

Cover Page for Protocol

Official Study Title:	Patient Factors Associated with Fragmentation of Copper Intrauterine Devices Requiring Hysteroscopic Removal
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University of Kansas Medical Center
RESEARCH PROTOCOL INVOLVING HUMAN SUBJECTS
TEMPLATE WITH GUIDANCE

Version date: 5/14/2024

Principal Investigator: irb

Study Title: Patient Factors Associated with Fragmentation of Copper Intrauterine Devices Requiring Hysteroscopic Removal

Co- Investigator(s): Dylan Vance, Olivia Pruss, Megan Geraghty, Sierra Reed

I. Purpose, Background and Rationale

A. Aim and Hypotheses

1. This study aims to define potential patient risk factors and associations with Copper IUD fragmentation upon removal that require hysteroscopy evaluation. We hypothesize that patients with uterine anatomic abnormalities and increased duration of ParaGard use will have higher associations with fragmentation requiring hysteroscopic removal. The results of this study may improve patient counseling of risk factors for Copper IUDs and provider understanding of IUD fragmentation

B. Background and Significance

1. Intrauterine devices (IUD) have been increasing in popularity as a contraception method over the past twenty years.¹⁻² Specifically, the copper IUD, known by its brand name ParaGard, is a non-hormonal IUD. While there is substantial evidence to support its efficacy and safety in patients, there are side effects and complications of its placement, utilization, and removal. Among these includes increased menstrual bleeding, discomfort, and possible perforation.³ The ParaGard IUD shares some of the same side effects and complications of hormonal IUDs such as Mirena, Liletta, Skyla, and Kyleena. However, fragmentation was disproportionately reported for copper IUDs when compared to hormonal IUDs.⁴⁻⁵ Regardless of how the breakage occurs, the broken fragments remain inside the uterus and may become embedded in the uterine wall. Removing the broken pieces can be painful, invasive, and even life-altering.⁶⁻⁷ Anecdotally, there have been cases within the University of Kansas Health System where patients have their ParaGard IUD removed and experience fragmentation necessitating hysteroscopy. This motivation in conjunction with our literature reviewing motivated the authors to further explore this topic. There are no studies identifying what patient factors contribute to fragmentation, and this study will provide valuable insight into this phenomenon.

C. Rationale

1. Latack & Nguyen reported a disproportionate breakage in copper versus hormonal IUDs through their study, however, they did not assess patient factors associated with breakage.⁴ Vitale et al. reported that the Copper IUD was the most common intracavitary retained and fragmented device among hysteroscopic removals.⁵ There are also various case series reporting fragmentation with lack of insight into potential etiologies.⁷ This should be disclosed by all IUD manufacturers if this is a known risk. This study can help determine if there are other factors that could be contributing to increased fragmentation or breakage to guide patient counseling.

II. Research Plan and Design

A. Study Objectives:

- a. To characterize and analyze the clinicopathologic factors of patients found to have IUD fragmentation requiring hysteroscopic removal.

B. Study Type and Design: The proposed study will be a retrospective chart review at KUMC to identify factors associated with IUD fragmentation/retention. Data will be collected and stored in the secure KUMC REDCap database. Patient charts that meet inclusion criteria will undergo review and extraction of relevant data points including demographic information, IUD characteristics, co-morbidities, IUD imaging findings, & pre-, intra-operative, and post-procedural information. These data points will be compared, and the analysis will allow for conclusions to be made regarding any common characteristics between patients who experienced IUD fragmentation requiring hysteroscopic removal.

C. Sample size, statistical methods, and power calculation

1. The maximum sample size will be a maximum of 700 patients. There will be no blinding or randomization of participants.
2. All power calculation and statistical analysis will be performed by KU employed biostatisticians. Characteristics of the study sample will be summarized using descriptive statistics (means, frequencies). The association between patient characteristics and IUD fragmentation will be assessed via bivariate logistic regression.

D. Subject Criteria (See Vulnerable Populations appendix, if applicable):

1. Inclusion criteria: Any patient who underwent IUD removal that required subsequent hysteroscopy to retrieve retained fragments of IUD in the last 20 years.
2. Exclusion criteria: <18 years old, patients who undergo IUD removal without requiring hysteroscopy, patient who undergo IUD removal without fragmentation of device, patients who do not undergo IUD removal.
3. Withdrawal/Termination criteria: N/A
4. Study subjects may participate in another research study while participating in this research study.

