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# The Major Complications of Colonoscopy: Sedation-Related, Hemorrhage Associated with Polypectomy and Colonic Perforation

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Paul Miskovitz

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## 1. Introduction

*“Complication, in medicine, is an unfavorable evolution of a disease, a health condition or a therapy. The disease can become worse in its severity or show a higher number of signs, symptoms, or new pathological changes, become widespread throughout the body or affect other organ systems. A new disease may also appear as a complication to a previous existing disease. A medical treatment, such as drugs or surgery may produce adverse effects and/or produce new health problem(s) by itself. Therefore, a complication may be iatrogenic, i.e., literally brought forth by the physician. Medical knowledge about a disease, procedure or treatment usually entails a list of the most common complications, so that they can be foreseen, prevented or recognized more easily and speedily.*

*Depending on the degree of vulnerability, susceptibility, age, health status, immune system condition, etc. complications may arise more easily. Complications affect adversely the prognosis of a disease. Non-invasive and minimally invasive medical procedures usually favor fewer complications in comparison to invasive ones.” [1]*

A currently popular focus in the gastroenterology and endoscopic literature is the quality of colonoscopy with regard to colorectal cancer screening [2]. This includes the collection of evidence regarding the use of colonoscopy as a tool for screening programs, defining and establishing quality indicators and minimum requirements that endoscopists involved in colorectal cancer screening programs should meet, and providing evidence about procedures that may improve the quality of colonoscopy. Those who have decades of experience performing colonoscopy will be quite familiar with the myriad of complications associated with the procedure, either through their reading of the gastrointestinal endoscopy literature, from personal experience or the experience of colleagues. That being said, three major cate-

gories of complications associated with colonoscopy are widely recognized. They are sedation-related complications, hemorrhage associated with colonic polypectomy and colonoscopy-related colonic perforation. Sedation-related complications are usually cardiovascular and/or pulmonary and include oxygen desaturation, respiratory arrest, alterations in heart rate (bradycardia and tachycardia), cardiac arrhythmias, myocardial infarction, stroke, seizures (at times attributed to the method of preparation) and shock. Hemorrhage is most often associated with snare electrocautery polypectomy but may also occur during the performance of diagnostic colonoscopy with or without biopsies. Two general subcategories of hemorrhage exist: hemorrhage immediately following the performance of polypectomy or delayed hemorrhage occurring up to several weeks after the therapeutic procedure. Colonic perforation resulting from colonoscopy may occur due to mechanical forces exerted against the colonic wall (colonoscope tip or shaft, biopsy forceps, dilatation of a stricture), barotrauma as a result of intraluminal air or carbon dioxide insufflation, or as a result of a therapeutic procedure such as polypectomy, foreign body extraction, or stent placement to name a few. A thorough understanding of these complications, their incidence and treatment, is part of the training of all those learning to perform colonoscopy and forms the basis for the physician obtaining informed consent (an explanation of the risks and benefits of the procedure) from the patient. This chapter will systematically review our current understanding of these complication categories and the methods of minimizing the likelihood of developing these complications. The latest treatments of specific complications will be reviewed with the intent of aiding the physician endoscopist's understanding of the principles of risk management as regards to performing colonoscopy.

*"Primum non nocere"* is the Latin phrase that means "First, do no harm". Non-maleficence, which is derived from this maxim, is one of the principal precepts of medical ethics taught to all medical students in medical school and is a fundamental principle for the provision of medical services world-wide. Another way to state it is that "given an existing problem, it may be better not to do something, or even to do nothing, than to risk causing more harm than good." It reminds the physician and other health care providers that they must consider the possible harm that any intervention might do. It is invoked when debating the use of an intervention that carries an obvious risk of harm but a less certain chance of benefit. This ancient principle should be kept in mind when contemplating colonoscopy and the possible complications of the procedure.

