

*«Randomized clinical trial to compare Underwater Cold Snare Polypectomy (UCSP) to Conventional Cold Snare Polypectomy (CCSP) for non pedunculated colon polyps of size 5-10mm [COLDWATER study]»*

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## **A. ABSTRACT**

### **Background**

Colon cancer is internationally the third cause of deaths from a malignant disease. Screening colonoscopy in adults >45 years of age aims at the early diagnosis and treatment colon polyps that are precancerous lesions. Endoscopic polyp removal (polypectomy) can be done with various techniques depending on the size, morphology, location of the polyp etc. According to updated guidelines, non-pedunculated polyps of small size are treated with a cold snare in air dilated intestinal lumen (conventional cold snare polypectomy - CCSP). In recent years, several studies have described the benefits of water aided colonoscopy, as well as safety and efficacy of underwater polypectomy in large colon polyps. However, there is not enough data on small polyps which are the most commonly diagnosed.

### **Methodology**

This is a prospective randomized double-blind clinical trial to compare the safety and efficacy of CCSP to underwater cold snare polypectomy (UCSP) for non-pedunculated polyps of size of 5-10 mm. A total of 398 polyps will be randomized and randomization will be performed via random numbers method of Microsoft Excel 2016. Primary outcome of this study is to determine muscularis mucosa resection rate. Secondary outcomes are the depth and percentage of R0 excisions, complications and the recurrence rate in follow up endoscopy 6-12 months after polypectomy

### **Discussion**

We expect UCSP to ensure a higher muscularis mucosa resection rate and we attempt examine whether it achieves a deeper resection in the submucosal layer. We will also examine if there are differences in complications and recurrence rate between the two treatment groups. These results will provide useful data for the development of guidelines in polypectomy techniques for non-pedunculated polyps 5-10mm.

## PROTOCOL INFORMATION PAGE

### **Trial Title**

*Randomized clinical trial to compare Underwater Cold Snare Polypectomy (UCSP) to Conventional Cold Snare Polypectomy (CCSP) for non pedunculated colon polyps of size 5-10mm»*

### **Acronym**

COLDWATER STUDY

### **Trial Identification Number**

PN61759 (Medical School, National and Kapodistrian University of Athens)

### **Sponsor**

Athens Medical School, National and Kapodistrian University of Athens

### **Funding**

No

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# **1. BACKGROUND**

## **1.1. OVERVIEW OF UNDERWATER POLYPECTOMY**

Polyp removal during colonoscopy is carried out in a dilated colon lumen after air insufflation. However, using water infusion to dilate the enteric lumen instead of standard air insufflations has been associated with higher patient comfort, less dose of intravenous sedation and higher adenoma detection rate [1-5]. Underwater Polypectomy (UP) was first described as Underwater Endoscopic Mucosal Resection (UEMR) in 2012. The term “EMR” (Endoscopic Mucosal Resection) has been improperly used to describe this new method, due to its unique feature to create a natural separation between mucosal/submucosal and muscular layer of the colon wall. In conventional EMR such separation is achieved by submucosal injection (lifting). During Endoscopic Ultrasound examination of the colon, where water is infused as an acoustic window, Binmoeller noticed that the water driven partial dilation of the colon lumen causes a “floating” effect on the colon wall. This causes the mucosal and submucosal layers to create protrusions towards the lumen (resembling the Gastric rugae) and to move away from the underlying muscular layer. The latter appears to remain circular and retain its normal thickness. [6-7]. Also, water due to its higher refractive index compared to air increases the sensitivity of the endoscopy, causing an optical zoom effect of the mucosal architecture [7-8]. This increases the sensitivity of the endoscopic overview [7-8], improving identification of the lesion margins before polypectomy and of any residual lesion or recurrence after polypectomy [7, 9]. Another advantage of UP is that the colon is not fully dilated, making mucosal lesions more compact with polypoid configuration in comparison with the flatter appearance of the same lesions in a fully dilated colon. This allows the endoscopist to capture larger mucosal surface with the snare increasing the chance of en-block resection even in larger lesions (eg. flat polyps of 20-40mm) [10]. As a result of all the above, UP offers shorter resection time, lower cost due to the reduced use of disposable materials (injection needles, syringes, lifting agents), higher en-block resection rates (89% vs 73%)

in large lesions and higher rates of R0 resection (based on histology results) in comparison with the conventional EMR. [10-17].

