 0.034) and the duration of postoperative ureteral stenting (less by 8 days; P = 0.011).

A group of authors led by N. Kang [52] has come to the same conclusions, where in 28 cases endoscopically controlled accesses to CPS of the kidney were performed under combined ultrasound and ureterorenoscopic guidance, while in 25 other cases, percutaneous renal access was performed using standard percutaneous technique under ultrasound guidance. The authors have noted that the implementation of endoscopically controlled accesses is a unique technique for the formation of percutaneous tract to CPS of the kidney in ECIRS, which minimizes the time to create access compared to its traditional performance (4.0 ± 0.7 min vs. 6.8 ± 2.6 min, P < 0.01) and significantly reduces second-look procedures (0 vs. 4 cases, P < 0.05, respectively).

Other experimental studies on the formation of percutaneous access in ECIRS are currently underway. An example is a study conducted by a group of authors led by E. Lima [53], where 10 patients underwent a puncture of the CPS under GPS guidance. After visual determination of the optimal renal calyx, an electromagnetic sensor was inserted through the working channel of the flexible ureterorenoscope, followed by percutaneous puncture of the selected calyx with a needle equipped by a GPS navigator at the tip, guided by a three-dimensional real-time image on the monitor. All 10 punctures of the collecting system were successfully performed on the first attempt without radiological guidance. The average time of a successful puncture, starting from the moment of needle insertion, was 20 seconds (from 15 to 35 seconds). No complications were observed. The authors have noted that the new technology allowed safe, accurate, fast and efficient puncture of the renal collecting system. These findings are reflected in the work from 2020 by medical physicists, who also studied this technique [54], mathematically confirmed the accuracy of the puncture of CPS with the help of electromagnetic control system and GPS navigation.

The introduction of ECIRS surgery has led to a change in the stereotypes of modern endourology. If traditionally percutaneous access to CPS of the kidney is performed with a puncture needle in the direction from the skin to the selected renal calyx (from the outside to the inside), then in ECIRS, this basic principle may be vice versa. In particular, a number of authors (C. A. Uribe et al. and K. S. Kaler et al.) propose to form percutaneous access by retrograde conduction of laser fiber through the channel of the inserted flexible ureterorenoscope, from the middle of the target renal calyx outwards (percutaneously), thus creating a nephrostomy tract. The externally conducted laser fiber is used as a guide wire for further standard formation of antegrade percutaneous access. The authors note in their studies that this access has two potential advantages, such as the accuracy of creating antegrade access and reducing the duration of radiography [55,56].

To date, the participation of robotic technologies in surgical treatment is increasingly becoming commonplace for modern surgery. Taking into consideration the growing popularity of ECIRS, the development of innovative equipment for this technique is particularly relevant.

In order to reduce percutaneous access complications, Nagoya University, Japan, has proposed to use the robotic X-ray access version RAF (robot-assisted fluoroscopy) ECIRS in combination with ANT-X (automated needle target with X-ray). According to a study conducted from January to June 2020, 19 patients underwent mini-ECIRS for calculi larger than 15.0 mm by a urologic surgeon who performed percutaneous access to the renal collecting system under fluoroscopic guidance for the first time, an average number of punctures with a guide needle accessing the lower calyx was equal to one. And the largest number of required repeated punctures, equal to four, was performed by puncturing the upper calyx. The obtained data confirm the efficacy of this technique and the possibility of its implementation by novice urologists [57].

In most cases, the development of technology is aimed at improving the results of the surgery, but some implementations are aimed at the comfort of the operating surgeon, including. This combination of qualities is predicted from the use of robotic system Avicenna Roboflex in retrograde access for ECIRS, which is confirmed by the results of a study conducted by Z. Tokati et al. high rates of single-stage SFR (95.5 %) with a low rate and severity of complications.
The incidence of nephrolithiasis increases the relevance of the patient during its implementation (the following advantages and disadvantages of ECIRS, reducing the total cost per patient. Ancillary procedures and surgeries, which also significantly reduces the cost of measures (blood transfusions, antibiotics, antibacterial medicines, etc.), necessary during ureteropyeloscopy, the TEC model received good scores from testers, especially for ultrasound-guided renal collecting system punctures, both in the prone and supine position of patients [59].

