Treatment rationale and design of a phase I single-arm open trial of a modified vaginal pipe for use in total laparoscopic hysterectomies

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Study protocol

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Abstract

Background: The Vagi-Pipe® is a useful device for performing total laparoscopic hysterectomy. The conventional model of the Vagi-Pipe® is unable to grasp the uterus during colpotomy for recovery of the resected uterus. However, the modified C-Type Vagi-Pipe® model has a shape that allows insertion into the vagina without removing the uterus manipulator. This study aimed to prospectively investigate the safety and efficacy of the C-Type Vagi-Pipe® in total laparoscopic hysterectomies.

Methods: A total of 25 female subjects between 20 and 60 years old with uterine fibroids or adenomyosis will be included in this study. Patients with complications considered unsuitable for this study by the investigators will be excluded. The C-Type Vagi-Pipe® will be used rather than the conventional Vagi-Pipe® when performing total laparoscopic hysterectomy. The primary outcome will be safety, and the secondary endpoints will be operation time, bleeding volume, and presence of complications. The protocol was approved by the institutional review board of Kyoto Prefectural University of Medicine. In accordance with the Declaration of Helsinki, written informed consent will be obtained from all patients before registration.

Discussion: This study seeks to confirm the safety and effectiveness of the C-Type Vagi-Pipe® for total laparoscopic hysterectomy. Once confirmed, the introduction of the C-Type Vagi-Pipe® is expected to make the total laparoscopic hysterectomy procedure easier to perform and thereby allow it to be performed in many more medical facilities. Results of the study will be disseminated via publications in peer-reviewed journals.

Trial registration: Japan Registry of Clinical Trials (jRCT), jRCTs052180221. Registered 18 March 2019 - Retrospectively registered, https://jrct.niph.go.jp/search

Background

Total laparoscopic hysterectomy (TLH) is becoming the standard radical surgical procedure for the treatment of common uterine tumors, such as fibroids and adenomyosis. Compared to open surgery, TLH is superior in terms of the degree of invasiveness and in terms of cosmetic concerns, but it requires advanced surgical skills, including those for a colpotomy.[1]

The Vagi-Pipe® is a widely used device when performing colpotomy as part of TLH. For the standard procedure of TLH, a uterus manipulator is inserted through the cervix into the uterine cavity to manipulate the uterus. This reduces the difficulty of the surgery. During colpotomy, the Vagi-Pipe® is inserted into the vagina to stretch the vaginal wall and clear the incision line. However, the uterus manipulator must be removed prior to insertion of the conventional model Vagi-Pipe®. The conventional model is unable to grasp the uterus, requiring more effort to manipulate the uterus during colpotomy and recovery of the resected uterus through the vagina.

The C-Type Vagi-Pipe® has a modified shape that allows it to be inserted into the vagina simultaneously with a uterus manipulator grasping the uterus. The uterus manipulator does not have to be removed beforehand. Therefore, the C-Type Vagi-Pipe® allows the manipulated uterus to be anteflexed and retroflexed during colpotomy and recovery procedures. This functionality can lead to reduced difficulty of the surgical procedure.

In this study, we seek to confirm the safety and effectiveness of the C-Type Vagi-Pipe®. If the safety and effectiveness are confirmed, introduction of the C-Type Vagi-Pipe® is expected to allow TLH to be performed at many more medical facilities, as it would make the procedure easier to perform.

Methods/design

Study Design

The study is a single-arm open trial. The primary endpoint is safety. The secondary endpoints are operation time, bleeding volume, and presence of complications.

Study setting

The protocol was approved by the Clinical Research Review Board at the Kyoto Prefectural University of Medicine. In accordance with the Declaration of Helsinki, written informed consent will be obtained from all patients before registration. At least annual independent monitoring is planned, in accordance with the Japanese clinical trial guidelines.

Participants

The inclusion criteria are as follows:

(1) Patients with clinically confirmed uterine fibroids

(2) Patients with clinically confirmed uterine adenomyosis

(3) Patients able to accept surgical treatment

(4) Patients capable of participating in this study for at least a 1-week hospital stay or corresponding management

(5) Patients who are between 20 and 60 years of age at the time of enrollment

(6) Patients who provide written informed consent to participate in the study

The exclusion criteria are as follows:

(1) Patients with malignant tumors

(2) Patients with infectious disorders requiring treatment with antibacterial drugs or antimycotics

(3) Patients with uncontrollable diabetes mellitus

(4) Patients who have complications of clinical concern (such as uncontrollable cardiac disease, severe cardiac arrhythmia requiring medical treatment, and sustained digestive diseases)

(5) Any other patients who are regarded as unsuitable for this study by the investigators

Treatment regimens

In this study, we will utilize the C-Type Vagi-Pipe® rather than the conventional Vagi-Pipe® when performing TLH. The C-Type Vagi-Pipe® has an improved morphology consisting of a tube structure with an opening only at the tip of the pipe (Fig. 1). This allows the device to be inserted into the vagina and then into the uterus along with the uterus manipulator.