## **1.2.OVERVIEW OF COLD VS HOT SNARE POLYPECTOMY**

UP has been applied in studies with colonic lesions >10mm and >20mm in particular. Nevertheless only 5% of the polyps found in everyday clinical practice are of large size with the majority of the polyps being smaller. In regard to small polyps European Guidelines recommend the use of Cold Snare (CS) over Hot Snare (HS) due to improved safety profile. [18] HSP can cause thermal injury of the vessels and of the colonic wall and lead to delayed bleeding (0,04%- 7,8%) [19-23], post polypectomy syndrome, abdominal pain or even perforation with the latter being a rare (1.4%- 1.5%), but clinically serious complication [24-25]. Complication risk after HSP is proportional to the polyp size, histological grade, use of antiplatelet agents and it is higher in Right Colon lesions [26-29]. Incomplete Resection Rate (IRR) in HSP is 6.8% based on CARE study [30]. Complete Resection Rate (CRR) using CSP (R0 resection proved on histology results) ranges from 32.9% to 96.6% in various studies, [31] with the highest rates being demonstrated in the most recent ones. [32-34] One disadvantage of CSP is that the depth of the vertical resection margin is shorter and that found in HSP. This is based on histological examination of the center of the resection specimen, where the muscularis mucosa layer is identified. This finding highlights the incomplete mucosal resection during CSP rendering the method suitable for resecting intraepithelial lesions. [35-36] A metanalysis in 2020 showed that using CSP for polyps up to 9mm IRR was 17.3% vs 14.2% when using HSP, [35] justifying the need for further research regarding the most suitable polypectomy method for this polyp group.

## **2.STUDY RATIONALE**

The aforementioned disadvantage has led many endoscopists to continue to use HS for the removal of small polyps despite the increased risks associated with the electrocautery. [36-37] In order to overcome the relatively short vertical resection margin found in CSP, UCSP has emerged given the theoretical advantage of improved complete polyp resection. Both the safety and efficiency of UCSP has been shown in a study published in Digestive Endoscopy in 2019. This study included 209 adenomatous colon lesions removed by UCSP which were compared with lesions removed previously by conventional CSP where air insufflation had been used to dilate the colon lumen. [38] The vast majority of colon polyps however were microscopic <5mm (157/209, 75.1%) and the rest were 6-8mm in size (52/209, 24.9%). The study showed that both techniques were equally safe, but R0 resection rate was 80.2% for UCSP vs 32.7% for CCSP respectively (p<0.001). The percentage of mucosal layer per polyp removed was 50% vs 35.3% (p= 0.015), in UCSP and CCSP respectively, while the presence of submucosa in the removed polyps was found to be 20.8% in UCSP and 12.9% in CCSP. The rate of R0 resections in this study was calculated similar to the rate of R0 resections with HSP as described in other studies. [38]

## **2.1. STUDY HYPOTHESIS**

Underwater cold snare polypectomy ensures a higher muscularis mucosa resection rate than conventional cold snare polypectomy

## **3. STUDY OBJECTIVES**

The aim of this study is to compare the safety and efficacy between the two endoscopic polypectomy techniques (UCSP vs CCSP) regarding resection of non-pedunculated colon polyps with size 5mm to 10mm

### **3.1. PRIMARY OBJECTIVE**

Primary outcome of the study is the investigation of the difference in the rate of area containing muscularis mucosa (%) between the two polypectomy techniques.

