Randomized controlled trial comparing adult to pediatric colonoscope in obese patients.

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Background

A colonoscopy is a routine procedure performed daily for various purposes, including colon cancer screening. Over time, colonoscopes have evolved and now come in different sizes, diameters, and flexibility levels. The choice of colonoscope typically depends on the endoscopist's preference, and anecdotal experience, with all types of instruments considered standard practice.

Several patient characteristics can make routine colonoscopy more challenging, such as diverticulosis and a history of previous surgeries, especially in the pelvic area. These challenging cases might influence the provider to choose one instrument over another, although there is a general lack of evidence demonstrating the superiority of specific colonoscopes in certain situations.

Obesity is one of the challenges encountered during routine colonoscopy. A retrospective study showed no difference in the performance of adult and pediatric scopes when matching the population's BMI. However, providers tend to choose adult scopes for higher BMI patients in unmatched populations. We designed this study to evaluate if adult and pediatric colonoscopes perform differently in obese patients, which both are considered standard practice in the study population.

Study objective.

The objective of this equivalence trial is to evaluate whether pediatric and adult colonoscopes achieve similar success rates in obese patients undergoing colonoscopy. Patients will be randomly assigned in a 1:1 ratio. The primary endpoint is the success rate of colonoscope completion without switching instruments (defined in the main protocol).

Study hypothesis.

There is no significant difference between adult and pediatric colonoscopes in the evaluation of obese patients.

Study design.

Prospective randomized single-blinded Equivalence trial

- ➔ The patient is blinded regarding the instruments used.
- ➔ The endoscopist is not blinded. blinding is not feasible as the endoscopist would recognize the different instrument dimensions before the procedure.

Primary outcome

A composite of reaching the cecum, requiring less than 10 min for cecal intubation, without changing the scope type.

Secondary outcome

- ➔ cecal intubation rate (CIR)
- ➔ Terminal ileum intubation rate (TIIR): The provider will attempt terminal ilium in every patient for at least 2 minutes and up to 5 min.
- ➔ Insertion time (IT): time from insertion photo, to first cecal photo
- ➔ Ancillary maneuvers use (position change, pressure application, increase stiffness)
- ➔ Withdrawal time: time from terminal ileum ilium picture or last cecal picture and rectal picture – 1 min per each intervention (polypectomy, cauterization…etc.)

Inclusion criteria

- BMI >30
- Screening and surveillance colonoscopy
- Male or female
- Age equal or more than 18 years

Exclusion criteria

- Colon surgery
- Therapeutic colonoscopy
- Inflammatory bowel disease
- Terminated procedure due to stool burden, stenosis, or obstructive mass.
- Colonoscopy for anemia
- History of incomplete colonoscopy due to technical difficulties

Randomization:

We will use the sealed envelope method for simple, stratified, randomization.

- Before the recruitment starts, we will prepare opaque sealed envelopes with a 1:1 ratio between the study groups, each envelope will have a serial number.
- On the day of the procedure, the endoscopist will be provided with a few envelopes (randomly selected serial numbers), he will choose one randomly and open it.
- All envelopes prepared before the recruitment process will be used during the study to ensure complete randomization and a 1:1 ratio between the study groups.
- The randomization will be stratified by providers performing the colonoscopy to ensure that each provider gets an equal assignment to both study groups to eliminate the bias that different providers' performances can introduce.

Study Operation:

1) Patient Invitation

- The research team will review the endoscopy schedule 1-2 weeks before the procedure date.

- All eligible candidates who meet the inclusion criteria will be invited to participate in the study.
- Candidates will be invited through A MyChart message or a mailed letter from the office of the provider performing the procedure.

2) Patient Consent

- The research coordinator will call the patient within 48 hours of sending the invitation. During this call, the study will be explained, and the consent process will be discussed (phone scripts attached). DocuSign will be used to send the consent form virtually. The patient will have 1-2 days to review the consent before a follow-up call is made.
- Patients who are interested in participating in the study, can elect to defer signing the paper consent to the day of the procedure.

Consent procedures for Patients at Coral Springs Family Health and Surgery Center

- For the patients who have not signed consent via DocuSign the endoscopist will obtain the signature for the consent prior to the procedure.
- Then the study coordinator will open the sealed envelope and communicate colonoscope randomization to the provider.
- The endoscopist will return the signed consents to the study coordinator when they are in Weston.

3) Colonoscopy

- Endoscopists participating in the study will be informed in advance of the candidate's scheduled procedure date.
- Patients will receive the usual pre-procedure care before the endoscopy.
- The endoscopist will randomly select a sealed envelope to determine the patient group and assign the type of colonoscope.
- As part of routine care, the endoscopist will capture photo documentation during the procedure, including insertion with time, cecum with time, terminal ileum with time, and end procedure with time.
- If the endoscopist is unable to intubate the terminal ileum, a second cecal photo will be taken before withdrawal.
- The endoscopist will document any additional maneuvers used, such as scope stiffening, changing patient position, applying pressure, or changing the scope.

- A brochure will be displayed near the computers used for procedure note documentation to remind providers of the required documentation elements after the procedure (attached).
- A research team member will retrospectively collect the study's primary and secondary outcomes from the endoscopy report and store them in REDCap.
- The patient's participation in the study will conclude at the end of the procedure.
- Trainees will not participate in the study procedures.