Power Calculations

The conventional Vagi-Pipe® model has been classified as a Class I device in terms of the risk it poses to the human body. However, its safety has never been verified via a clinical study. The C-Type Vagi-Pipe® has not been subjected to a multicenter clinical study and assessments of its safety and other features have yet to be performed. As a result, its use in Japan is not yet approved. To our knowledge, this will be the first clinical study on the C-Type device in humans conducted in Japan. It is, therefore, a pilot study whose primary endpoint is safety. The incidence of complications reported following a TLH is approximately 1.5%.[2] Therefore, we calculated that 23 subjects will be required to assess the safety of the device with a reliability of 95% and an error of within 5%.

Statistical methods

For this study, safety is defined as grade and frequency of each adverse event. Operation time is defined as the total surgery time. Bleeding volume is defined as the total amount of blood loss during surgery. Presence of complications involves grade and frequency of each complication.

Population to be analyzed

We will analyze all subjects enrolled in this study, who will comprise the full analysis set (FAS). The study subjects, excluding patients with serious violations, such as serious protocol deviation, violation of inclusion/exclusion criteria, and violation of prohibited concomitant medication/therapy from the FAS,

will be also analyzed per protocol. Moreover, subjects in the FAS in which the protocol treatment is provided at least once will be evaluated for the safety analysis set.

Discussion

The current standard surgical procedure used in cases of benign uterine diseases is TLH, and its indications are to be expanded to include uterine malignancies, such as uterine and cervical cancers.[1, 3] Furthermore, robot-assisted laparoscopic hysterectomy (LH) has been performed in recent years, which also marked the expansion of laparoscopic surgeries.[4, 5] Nevertheless, the current number of facilities capable of performing TLH on malignancies or robot-assisted LH remains limited.[6] One reason for this limitation is that the entire surgical team, including the surgical assistants, must have a certain level of expertise in the TLH procedure.

During TLH, the second surgical assistant manipulates the uterus using the uterus manipulator. When performing colpotomy in TLH, the uterus is displaced in the cranial direction while simultaneously maintaining a fixed degree of tension on the incision line on the vaginal wall to allow for a keen incision. However, this process can be quite difficult to perform without the uterus manipulator.

The morphology of the modified vaginal pipe utilized in this study is different from that of the conventional model, as the modified vaginal pipe does not have a perfect cylindrical shape. Only the tip has a cylindrical shape with a space on the side, making it C-shaped. This space allows the uterus manipulator to pass through along the side of the modified vaginal pipe, allowing the device to be used in the same way as the conventional device but does not require removal of the uterus manipulator prior to insertion. This modification allows the uterus manipulator to grasp the uterus during colpotomy and recover the uterus. It may lead to greater uterine mobility, making it easier for the first surgical assistant to ensure the surgical field, allowing the surgeon to make the vaginal wall incision and the recovery of the resected uterus with less difficulty. As a result, the use of the modified vaginal pipe may allow the conventional TLH to be more easily performed with shorter surgical duration, decreased blood loss, and fewer complications.

If this study shows that the modified vaginal pipe is safe, TLH may be performed more safely and with less difficulty using this device. This may encourage larger numbers of medical facilities to adopt TLH.

Trial Status

This study opened to recruitment in July 2016, with a planned last follow-up in March 2020. As of September 2019, eight subjects have been enrolled.

Abbreviations

TLH: total laparoscopic hysterectomy

LH: laparoscopic hysterectomy

FAS: full analysis set

Declarations

Ethics approval and consent to participate

The trial received ethical approval from the Ethics Committee of Kyoto Prefectural University of Medicine, Kyoto, Japan (number: ERB-C–609–3, the last edition ver 2 17/Jun/2016). The trial is subject to the supervision and management of the Ethics Committee.

Consent for publication

As per the Declaration of Helsinki, written informed consent will be obtained from all patients before registration.