E. Specific methods and techniques used throughout the study

1. Study Procedures: N/A
2. Laboratory Tests: N/A
3. There are no validated instruments, medical procedures, or tests being utilized for the proposed project.
4. No body components utilized in the study.
5. Timeline: Upon IRB approval and obtaining data from HERON request, chart review will take about 2 months. Data analysis is expected to take around 2 months. Abstracts will be submitted to a national reproductive and gynecologic conference. Upon presentation of abstract data, a manuscript will follow.

F. Risk/benefit assessment:

1. Physical risk: N/A
2. Psychological risk: N/A
3. Social risk: N/A
4. Economic risk: N/A

5. Potential benefit of participating in the study
 - a. to the individual subject and/or parent if any: N/A
 - b. to the population from which the subject is drawn: to identify associated factors that predispose patients to an increased likelihood of IUD fragmentation and retention during removal.
 - c. to science, society, and humanity in general: to identify associated factors that predispose patients to an increased likelihood of IUD fragmentation and retention during removal to guide future counseling of patients.

G. Location where study will be performed: Research team will conduct chart review on-site at the University of Kansas Medical and remote locations via secure connection to KUMC server.

H. Collaboration (with another institution, if applicable): N/A

I. Community-Based Participatory Research (if applicable): N/A

J. Personnel who will conduct the study, including:

1. Indicate, by title, who will be present during study procedure(s):
 - a. Dylan Vance (Medical Student)
 - b. Olivia Pruss (Medical Student)
 - c. Megan Geraghty (Medical Student)
 - d. Dr. Neha Singh, DO (Resident doctor, Department of Obstetrics and Gynecology)
 - e. Dr. Annabel Mancillas, MD MPH FACOG, Assistant Professor of Obstetrics & Gynecology (Principal investigator)
2. Primary responsibility for the following activities, for example:
 - a. Determining eligibility: Dylan Vance (Medical Student), Olivia Pruss (Medical Student), Megan Geraghty (Medical Student), Dr. Annabel Mancillas, MD (Principal investigator)
 - b. Obtaining informed consent: Dylan Vance (Medical Student), Olivia Pruss (Medical Student), Megan Geraghty (Medical Student), Dr. Neha Singh, Dr. Annabel Mancillas, MD (Principal investigator)
 - c. Providing on-going information to the study sponsor and the IRB: Dylan Vance (Medical Student), Olivia Pruss (Medical Student), Megan Geraghty (Medical Student), Dr. Neha Singh, Dr. Annabel Mancillas, MD (Principal investigator)
 - d. Maintaining participant's research records: Dylan Vance (Medical Student), Olivia Pruss (Medical Student), Megan Geraghty (Medical Student), Dr. Neha Singh, Dr. Annabel Mancillas, MD (Principal investigator)
 - e. Completing study data forms: Dylan Vance (Medical Student), Olivia Pruss (Medical Student), Megan Geraghty (Medical Student), Dr. Neha Singh, Dr. Annabel Mancillas, MD (Principal investigator)

- f. Managing study database: Dylan Vance (Medical Student), Olivia Pruss (Medical Student), Megan Geraghty (Medical Student), Dr. Neha Singh, Dr. Annabel Mancillas, MD (Principal investigator)

K. Assessment of Subject Safety and Development of a Data and Safety Monitoring Plan – N/a

1. Please note that any study proposal with more than minimal risk must include a data and safety monitoring plan. Elements of the plan include:
 - a. Persons/groups who will review the data (study team; independent safety monitor, data monitoring committee or formal DSMB)
 - b. Data/events that will be reviewed
 - c. Frequency of review
 - d. Types of analyses to be performed
 - e. Safety-related triggers that would cause the PI to stop or alter the study
2. Describe how adverse events and unanticipated problems will be ascertained and handled. Explain exactly which type of problems will be considered serious and reported to the IRB. The reporting timeframe should also be detailed.
3. Explain exactly what will happen if a patient experiences an adverse event or other problem (for example, will discontinue study participation).