Electronic Consent Process

- An investigator or research coordinator will contact the invited candidates by phone one week before the scheduled procedure. The study's purpose, intervention, and consent process will be discussed during this call, which will be documented in the patient's chart.
- Patients interested in participating will receive the consent form through DocuSign, with instructions on how to complete it online.
- A follow-up phone call will be made 1-2 days later to answer any questions the patient may have.

Rationale for Electronic Consent (E-Consent)

- Many procedures are scheduled through open access, meaning the patient is scheduled by a provider other than the one performing the procedure, often from a different department. In these cases, the patient may not meet the performing physician until the day of the procedure.
- E-consent allows patients more time to consider participation without the pressure of deciding on the day of the procedure.

Sample size calculations

Assuming a 93% success rate in both arms and no true difference between colonoscope types, we aim to test statistical equivalence using a two-sided type I error of 0.05 and power of 80%. A 10% margin (±0.10) in success rate is considered clinically acceptable and forms the basis for the equivalence hypothesis:

$$H_0: |p_1 - p_2| \geq 0.1$$

$$H_1: |p_1 - p_2| < 0.1$$

Based on these assumptions, a fixed sample size of 112 participants per group (total N = 224) is required. To preserve operating characteristics under the group sequential framework, the maximum sample size is inflated by an estimated factor of 1.082, yielding a maximum of 122 participants per group (total N = 244). The interim analysis will occur after enrollment of 122 participants (61 per group). (Group Sequential Methods with Applications to Clinical Trials by Jennison and Turnbull (pages 149–150) [2].

Study Variables

Date of birth, gender, race, BMI, previous pelvic\abdominal surgery, diverticulosis, colon prep (adequate- inadequate), type of colonoscopy, insertion time, cecum and terminal ileum intubation success, and procedure time. Please refer to the data collection sheet for details of the variables above.

Data Analysis

All statistical analyses will be conducted by a statistician from the Cleveland Clinic’s Quantitative Health Sciences (CCF QHS) team, following the intention-to-treat (ITT) principle. This means that all randomized patients who receive one of the study interventions will be included in the primary analysis.

Baseline characteristics will be assessed for balance using standardized mean differences (SMDs), with a value less than 0.10 (absolute) indicating acceptable balance.

Missing data in baseline variables are expected to be minimal. If more than 5% of data are missing for any key variable, multiple imputation methods will be employed.

The primary outcome—successful completion of the colonoscopy (Yes/No)—will be analyzed as a binary endpoint. The effect of colonoscope type (adult vs. pediatric) will be evaluated using the Two One-Sided Tests (TOST) procedure, with a pre-specified equivalence margin of ±10%. The absolute risk difference of 10% will also be translated into corresponding thresholds for odds ratios (OR = 2.72 or OR = 0.36) and relative risks (RR = 1.12 or RR = 0.893). Both unadjusted and adjusted logistic regression models, incorporating pre-specified covariates, will be used to estimate treatment

effects. Results will be presented as risk differences, relative risks, and odds ratios, with 95% confidence intervals derived via the g-computation method. Equivalence will be declared if the full confidence interval lies entirely within the specified equivalence range on each metric.

A per-protocol analysis will be conducted as a sensitivity analysis if there is substantial non-compliance. Additional sensitivity analyses will be considered to address missing data in outcome variables.

Secondary outcomes including cecal intubation rate (CIR), terminal ileum intubation rate (TIIR), insertion time (IT), use of ancillary maneuvers, withdrawal time, are considered independent of the primary outcome. Categorical secondary outcomes will be compared using chi-squared or Fisher’s exact tests, while continuous variables will be analyzed using two-sample t-tests or Wilcoxon rank-sum tests as appropriate. Regression models adjusting for pre-specified covariates will also be considered.

Repeatedly measured outcomes will be analyzed using mixed-effects models, with study group and time point included as fixed effects, and subject ID as a random effect to account for within-subject correlation. This approach is robust to data that are missing at random (MAR) or missing completely at random (MCAR).

Data Security

Data, including patient information and consent, will be stored electronically in the Redcap system\DocuSign which is password-protected and on the secure Cleveland Clinic network. If physical paper sheets were used, the physical paper sheets' information would be transferred to Redcap and shredded on the day of data gathering.

Interim analysis

A group sequential design with a single interim analysis at 50% enrollment is proposed. This design allows early trial termination for either efficacy (equivalence) or futility (non-equivalence), while preserving the overall type I error ($\alpha = 0.05$) and power ($1 - \beta = 0.80$).

The design employs Hwang-Shih-DeCani gamma error spending functions [1]:

- Type I error: γ = –4 (O’Brien-Fleming–like)
- Type II error: γ = 1 (Pocock-like)

Analysis Stage	Type I Error Spending (Cumulative)	Type II Error Spending (Cumulvative)
Interim (50%)	0.00596	0.124
Final (100%)	0.05	0.2

A non-binding futility boundary is used. Z-stopping-boundaries are shown below.

Analysis Stage	Equivalence upper	Equivalence lower	Non-equivalence upper	Non-equivalence lower
Interim (50%)	2.749966	-2.749966	1.152821	-1.152821
Final (100%)	1.959964	-1.959964	1.959964	-1.959964

Possible Harm to Subjects

Both study arms are considered standard treatment, and no anticipated harm is related to the study.