Availability of data and materials

The authors make every effort to grant all reasonable requests for access to data and materials.

Competing interests

The authors have no competing interests to declare.

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Authors’ contributions

F. I. and J. K. conceived and designed the study; F. I., T. K., H. M., A. K., and I. K. performed the study; F. I., T. M., and J. K. will analyze the data and interpret the results of the study; F. I., T. M., and J. K. edited and revised the manuscript. All authors have read and approved the manuscript.

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Figures

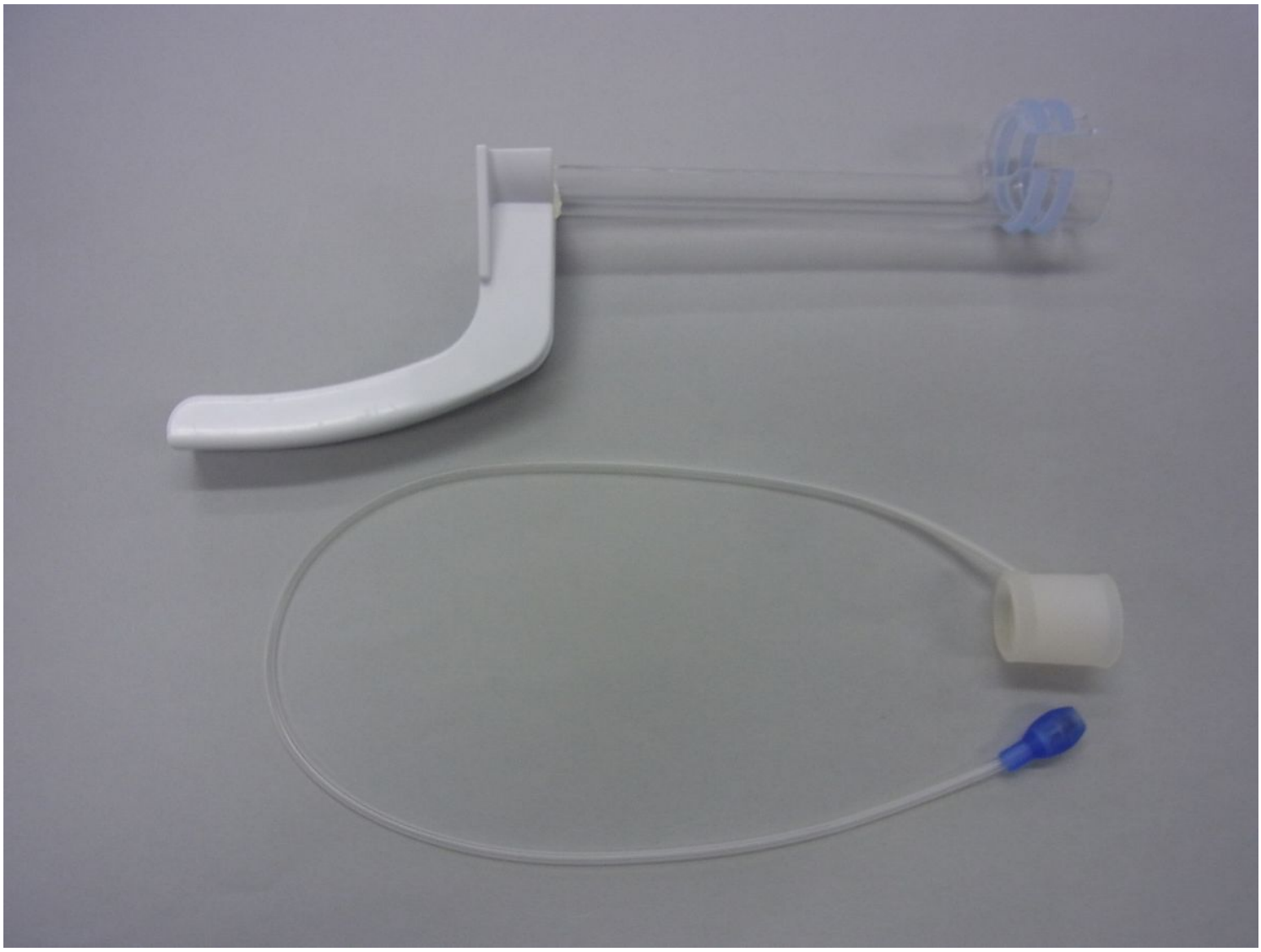

Figure 1

The C-Type Vagi-Pipe®