### **3.2. SECONDARY OBJECTIVES**

Investigation of the difference at the following points between UCSP and CCSP group

- Presence or absence of submucosal in the specimen and its depth (if present)
- R0 Resection Rate (R0RR)
- Incomplete Resection Rate (IRR)
- Complication rate
- Residual lesion rate during repeat colonoscopy in 12months

## **4. METHODS AND DESIGN**

### **4.1. STUDY DESIGN**

This is a prospective randomized, double-blind, controlled study to compare underwater cold snare polypectomy (UCSP) to conventional cold snare polypectomy (CCSP) for non-pedunculated colon polyps of size 5-10mm.

Prior to this study, the safety and effectiveness of the UCSP method was confirmed in the literature and by the experience of two qualified endoscopists of the General Hospital Sismanogleio in 35 patients who agreed to undergo UCSP.

### **4.2 STUDY SITES**

The Gastroenterology Department of General Hospital of Athens "Sismanogleio" will participate in this trial.

### 4.3. STUDY PATIENTS

Patients scheduled for colonoscopy will be prospectively screened for eligibility. The workflow is shown in Fig.4

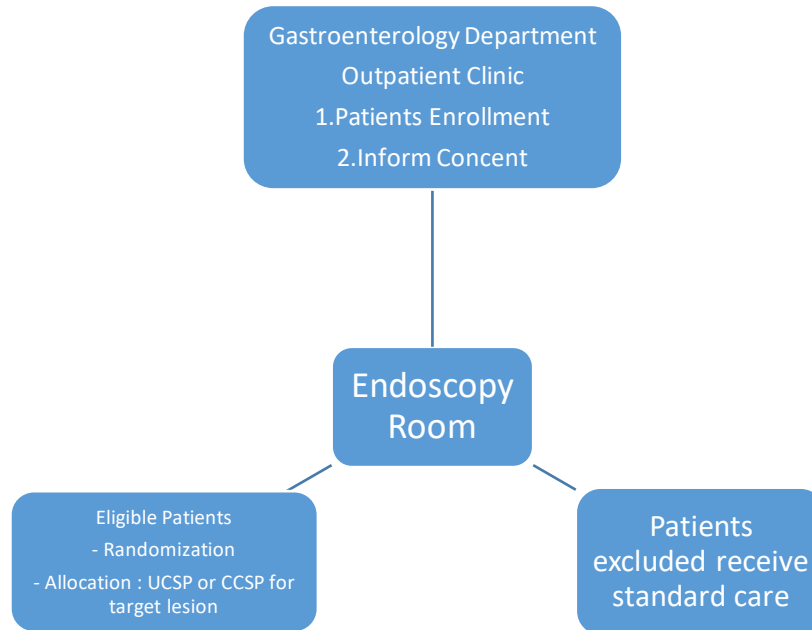


Figure 4. Study Workflow

#### 4.3.1. INCLUSION CRITERIA

The inclusion criteria for this study are:

1. Age > 20 years
2. Non pedunculated polyps (Paris classification Isp, Is, IIa, IIb)
3. Polyp size: diameter of 5 to 10mm
4. Endoscopic diagnosis of mucosal lesions – must not present malignant submucosal infiltration evidence (NICE 1, NICE 2A, BASIC)
5. Informed consent

Patients > 20 years of age with non-pedunculated polyps (Paris classification Isp, Is, IIa, IIb – figure 1) with a diameter of 5 to 10 mm. The endoscopic diagnosis of mucosal lesions will be based on their macroscopic appearance depending on the available equipment of the Endoscopy Department. Narrow-Band Imaging (NBI) findings or Blue Light Imaging (BLI) may be used. Endoscopic polypectomy will only be indicated for lesions that:

- ✓ According to the NICE (Narrow-Band Imaging International Colorectal Endoscopic Classification) are classified as type 1 or 2A. (Attached classification table - figure 2)



- ✓ According to the BASIC (Blue Light Imaging Adenoma Serrated International Classification) classification do not show evidence of malignant submucosal infiltration. (Attachment classification table - figure 3)
- ✓ Do not present macroscopic malignant submucosal infiltration evidence (deepening, ulceration / ulcer, abnormal vessels, irregular surface)

The size of the lesion will be determined according to its endoscopic appearance by comparing the lesion with the closed (2mm) or open (7mm) biopsy forceps and will be confirmed before resection by comparing it with the open snare (10mm).