### **1.1. Informed consent for colonoscopy**

The doctrine of informed consent (and its antithesis, informed refusal) for colonoscopy involves an assessment of the competence of the patient by the physician, disclosure of, in an understandable way, the information necessary to allow the patient to make an informed decision (risks and benefits considered) regarding the role of colonoscopy in his care, and the documentation of these proceedings in the medical record [3]. It is an intrinsic part of the doctor-patient relationship and an ethical obligation on the part of the physician in the clinical practice of medicine. In the United States, the doctrine of medical informed consent is most famously traced back to a 1914 New York court decision centered about the observa-

tion that since most surgical operations involve some use of force, there must be consent on the part of the patient. Because the nature of surgery is outside the experience of most patients, the consent must be granted only after the patient is properly informed of the risks and benefits. The most famous description of informed consent is a quote from New York Justice Benjamin Cardozo who, in 1914, stated that:

*"Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault for which he is liable in damages" [4].*

This advice is still applicable in the 21<sup>st</sup> century! Most important in considering the complications of colonoscopy is the need to meticulously document the obtaining of informed consent from the patient and the procedural technique, findings and outcome including any complications [5].

## 2. Sedation-related complications of colonoscopy

Sedation-related complications of colonoscopy are usually cardiovascular, pulmonary and occasionally neurological. The risk of these events occurring is associated with advancing age, higher American Society of Anesthesiologists Physical Status Classification System scores (ASA score – with category 6 not being applicable), and the patient's co-morbidities [6-8].

ASA Physical Status Classification System (I-VI)

ASA-I A normal healthy patient.

ASA-II A patient with mild systemic disease.

ASA-III A patient with severe systemic disease.

ASA-IV A patient with severe systemic disease that is a constant threat to life.

ASA-V A moribund patient who is not expected to survive without the operation.

ASA-VI A declared brain-dead patient whose organs are being removed for donor purposes.

ASA-E Emergency operation of any variety (used to modify one of the above classifications, i.e., ASA III-E)

In general, patients' inpatient status, trainee participation and the routine use of supplemental oxygen (the latter by possibly masking hypercapnea and hypoventilation) are associated with a higher risk of unplanned cardiopulmonary events [9]. The monitoring period for the "event rate" should likely include the 30 days post procedure [10].

### 2.1. Hypoxemia

Hypoxemia, which is usually transient but often anxiety provoking for the colonoscopist, is a common occurrence during sedation for colonoscopy and has lead to the often "routine"

practice by colonoscopists and attending anesthesiologists and nurse anesthetists of providing patients with supplemental oxygen [9] delivered by nasal cannula and on occasion by a venturi air-entrainment mask (the latter providing a fixed and predictable oxygen concentration despite a variable respiration pattern). Prolonged hypoxemia associated with colonoscopy is rare. The etiology of hypoxemia is often multifactorial but not to be overlooked is the amount of air (or carbon dioxide) insufflated into the colon for adequate luminal distention and in some cases the passing of this gas into the small bowel through an incompetent ileocecal valve thereby affecting diaphragmatic function. This has lead most endoscopists to periodically monitor the degree of abdominal distention (“softness”) by direct palpation of the abdomen either routinely during the procedure or when there are drops in the monitored oxygen saturation.

## 2.2. Hypercapnea

Capnography monitor use is widespread in hospitals but these devices are less commonly used in the gastrointestinal endoscopy suite and other ambulatory settings where propofol is often used. In 2012 the American Society of Anesthesiologists (ASA) advised its member to use such carbon dioxide monitoring devices that detect changes in the amount of carbon dioxide the patient is exhaling during monitored anesthesia care for upper gastrointestinal endoscopies [11]. The new policy states:

*“Monitoring for exhaled carbon dioxide should be considered during endoscopic procedures in which sedation is provided with propofol alone or in combination with opioids and/or benzodiazepines, and especially during these procedures on the upper gastrointestinal tract. Careful attention to airway management must be provided during endoscopic retrograde cholangiopancreatography (ERCP) procedures performed in the prone position where ventilatory monitoring, airway maintenance and resuscitation may be especially difficult.”*

It has only been a matter of time since this recommendation has found application in the monitoring of sedated patients undergoing colonoscopy. The new policy has met with mixed reviews in the gastrointestinal endoscopy and anesthesiology communities but most have agreed that there is little downside to such monitoring.

It is important to emphasize that at least one individual with training in advanced cardiac life support (tracheal intubation, defibrillation, use of resuscitation medications, ACLS certification) that is capable of establishing an airway and providing positive-pressure ventilation should be present during colonoscopy sedation. Ability for communication with “back up” local paramedics or life support personnel should be confirmed.

