

Official Title: Triple-Zero Retrograde Intrarenal Surgery (TZ-RIRS) versus Conventional Retrograde Intrarenal Surgery (C-RIRS): Development and Internal Validation of the Novel TZ-STONE Feasibility Score

Document Date: 10-01-2023

1. Introduction

You are being invited to take part in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

2. Purpose of the Study

The purpose of this study is to evaluate a new minimally invasive surgical technique for kidney stones called Triple-Zero RIRS. This technique avoids the use of X-ray guidance, a plastic tube (UAS), and a stent placed before surgery. We are also testing a new scoring system (the TZ-STONE score) to see if it can predict which patients are the best candidates for this approach.

3. Why Have I Been Chosen?

You have been chosen because you have a kidney stone that requires surgical removal, and your stone characteristics fit the criteria for this study.

4. Do I Have to Take Part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You can withdraw at any time without giving a reason. Your standard medical care will not be affected.

5. What Will Happen to Me if I Take Part?

If you agree to take part, you will undergo the Triple-Zero RIRS procedure. This involves:

- You will receive general or spinal anesthesia.
- The surgeon will use a thin, flexible camera to locate and break up your kidney stone using a laser.
- No X-ray guidance will be used unless absolutely necessary.
- No plastic access tube will be used.
- No stent will be placed before the surgery.
- A stent may be placed at the end of the surgery, if your surgeon deems it necessary.
- You will be followed up at 3 months with a CT scan to check if the stone is gone.

6. What Are the Possible Risks?

- Standard risks of surgery: Bleeding, infection, injury to the ureter or kidney.
- Study-specific risks: Because this technique does not use standard X-ray guidance, the surgeon relies entirely on direct vision. While this reduces radiation exposure, there is a

small risk that the surgeon may need to convert to standard X-ray guidance mid-surgery if the anatomy is complex. The risk of needing a rescue UAS placement is also present.

7. What Are the Possible Benefits?

- You will be exposed to significantly less radiation than a standard kidney stone surgery.
- You will avoid the discomfort of a stent being placed before surgery.
- You may have a lower risk of injury to your ureter.

8. Confidentiality

All information collected about you during the course of the research will be kept strictly confidential and anonymized before being analyzed or published.

9. Contact Details

If you have any questions or concerns, please contact:

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Statistical Analysis Plan (SAP)

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1. Study Populations

Development Cohort: 312 patients (TZ-RIRS).

Matching Cohort: 1:1 propensity score matching (nearest-neighbor, caliper 0.2) yielding 250 patients per group (TZ-RIRS vs. C-RIRS).

2. Propensity Score Matching

A multivariable logistic regression model will generate propensity scores based on age, sex, BMI, stone size, stone location, stone density, and number of stones. Standardized mean differences (SMD) will be calculated, with an SMD <0.1 indicating adequate balance.

3. Analysis of the TZ-STONE Score

Derivation and Validation: The TZ-RIRS cohort will be randomly split into a 70% training set (n=218) and a 30% validation set (n=94).

Discrimination: Receiver operating characteristic (ROC) curves will be generated. The area under the curve (AUC) and 95% confidence intervals (DeLong method) will be calculated.

Calibration: Assessed via the Hosmer-Lemeshow goodness-of-fit test and calibration plots (slope and intercept).

Clinical Utility: Decision curve analysis (DCA) will evaluate net benefit across threshold probabilities.

Optimal Threshold: Determined using the Youden index (Target ≥ 8).

4. Comparative Outcomes Analysis

Continuous Variables: Analyzed using Student's t-test or One-way ANOVA (with Tukey post-hoc tests for TZ-STONE tiers). Non-parametric alternatives (Mann-Whitney U) will be used if data are not normally distributed.

Categorical Variables: Analyzed using the χ^2 test or Fisher's exact test.

Noninferiority: Stone-free rates between TZ-RIRS and C-RIRS will be assessed for noninferiority using a margin of -10%. A two-sided p-value < 0.05 is considered significant.

Software: R version 4.3.1.