Patients who receive antiplatelet / anticoagulant therapy are included in the study only if their treatment has been modified according to ESGE guidelines.

All patients will complete a written consent to participate in the study, after being thoroughly informed about the procedure.

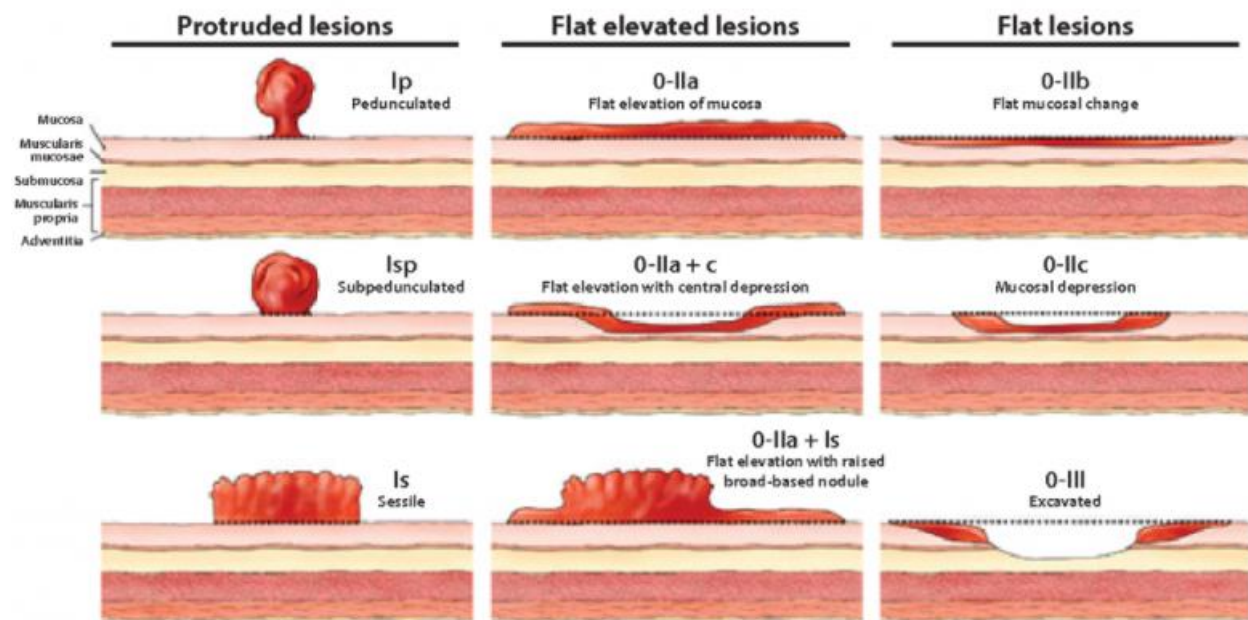


Figure 1 Paris classification for polyps

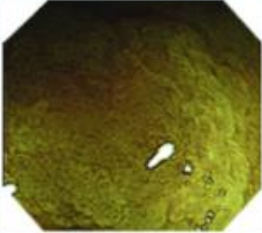
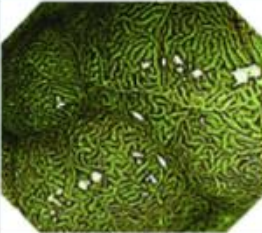

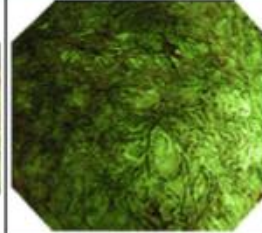
#### 4.3.2. EXCLUSION CRITERIA

The exclusion criteria for this study are:

1. Age <20 years old
2. Pedunculated polyps
3. Lesions with macroscopic elements of high-grade dysplasia or submucosal infiltration
4. Sites with previous polypectomy
5. Patients with idiopathic inflammatory bowel disease
6. Patients with coagulation disorders
7. Patients with severe organ failure

7. Patients who during endoscopy will undergo any technique using electrocautery / electrocoagulation will not be eligible for participation in the study.