## 2.3. Hypotension

The etiology of hypotension during colonoscopy is also multifactorial (pre-procedure anti-hypertensive medications, sedatives and analgesics used during the performance of the procedure, arrhythmias, pre-procedure cardiac performance status, etc.) but the state of hydration of the patient after (usually a polyethylene glycol containing) bowel preparation

may reign supreme among the factors to consider. Intravenous replacement with crystalloid solutions should be considered during such events and in anticipation of such events in appropriately screened patients.

#### **2.4. Arrhythmia**

Cardiac arrhythmias including bradycardia, less often tachycardia, atrial premature contractions, paroxysms of atrial fibrillation, and ventricular premature contractions have been documented during procedural sedation. Most resolve with the intravenous administration of fluids or increased sedation. With regard to bradycardia there is asymptomatic bradycardia (heart rate less than 60 bpm) and symptomatic bradycardia defined as a heart rate less than 60/min that elicits signs and symptoms. In symptomatic bradycardia the heart rate will usually be less than 50/min. Symptomatic bradycardia exists when the following 3 criteria are present: 1.) The heart rate is slow; 2.) The patient has symptoms; and 3.) The symptoms are due to the slow heart rate. Atropine is the first drug of choice for symptomatic bradycardia [12]. The dose in the bradycardia ACLS algorithm is 0.5 mg IV push which may be repeated up to a total dose of 3 mg. (Anesthesiologists often choose glycopyrrolate [Robinul®] as an alternative to atropine.) Dopamine is a second line drug for symptomatic bradycardia when atropine is not effective. The dosage is 2-10 micrograms/kg/min infusion. Epinephrine can be used as an equal alternative to dopamine when atropine is not effective. The dosage is 2-10 micrograms/min. Rare cases of ventricular tachycardia and cardiac arrest during ventricular fibrillation have been reported necessitating the need for continuous EKG monitoring, the availability of ACLS trained personnel, as well as obtaining a history of cardiac or pulmonary disease prior to initiating the procedure.

#### **2.5. Pulmonary embolism**

Although the prevalence of coexistent pulmonary embolism at the time of colon cancer detection has been estimated to be as high as 2% (with the concurrent prevalence of deep venous thrombosis being as high as 8%) there are no accepted statistics for the incidence of pulmonary embolism complicating diagnostic or therapeutic colonoscopy [13].

#### **2.6. TIA/stroke**

The risk of stroke in patients with AF whose anticoagulation is adjusted for endoscopies is low, but almost tenfold higher in patients with complex clinical situations [14]. Age, history of stroke, hypertension, hyperlipidemia, and family history of vascular disease may increase the risk of suffering a stroke during or immediately after undergoing a gastrointestinal endoscopic procedure. Comprehensive guidelines for the management of anticoagulation and antiplatelet therapy in patients undergoing gastrointestinal endoscopic procedures including colonoscopy have recently been published [15] and should serve as a reference and guide when dealing with such patients.

## 2.7. Myocardial infarction

Recent myocardial infarction has traditionally precluded the performance of elective colonoscopy for at least several months but recently this issue has been closely addressed in the literature [16]. Colonoscopy performed in patients who have experienced a recent myocardial infarction is associated with a higher rate of minor, transient, and primarily cardiovascular complications when compared with control patients but is relatively infrequently associated with major complications. In certain circumstances, despite the higher risk, colonoscopy may be beneficial in this setting, particularly given the higher frequency of ischemic colitis in this patient population. The occurrence of cardiac ischemia (and concomitant cardiac rhythm disturbances) in patients undergoing colonoscopy who have known cardiac disease or cardiac risk factors has recently been quantified [17]. Holter EKG recordings and measurement of cTnI troponin I levels showed a high incidence of new but silent ischemic and arrhythmic EKG changes during colonoscopy and do a lesser extent those patients with one or more risk factors for heart disease. Two patients with known heart disease died within 30 days of colonoscopy.