III. Subject Participation

A. Recruitment:

1. Subjects will be recruited from KUMC via chart query using ICD-10 codes and CPT codes. No other institutions will be involved.
 - 1 CPT Code:
 - a) 58562 Hysteroscopy, surgical; with removal of impacted foreign body
 - 2 ICD-10 Codes:
 - a) Z53.8 Procedure and treatment not carried out for other reasons
 - b) Z30.432 Encounter for removal of intrauterine contraceptive device
 - c) T83.32 Displacement of intrauterine contraceptive device
 - d) Z30.431 Encounter for routine checking of intrauterine contraceptive device
 - e) T83.9XXS Unspecified complication of genitourinary prosthetic device, implant of graft, sequela
 - f) T83.9XXA Unspecified complication of genitourinary prosthetic device, implant of graft, initial encounter
 - g) T83.9XXD Unspecified complication of genitourinary prosthetic device, implant of graft, subsequent encounter
 - h) T83.39 Other mechanical complication of intrauterine contraceptive device
2. Queries for participants will be requested in Heron by Dylan Vance.
3. There will be no advertisements or fliers utilized to recruit participants.
4. There will be no recruitment letter or introductory statement.

B. Screening Interview/questionnaire: N/A

C. Informed consent process and timing of obtaining of consent: N/A

D. Alternatives to participation: N/A

E. Costs to Subjects: N/A

F. How new information will be conveyed to the study subject and how it will be documented: After completion of the study, de-identified data and results will be shared with participants via publication of research results.

G. Payment, including a prorated plan for payment: There will be no payment for participation in this study.

H. Payment for a research-related injury: N/A

IV. Data Collection and Protection

A. Data Management and Security:

1. Principle and co-investigators will be the individuals with access to the study data. Individual subjects will be identified by their UKHS medical record numbers during the initial chart review and data collection phase. Once eligibility for the study is confirmed and unidentifiable data points have been extracted from the subject's medical record, the MRN will be removed from the subject's research record. After initial chart review and data collection, the study subjects will no longer be identifiable directly or indirectly.
2. Study data will be compiled and stored in a secure RedCap database.
3. All patient information will be deidentified.
4. Data will be linked to subjects via record number assigned through REDCap.
5. All data will be stored in REDCap.
6. There will be no mobile devices utilized for data collection or storage.
7. No identifiable or de-identified data will be sent outside of KUMC.

B. Sample / Specimen Collection: N/A

C. Tissue Banking Considerations: N/A

D. Procedures to protect subject confidentiality: Subject confidentiality will be protected via data collection taking place in the secure KUMC REDCap. Patients will be de-identified for analysis. Only members of the team as listed above will have access to this database.

E. Quality Assurance / Monitoring

1. To ensure that the collected data is accurate, consistent, complete and reliable, Dylan Vance, Olivia Pruss, and Megan Geraghty will provide audits of data. There are no plans to have ongoing third-party monitoring.

V. Data Analysis and Reporting

A. Statistical and Data Analysis: All statistical and data analysis to be performed by KU Medical Center biostatisticians. Data will be analyzed via Chi-square or Fisher exact tests for categorical variables, and two-sample paired t-tests or Wilcoxon rank sum tests for continuous variables.

B. Outcome: Data from the research will be utilized to inform and validate current and future practice patterns and lead to improved patient outcomes in the future.

C. Study results to participants: N/A

D. Publication Plan: This research will be submitted for presentation at an upcoming meeting, anticipated regionally and/or nationally. All data will be presented in aggregate without identifying information. A manuscript will be prepared for submission to be considered for publication in relevant reproductive health obstetrics and gynecology journals.

VI. Bibliography

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APPENDIX I: VULNERABLE POPULATIONS – N/A

- I.** If the recruitment plan includes any of the groups noted below, explain how they will be protected and how consent will be obtained. In general, regulations allow subjects identified as part of vulnerable populations to be included if the research cannot be accomplished without their involvement.
- II.** Cognitively or decisionally impaired individuals: N/A
- III.** Children: N/A
- IV.** Pregnant women: N/A
- V.** Prisoners: N/A
- VI.** Students and/or Employees: N/A