**Japanese NBI Expert Team (JNET) classification**

NBI	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	• Invisible <sup>01</sup>	• Regular caliber • Regular distribution <sup>02</sup> (meshed/spiral pattern)	• Variable caliber • Irregular distribution	• Loose vessel areas • Interruption of thick vessels
Surface pattern	• Regular dark or white spots • Similar to surrounding normal mucosa	• Regular (tubular/branched/papillary)	• Irregular or obscure	• Amorphous areas
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low-grade intramucosal neoplasia <sup>04</sup>	High-grade intramucosal neoplasia/ Superficial <sup>05</sup> submucosal invasive cancer <sup>03</sup>	Deep submucosal invasive cancer
Examples				

- \* 1. If visible, the caliber in the lesion is similar to surrounding normal mucosa.
- \* 2. Microvessels are often distributed in a punctate pattern and well-ordered reticular or spiral vessels may not be observed in depressed lesions.
- \* 3. Deep submucosal invasive cancer may be included.
- \* 4. Low-grade intramucosal neoplasia: low-grade dysplasia.
- \* 5. High-grade intramucosal neoplasia: high-grade dysplasia.

Figure 2. Diagnostic performance of Japan NBI Expert Team classification for differentiation among noninvasive, superficially invasive, and deeply invasive colorectal neoplasia. Sumimoto K. *GastrointestEndosc.* 2017 Oct;86(4):700-709. doi: 10.1016/j.gie.2017.02.018. Epub 2017 Feb 28. PMID: 28257790.


BASIC Algorithm 					
		HYPERPLASTIC	ADENOMA	SESSILE SERRATED	CANCER
SURFACE	Mucus present	No	No	Yes	No
	Regular (smooth) or irregular	Regular	Regular/irregular	Regular/irregular	Irregular
	Pseudodepression	No	Yes	No	No
	Depression	No	No	No	Yes
PITS	Featureless?	Yes	No	No	No
	Type (round/not round)	Round pits	Not round (e.g tubular)	Round pits with/without dark spots	Round or non round
	Distribution (regular = homogenous/irregular = heterogenous - >1 pit pattern)	Homogenous	Homogenous or heterogenous without focal loss	Homogenous/heterogenous	Heterogenous with focal loss
VESSELS	Present?	Yes or no	Yes	Yes or no	Yes
	Type	Lacy	Pericryptal	Pericryptal	Irregular

Figure3.

Optical diagnosis of colorectal polyps with Blue Light Imaging using a new international classification. Subramaniam S. United European Gastroenterol J. 2019 Mar;7(2):316-325. doi:10.1177/2050640618822402. PMID: 31080616

## 5. STUDY INTERVENTIONS

### 5.1. POLYPECTOMY

All endoscopic procedures will be performed with High Definition (HD) instruments. In both groups of patients, the use of a cap and the performance of the colonoscopy with water / air / CO2 will be chosen according to the preferences of the physician. Additionally, in both groups, a 0.3mm dedicated cold snare will be used for polypectomy.