## 3. Colonic hemorrhage associated with polypectomy

Although hemorrhage can occur during diagnostic colonoscopy (particularly when “cold” or “hot” forceps biopsy techniques are used) it most often complicates polypectomy occurring immediately or being delayed for several weeks after the procedure [18]. The overall incidence of hemorrhage has been reported to be in the range of 1 to 6 per 1,000 colonoscopies [19,6] (this being a useful figure to quote when obtaining informed consent from the patient) with the number of polyps [20], polyp size [19] recent anticoagulant use [22,23] and even polyp histology(!) [6,24,25] being modifying factors! The effects of aspirin, nonsteroidal anti-inflammatory drugs and clopidogrel both alone and in combination on this complication of colonoscopy have also been addressed [26,27].

Patients requiring colonoscopy with or without biopsy and/or polypectomy are often taking antithrombotic agents including anticoagulants such as warfarin, heparin, and low molecular weight heparin, and antiplatelet agents such as aspirin, non-steroidal anti-inflammatory drugs, thienopyridines such as clopidogrel and ticlopidine, and glycoprotein IIb/IIIa receptor inhibitors. The indications for the use of these medications include atrial fibrillation, acute coronary syndrome, deep venous thrombosis, hypercoagulable states and indwelling endoprostheses such as coronary artery stents. When hemorrhage does occur in patients taking these agents it is most commonly from the gastrointestinal tract [28]. Risk stratification for these patients can generally be relegated to two categories. Low risk procedures include diagnostic colonoscopy including mucosal biopsy [29,30] and high-risk procedures include colonoscopy with polypectomy and the dilatation of either benign or malignant colonic strictures (guidelines extrapolated in part from experience reported in the upper gastrointestinal endoscopy literature) [31-33]. A comprehensive review of the types of antithrombotic therapies, their implications for patients undergoing colonoscopy, and recommendations and a management

algorithm for such patients using these agents has recently been published [34]. Newer anticoagulants, for which current guidelines regarding their being held for endoscopic procedures, are lacking and these agents are reaching the market at an increasing rate. They include danaparoid, a low molecular weight heparinoid consisting of a mixture of heparin sulfate, dermatan sulfate, and chondroitin sulfate [35,36] which was recently removed from the US market due to shortages; the direct thrombin inhibitors recombinant hirudin (lepirudin), argatroban, desirudin and bivalirudin [37-39]; the recently available orally active direct thrombin inhibitor dabigatran etexlate [40]; and the factor Xa inhibitors idraparinux, rivaroxaban, and apixaban [41]. There is no doubt that as these agents are used they will affect practice standards with regard to colonoscopy and polypectomy.

Acute postpolypectomy bleeding is often immediately localizable by or apparent on colonoscopy and amenable to endoscopic therapy using clips, ligatures, cautery or argon plasma coagulation [42,43] or nonendoscopic techniques such as angiographic embolization or surgery [44]. Recent endoscopic clip application devices have undergone redesign and improvements to optimize their clinical effectiveness [45]. The site of delayed postpolypectomy colonic hemorrhage can be identified by colonoscopy, by red cell nuclear scintigraphy and/or by selective angiography [46] and dealt with in a similar fashion.

A variety of procedural techniques have been proposed to minimize the risk of hemorrhage complicating polypectomy. These include the avoidance of the use of the "hot biopsy" technique [47], the use of clips or detachable snares [48,49] and possibly the use of epinephrine injections to the base of the polyp prior to initiating the polypectomy [50,51]. Proper technique for the removal of pedunculated polyps includes planning for the application of pressure by regrasping the pedicle with the snare if immediate bleeding occurs, the injection of epinephrine 1:10,000 to 1:20,000 dilution into the bleeding site, the application of cautery (with thermal probes, bipolar cautery [BICAP], the argon plasma coagulator, or the tip of the polypectomy snare), the use of hemoclips, and/or the use of loops and band ligators on the pedicle. Similar techniques may be used in those with delayed bleeding who seem to be actively bleeding. Up to 50 percent of patients with delayed hemorrhage may require blood transfusion [23].

#### **4. Colonic perforation associated with polypectomy**

Perforation of the colon is the most dreaded complication of colonoscopy and polypectomy and this risk, albeit small, should be cited in the process of obtaining informed consent from the patient for the procedure.

