STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Effectiveness and Safety of Single-port Versus Multi-port Laparoscopic Surgery in the Treatment of Ectopic Pregnancy

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1. Introduction

Single-port laparoscopic surgery has become one of the treatment options for ectopic pregnancy with certain advantages such as reduced numbers of incision and scars, fast recovery, and increased patient's satisfaction post-surgery. Although several research groups have investigated the differences between single-port and traditional multi-port laparoscopic surgery, the investigators have not had such studies carried out at Hung Vuong hospital. Therefore, the investigators set out this project to compare the effectiveness and safety of single-port versus conventional multi-port laparoscopic surgery in the treatment of ectopic pregnancy at Hung Vuong hospital, aiming to gain insights into the application potential of this technique to the gynecologic laparoscopy procedures.

2. Study design

Study subjects will be recruited from November 2023 to May 2024 at Hung Vuong hospital, Ho Chi Minh city, Vietnam. Inclusion criteria for participants in this study include pregnant women who are 18 years old or older; who are indicated for laparoscopic surgery to treat ectopic pregnancy; and who agree to participate and provide a consent. Exclusion criteria include pregnant women who are allergic to anesthesia; who have hemodynamic instability; or who have ruptured ectopic pregnancies. The study is a parallel-group randomized control trial with 2 arms and no blinding. Arm 1 includes patients who will undergo single-port laparoscopy while aim 2 have patients undergo multi-port laparoscopy. All patients are randomized using computer-generated sequences with allocation ratio 1:1. Primary outcomes include blood loss, and surgical time. Secondary outcomes include pain intensity, surgical complications, hospital stay, and pneumoperitoneum. Blood loss and surgical time will be measured right after surgery while other outcomes will be measured during hospital stay. Technically, the investigators will perform examination 3-4 days post-surgery. Sampling will be stopped and the study will be concluded when patients are discharged from the hospital. The study design is visualized in Figure 1 below.