### 5.2. EXCISION PROCEDURE

The procedure of Underwater Cold Snare Polypectomy (UP) will be as follows:

1. Complete suction of air from the intestinal tract
2. Partial opening of the intestinal lumen by using sterile room temperature water via a water pump
3. Complete immersion of the lesion in water
4. Snaring of the lesion and a small amount of surrounding healthy tissue (1-2mm)
5. Excision

The procedure of Conventional Cold Snare Polypectomy (CCSP) will be as follows:

1. If the entry during the endoscopy has been made with water, the water will be aspirated, and the intestinal lumen will be re-stretched using air / CO2

2. Snaring of the lesion and a small amount of surrounding healthy tissue (1-2mm)
3. Excision

In both groups of patients, the objective will be the en bloc resection of the lesion including healthy tissue (about 2mm). If the en bloc resection fails, a piecemeal resection will be performed on as few specimens as possible.

The tissue specimen(s) will be placed in a vial with formol (Vial 1).

### **5.3. RESECTION POINT OVERVIEW**

After the resection of the lesion, a careful review of the resection point for bleeding or perforation will follow.

- Bleeding that lasts over a period of < 60 seconds will not be treated with endoscopic hemostasis (endoscopic clips) and will be recorded as self-limited.
- Bleeding that will persist > 60 seconds is characterized according to the instructions of ESGE 2017 as intraprocedural bleeding and can be treated either by water sprinkling or by placing hemostatic clips. The use of electrocautery or electrocoagulation methods will not be permitted.

This will be followed by a meticulous evaluation of the resection margins with digital endoscopy and a photograph of the site after the polypectomy if possible.

Where residual damage is observed, it will be removed using Cold Snare or biopsy forceps, but once again without using electrocautery or electrocoagulation methods. In any case, in the end of the procedure the resection should be judged as endoscopically complete.

### **5.4. BIOPSIES FROM RESECTION SITE**

Often the resection margins cannot be clearly defined during the pathological examination for reasons such as : the destruction of the tissue particles during aspiration into the working canal of the endoscope, specimens' autolysis and orientation inability. In order to determine the R0 resection rate and the incomplete resection rate, additional biopsies will be taken from the resection site as follows :

Horizontal margins :

In order to determine the horizontal margins, 2-4 biopsies will be taken from the resection area (2 biopsies antidiagonally in polyps of 5-7 mm size, 4 biopsies in polyps of 8-10 mm size). One cup of forceps will be placed in the defect and the second in the macroscopically normal mucosa.

The received tissue pieces will be placed in a new vial with formol (Vial 1A)

At the end of the endoscopic removal there will be 2 vials.

## **5.5. MARKING OF LESION'S POSITION**

In order to easily locate the point of the polypectomy in the repeated colonoscopy, a submucosal tattoo should be made 2-3 cm peripherally of the lesion. The tattoo will always be performed after the polypectomy and biopsy. For rectal or cecum polyps, positioning does not require a submucosal tattoo, and may be aided by photographic recording prior to polypectomy.

## **6. STUDY PROCEDURES**

### **6.1. RANDOMIZATION**

Randomization will be conducted at the patient level. If more than one polyp is diagnosed in a patient, then all will be resected by the same method. Specifically, the randomization process will be done by using the random numbers method of Microsoft Excel 2016. A research assistant, who will not participate in clinical practice, will allocate patients with a 1:1 ratio to the UCSP and CCSP group and will inform the endoscopist of the polypectomy method when a polyp is found. The Excel distribution table will not be accessible by the endoscopists. After written consent, patients will not be aware of the polypectomy method that will be applied (blinding)

### **6.2. PATHOLOGICAL EXAMINATION**

Specimens will be placed in vials with 10% formol (a total of 2 vials as mentioned above) and will be sent to the Pathological Laboratory. The slides will be stained in the DAKO CoverStainer using the DAKO Hematoxylin&Eosin Staining Kit. The slides will be then evaluated by two independent experienced pathologists, under a Nikon Eclipse 50i and a Nikon Eclipse E400 optical microscope (4X). Dysplastic changes will be classified using the Vienna classification system. In case multiple tissue fragments were biopsied, the aforementioned parameters will be calculated cumulatively.

Pathologists examining the tissues will be blinded and will not know the resection method (CCSP or UCSP) of each specimen.