It is important to note that ECIRS has not yet become widespread in clinical practice due to a number of problems. Firstly, the need for two endoscopic systems and teamwork between two surgeons, which can be a challenge in a resource-constrained environment. Secondly, the problem of high cost of ECIRS, mentioned in the study of H. D. Jung et al., where the authors pointed out the difficulties in calculating the cost of these procedures, which can be problematic for the hospital [17]. Thirdly, when combining the two procedures, the surgery duration of ECIRS is sometimes considered longer, but a number of studies have not found a significant difference in the surgery duration between ECIRS and PNL [35,42].

The above-mentioned concerns need to be analyzed carefully, as the incidence of potential complications reduces the cost of measures (blood transfusions, long-term use of antibacterial medicines, etc.), necessary to eliminate them. And higher SFR eliminates the need for ancillary procedures and surgeries, which also significantly reduces the total cost per patient.

Summarizing the analyzed data, we can emphasize the following advantages and disadvantages of ECIRS, which are related to both the method itself and the position of the patient during its implementation (Table 1).

Thus, the current trend towards a steady increase in the incidence of nephrolithiasis increases the relevance of the innovative technical equipment introduction and new types of surgeries. Our review of current data shows that ECIRS is more effective and safer than PNL in mono-mode. That is why the combination of PNL and RIRS, otherwise known as ECIRS, is presented as a new effective method of surgical treatment of nephrolithiasis and proximal ureterolithiasis, aimed at eliminating disadvantages of these techniques in mono-mode. Despite the spread of interest in this method, the world scientific literature provides a small amount of data on the evaluation of the results related to the combination of these methods. At the same time, ECIRS, as a new treatment, looks promising for the treatment of nephrolithiasis and UUT calculi.

**Table 1. Advantages and disadvantages of ECIRS**

| Advantages of ECIRS | Disadvantages of ECIRS
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<td>– removal of an UUT calculus of any localization through one percutaneous tract;</td>
<td>– the need for two experienced operating doctors [29];</td>
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<td>– performing endoscopic-guided access [65], which reduces radiation dose on the patient [27], the duration of the percutaneous tract formation and the level of related complications [52];</td>
<td>– availability of two endoscopic sets [29];</td>
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<td>– forming a space for performing a transcutaneous tract, with tight calculus positioning in the calyx in the potential access [35];</td>
<td>– lower rate of infectious complications due to reduction of intrarenal pressure [21,22];</td>
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<td>– reduction of renal mobility during tract formation;</td>
<td>– reduction of the surgery duration by eliminating the need to change the position of patients [29];</td>
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<td>– antegrade insertion of a guide wire (the first surgeon – a puncture needle – a collecting system</td>
<td>– increasing the evacuation rate of calculus fragments due to the horizontal or acute angle of the nephroscope [32];</td>
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<td>– a ureteral sheath – the second surgeon) [21];</td>
<td>– reduction of cardiovascular and respiratory load on patients [27];</td>
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<td>– the ability to work simultaneously in the UUT with two tools [60];</td>
<td>– deterioration of endoscopic visibility caused by the decrease in the renal cavity system due to better outflow of lavage fluid [19];</td>
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<td>– moving the calculus with the help of flexible instruments in the access area of the rigid nephroscope by “passing the ball” [19];</td>
<td>– smaller safe area for percutaneous puncture of the renal collecting system [61];</td>
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<td>– improving the local image quality of hematuria, due to the bilateral supply of lavage fluid [60];</td>
<td>– longer access tract, which reduces the mobility of tools [17];</td>
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<td>– greater renal mobility [21];</td>
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<td>– more difficult to perform a puncture of the upper group of calyces [21].</td>
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Conclusions

1. The use of ECIRS increases SFR with minimal complications rate and reduces the number of required second-look surgeries.
2. Performing ECIRS in the supine position involves a number of anesthetic complications.
3. ECIRS is a method of treatment that can become a priority in the treatment of complex forms of nephrolithiasis.
4. The main disadvantages of ECIRS are the need for simultaneous work of two operating surgeons and the availability of two sets of endoscopic equipment, which make this procedure expensive.

Conflicts of interest: authors have no conflict of interest to declare.

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