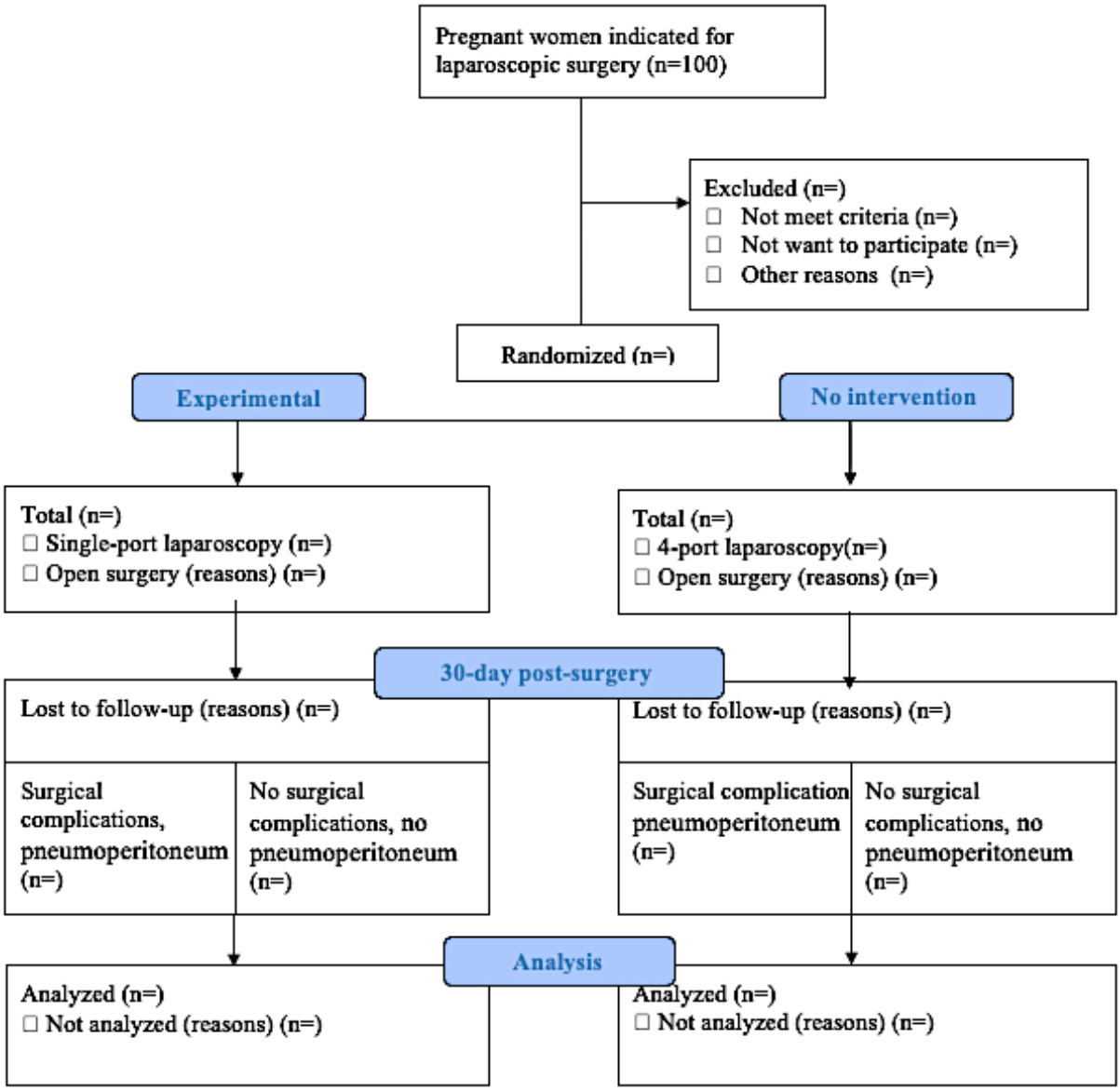

Figure 1: The CONSORT flow diagram of the study

Sample size calculation

The sample size is calculated based on the following formula:

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2[\sigma_1^2 + \frac{\sigma_2^2}{r}]}{\Delta^2}$$

$$r = \frac{n_1}{n_2}$$

$$\Delta = \mu 1 - \mu 2$$

Where:

n: required minimum sample size in each group

μ: outcome in each group

σ: standard deviation in each group

z: z score

α: type I error, α = 0,05

β: type II error, β = 0,15 (statistical power = 0,85)

Based on Hsu-Dong Sun's group [1], sample sizes for each variable are as follows

Variables	4-port	1-port	Sample size
Bowel recovery time	6,2 ± 1	7,2 ± 1,4	24
Blood loss	125 ± 156,9	335 ± 104	50
Visual analogue scale	3 ± 0,5	3,6 ± 0,6	14

The investigators anticipate to obtain the sample size of 50 for each group.

3. Aims and objectives

The aim is to compare the effectiveness and safety of single-port versus traditional multi-port laparoscopic surgery in the treatment of ectopic pregnancy. Specifically, the surgical effectiveness will be evaluated via beta-hCG values, ultrasound imaging, and rate of switching to open surgery. The surgical safety will be evaluated via surgical time, blood loss, pain intensity, and surgical complications.

4. Outcomes

The primary outcomes of interest are the amount of blood loss during surgery, and surgical time. Secondary outcomes include pain intensity as indicated by visual analogue scale, surgical complications such as organ damages and surgical site infections, hospital stay, and pneumoperitoneum. The primary outcomes will be evaluated immediately post-surgery while the secondary outcomes will be evaluated within 4 weeks post-surgery by qualified practitioners.

5. Populations and subgroups to be analyzed

Populations: intention-to-treat
Subgroups: single-port versus multi-port group. These 2 subgroups will be analyzed using intention-to-treat populations.

6. Analyses

Data will be analyzed using Stata 16 (StataCorp LLC, College Station, TX). Normally distributed data will be expressed as mean ± standard deviation, while non-normally distributed data will be shown as medians with interquartile ranges. T-test for normally distributed continuous variables and Mann-Whitney-U test for non-normally distributed continuous variables will be used to compare between groups. Categorical variables will be reported as absolute numbers and percentages; the Chi-square test or Fisher's exact test will be utilized for comparison A p-value of <0.05 will be considered statistically significant.

7. References

[1] Sun, Hsu-Dong, et al. "Comparison of single-port and three-port laparoscopic salpingectomy in the management for tubal pregnancy." *Journal of the Chinese Medical Association* 81.5 (2018): 469-474.