Abdominal pain, abdominal distention, +/- abdominal tenderness, hiccoughs, loss of bowel sounds indicative of ileus, and late developing peritoneal signs are the hallmarks of perforation following colonoscopy. As physical examination, chest x-ray and abdominal flat and upright x-ray alone or in combination may not be diagnostic of colonic perforation patients



suspected of having this complication should undergo CT scanning of the abdomen and pelvis [52]. The rate of perforation after colonoscopy ranges from 0.1-0.3% [19] and may be increased (along with the risk of hemorrhage) in those physicians who have a low procedure volume [53]. It has been suggested that physicians who have a high perforation rate should be evaluated for inappropriate colonoscopy practice technique [54].

Perforation risk for polypectomy may be minimized by proper technique. One should avoid ensnaring colonic folds, particularly when the anatomy is obscured by large pedunculated or sessile lesions. By not properly lifting an ensnare polyp into the lumen of the colon before applying current, there may be spread of thermal injury to the deeper layers of the bowel wall increasing the risk of delayed perforation. Likewise, a pedunculated polyp should not be resected close to the bowel wall. Care should be taken to leave some residual stalk. The polypectomy snare should be tightly closed before applying coagulation in order to avoid the tip of the snare behind the polyp from touching the bowel wall.

Endoscopic mucosal resection for the piecemeal removal of benign appearing sessile colonic adenomas has become routine. Endoscopic submucosal dissection is a resection technique applied to early gastrointestinal cancers. Complications rates are higher with endoscopic submucosal dissection than with endoscopic mucosal resection with perforations occurring in up to 10 percent of patients. Often these perforations can be managed by endoscopic clipping and conservative therapy, however surgery is still required in some cases and prolonged hospital stays are common. [55-57].

All patients found to have evidence of colonic perforation following colonoscopy should be seen in surgical consultation because perforation often requires surgical repair which in some cases may be accomplished using a laparoscopic technique with avoidance of diverting colostomy formation [58,59]. It has been reported that nonsurgical management may be appropriate for some individuals [60,61] but these patients should still undergo surgical consultation and close monitoring for signs of deterioration. Successful endoscopic repair of an iatrogenic colonic perforation occurring during *diagnostic* colonoscopy has been reported [62] and the efficacy of a new Over-the-Scope-Clip (OTSC-Ovesco Endoscopy AG, Tübingen, Germany) device (a bear trap-like, large clip with a wingspan of 12 mms. that grasps much more tissue than the small endoscopic clips used previously and can create a full-thickness closure of perforations up to 3 cms. in diameter) in treating acute perforation of the gastrointestinal tract has been reported [63].

## **5. Miscellaneous complications of colonoscopy with and without polypectomy**

### **5.1. Abdominal discomfort**

Commonly reported but minor complications of colonoscopy include bloating and abdominal discomfort and or pain [64-66]. The incidence of these complications may be reduced by



avoiding “looping” of the colonoscope, avoiding excess traction applied to the bowel mesentery, adequately removing insufflated gas, using carbon dioxide instead of insufflated air [67] and by using a water insufflation technique instead of the insufflation of gas [68].

### **5.2. Postpolypectomy electrocoagulation syndrome**

Postpolypectomy electrocoagulation syndrome refers to a transmural burn and localized peritonitis occurring up to a few days after the removal of a polyp without clinical or radiographic evidence of perforation of the viscus. Patients may present with localized abdominal pain, fever, and leukocytosis. Inpatient [69] and outpatient [70] therapy have both proven to be successful in treatment of this complication.

### **5.3. Infection**

Transient bacteremia after colonoscopy with polypectomy is rare and signs and symptoms of infection are even rarer [71,72]. Current guidelines exist generally advocating against antibiotic prophylaxis for those undergoing colonoscopy with or without polypectomy [73]. As these represent only guidelines it is best for the endoscopist to consult with the patient and the referring physician before deciding to forego the use of antibiotic prophylaxis in certain clinical situations (prosthetic heart valve, history of endocarditis, newly placed prosthetic joint, etc.). Both diverticulitis [74] and appendicitis [75] the latter possibly due to barotrauma have been reported complicating colonoscopy done with and without polypectomy. These clinical possibilities must be kept in mind in patients with post-procedure abdominal pain.