Vial 1:

- Determination of polypectomy margin according to Residual Tumor Classification
- Determination of percentage of muscularis mucosa included in specimen. The determination of the area containing muscularis mucosa layer will be done by measuring the length of muscularis mucosa  $\text{mm}^2$  / length of specimen  $\text{mm}^2 \times 100\%$ . Using an ocular and stage micrometer, the length of the muscularis

mucosa underlining a neoplastic lesion was measured, along with the maximum depth of the muscularis mucosae and the specimen's maximum diameter

- Presence or absence of submucosa
- Measurement of submucosa depth in  $\mu\text{m}$  (when submucosa is present in the specimen)

Vial 1A :

- Determination of horizontal margins: presence of residual damage or not

A Nikon 10X microscope lens is used for microscopic measurement.

### **6.3. BLINDING**

This is a double blinded study. As it was mentioned above, pathologists and patients will be blinded. Blinding cannot be applied in the endoscopist level because of the nature of the intervention.

## **7. SAFETY ASSESSMENTS**

### **7.1. RISKS**

Regardless patients' participation in the study, those who are diagnosed with colon polyps will undergo polypectomy according to ESGE & ASGE guidelines in order to prevent malignancy in the future. UCSP and CCSP are both safe methods used in everyday clinical practice. Although as polypectomy is an interventional procedure, adverse events may occur but they are not study-related.

- Intraprocedural bleeding - IPB (bleeding during polypectomy), is defined according to the guidelines of ESGE (2017) bleeding that occurs during polypectomy and lasts more than 60 secs or bleeding that requires endoscopic intervention. In these cases, the hemostasis will be performed by using hemostatic clips. Bleeding episode during polypectomy that lasts less than 60 secs will be characterized as self-limited.
- Post-procedural bleeding - PPB (bleeding after polypectomy), is defined according to the guidelines of ESGE (2017) bleeding that occurs up to 30 days after polypectomy, and leads to the need for unplanned medical evaluation, or as a visit to the emergency room, or as the need for hospitalization or invasive treatment (repeated endoscopy for hemostasis, transfusion, angiography, surgery).  
>Early post procedural bleeding (after polypectomy) is defined as rectal bleeding within 48 hours of polypectomy.

>Late bleeding (after polypectomy) is defined as rectal bleeding from 48 hours to 30 days after polypectomy

New endoscopy is indicated in patients with two or more episodes of moderate / severe bleeding, drop in hemoglobin of at least 2 g / dl, and / or hemodynamic instability.

- Perforation: presence of air or intestinal contents outside the gastrointestinal tract [39] Perforation is a rare adverse events and occurs in polypectomies of large size lesions and when electrocautery is used.
- Abdominal pain not due to perforation [39]

All complications and treatment of them will be recorded.

## **7.2 FOLLOW UP FOR ADVERSE EVENTS**

The aforementioned complications will be evaluated by a study physician of the Gastroenterology Department 30 days after the polypectomy with a phone call and clinical examination if needed. Patients will be able to communicate with a physician who participates in the study 24h/24h.

## **7.3. FOLLOW UP ENDOSCOPY**

After 6-12 months, endoscopy will be repeated to check for recurrence of the lesion. The procedure will be done with a careful overview of the area of the previous resection. The area of the previous resection will be indicated by the tattoo or by the photofile or by the endoscopists descriptions at their reports. If the scar from the prior polypectomy can be located, two biopsies will be conducted from the scar area to determine the occurrence or absence of a microscopic recurrence.

# **8. STATISTICAL CONSIDERATIONS**

## **8.1. SAMPLE SIZE**

It was estimated that to find a mean difference of 15% at the main endpoint of the study (rate of the area containing muscularis mucosa%) and based on the literature data provided by a relevant research [Ref: 38], 198 people will be required per group (total 396) in order to find differences in significance level 0.05.