### **5.4. Rare complications**

Rare complications of colonoscopy with and without polypectomy have been reported and include infections related to instrument cleanliness [76] incarceration of the colonoscope in an inguinal hernia [77], splenic injury during colonoscopy [78], and intracolonic gas explosion during colonoscopic polypectomy [79,80]. CT colonography, the alternative to colonoscopy in many patients, however, is not without its own complications and adverse events [81].

## **6. Conclusion**

It is incumbent upon physicians performing colonoscopy to stay current in their field, keep abreast of the medical literature and the ongoing technological advances associated with endoscopic equipment and technique, and to be meticulous in their approach to detail in caring for their patients, particularly when gastrointestinal endoscopic diagnostic and therapeutic procedures are involved.

<p>GENERAL</p> <ul style="list-style-type: none"> <li>♥Obtain informed consent from the patient prior to the colonoscopy procedure with emphasis on the risks of, benefits of and alternatives to the proposed procedure</li> <li>♥Be cognizant of your limitations as an endoscopist</li> <li>♥Be certain that all necessary equipment to perform the colonoscopy procedure (diagnostic and therapeutic) is available and in working order</li> </ul> <p>SEDATION RELATED COMPLICATIONS</p> <ul style="list-style-type: none"> <li>♥Perform and document a medical history and physical examination prior to the initiation of the procedure. Include a review of the patient’s current medications, known allergies, past experiences with anesthesia, Mallampati score and ASA Physical Status Classification</li> <li>♥Ensure that the patient is properly monitored during the procedure including blood pressure, pulse, oximetry, capnography monitoring if available, cardiac rhythm monitoring, and airway management. If working with an anesthesiologist thoroughly discuss with your colleague the patient’s medical history and the goals of the procedure. Maintain a dialogue with the anesthesiologist throughout the procedure</li> <li>♥Ensure that tracheal intubation and cardiac defibrillation equipment as well as resuscitation medications are available and have up to date certification in Advanced Cardiac Life Support</li> </ul> <p>COLONIC HEMORRHAGE ASSOCIATED WITH POLYPECTOMY</p> <ul style="list-style-type: none"> <li>♥Take a history of the patient’s anticoagulant use, antiplatelet agent use, and past history of bleeding diathesis if any</li> <li>♥Be thoroughly familiar with proper snare electrocautery polypectomy technique including the use of saline or epinephrine injection into the base of the polyp before initiating electrocautery</li> <li>♥Avoid the use of the “hot biopsy” technique for small (several millimeter) polyps</li> <li>♥Have available for use if necessary clips, ligatures, epinephrine, a bipolar electrocautery device and/or an argon plasma coagulation device or heater probe</li> <li>♥Give specific written post-procedure instructions to the patient regarding the use of anticoagulants and antiplatelet agents</li> </ul> <p>COLONIC PERFORATION ASSOCIATED WITH POLYPECTOMY</p> <ul style="list-style-type: none"> <li>♥Cite the risk of colonic perforation when obtaining informed consent</li> <li>♥Avoid ensnaring colonic folds</li> <li>♥Do not perform polypectomy when the anatomy is obscured by the size or shape of the lesion or the adequacy of the preparation</li> <li>♥Have training and familiarity with endoscopic clipping techniques</li> <li>♥Have a predetermined “game plan” to expeditiously evaluate a patient suspected of having a perforation</li> </ul> <p>MISCELLANEOUS COMPLICATIONS OF COLONOSCOPY WITH AND WITHOUT POLYPECTOMY</p> <ul style="list-style-type: none"> <li>♥If available, use carbon dioxide for colonic insufflation</li> <li>♥Monitor the degree of abdominal distension by palpation throughout the procedure</li> <li>♥Examine the patient in the recovery area post procedure to ensure that there has been adequate evacuation of colonic gas</li> <li>♥Be cognizant of and practice infection control measures routinely</li> <li>♥Keep abreast of the medical literature and ongoing technological advances associated with endoscopic equipment and technique</li> </ul>
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**Table 1.** Recommendations to prevent specific colonoscopy complications

## Author details

Paul Miskovitz

Division of Gastroenterology and Hepatology, Department of Medicine, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, USA

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