## **8.2. DATA ANALYSIS**

Absolute and relative frequencies, 95% confidence intervals and frequency graphs will be used to illustrate the qualitative variables of the study. The mean values, standard deviations, median values, intra-quadratic ranges (25th-75th percentage points).

Histograms and boxplots will be used to describe the quantitative variables. The Kolmogorov - Smirnov test will be run to check the normality of the distributions. Pearson's chi-square and Fisher's exact test will be applied to compare the ratios between the study groups. On the other hand, the Student's t-test or the non-parametric Mann-Whitney test will be used to compare quantitative variables between the two groups, depending on whether the data follow the normal distribution. Moreover, linear or logarithmic models will be used to check for differences between the studied groups, taking into account other factors (e.g. demographic and clinical characteristics). In case of asymmetrical distribution, logarithmic transformations of the variables will be used. Significance levels will be bilateral and the statistical significance will be set at 0.05. The analysis will be run with the statistical program SPSS 26.0.

## **9. DATA QUALITY**

### **9.1. DATA COLLECTION AND MANAGEMENT**

A data collection form (source document) will be completed for each patient including all patient's details according to the study protocol. Especially trained investigator staff will enter the data required by the protocol into the case report forms (CRFs) and into the database. The Primary Investigator must check and certify that CRFs are complete and accurate. According to GCP patients' data will be available for sponsor's essential documents too.

### **9.2. QUALITY ASSESSMENT**

#### **9.2.1 MONITORING**

Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Monitor will verify that the rights of human subjects are protected, the reported trial data are accurate, complete, and verifiable from source documents, the conduct of the trial is in compliance with the currently approved protocol, with GCP, and with the applicable regulatory requirements. Monitoring plan: first visit before initiation of patients enrollment and following regular visits site according to an agreed monitoring plan every 4-6 weeks.

## **10. ETHICAL CONSIDERATIONS**

### **10.1. ETHICAL COMPLIANCE**

The study design conforms with ICH-GCP, the Declaration of Helsinki, and local ethical and legal requirements. The study protocol is approved by the Institutional Review Board



of Sismanogleio General Hospital of Athens and approval by the Committee of Bioethics and Ethics of the Medical School - National and Kapodistrian University of Athens is pending. This trial protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT).

## **10.2. INFORMED CONSENT**

IRB-approved, written informed consent (witnessed, where required by law or regulation) will be obtained from all participants during the visit at the out-patient clinic before enrollment in the study. All participants will take a copy document, and the original document will be kept as one of the essential documents for trial's master file (TMF).

## **10.3. PUBLICATION POLICY**

This protocol will be posted in [clinicaltrials.gov](https://clinicaltrials.gov) which is a publicly accessible database. Study's results and outcomes will be submitted for publication in international medical journal and presented in medical conferences related to interventional gastrointestinal endoscopy and polypectomy techniques.

## **11. REFERENCES**

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## 12. ABBREVIATIONS

ASGE : American Society for Gastrointestinal Endoscopy

CCSP : Conventional Cold Snare Polypectomy  
CRF : Case Report Form  
CRR : Complete Resection Rate  
CS : Cold Snare  
CSP : Cold Snare Polypectomy  
EMR : Endoscopic Mucosal Resection  
ESGE : European Society of Gastrointestinal Endoscopy  
GCP : Good Clinical Practice  
HS : Hot Snare  
HSP : Hot Snare Polypectomy  
IPB : Intraprocedural Bleeding  
IRR : Incomplete Resection Rate  
MM :Millimetre  
UCSP : Underwater Cold Snare Polypectomy  
UEMR : Underwater Endoscopic Mucosal Resection  
UP : Underwater Polypectomy  
PPB :Postprocedural bleeding  
R0RR : R0 Resection Rate  
RCT : Randomized Controlled Trial  
SOP :Sponsor's Standard Operating Procedures  
SPIRIT :Standard Protocol Items: Recommendations for Interventional Trials  
TMF : Trial's Master File