Insights into the management of anorectal disease in the coronavirus 2019 disease era

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Abstract: Coronavirus 2019 disease (COVID-19) has created major impacts on public health. The virus has plagued a large population requiring hospitalization and resource utilization. Knowledge about the COVID-19 virus continues to grow. It can commonly present with gastrointestinal symptoms; initially, this was considered an atypical presentation, which led to delays in care. The pandemic has posed serious threats to the care of anorectal diseases. Urgent surgeries have been delayed, and the care of cancer patients and cancer screenings disrupted. This had added to patient discomfort and the adverse outcomes on healthcare will continue into the future. The better availability of personal protective equipment to providers and standard checklist protocols in operating rooms can help minimize healthcare-related spread of the virus. Telehealth, outpatient procedures, and biochemical tumor marker tests can help with mitigation of anorectal-disease-related problems. There is limited literature about the clinical management of anorectal diseases during the pandemic. We performed a detailed literature review to guide clinicians around management options for anorectal disease patients. We also highlighted the health challenges seen during the pandemic.

Keywords: anorectal disease, Coronavirus disease 2019, telehealth

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Introduction
Coronavirus disease 2019 (COVID-19), caused by a single-stranded enveloped RNA virus called SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), originated in Wuhan province in China in December 2019. COVID-19 later progressed to a global pandemic that until now has claimed more than 3.0 million deaths and cases continue to grow.1 High infectivity and transmission through asymptomatic patients have led to rapid transmission across geographical borders.2 COVID-19 has impacted healthcare and socioeconomic worldwide. Investigations on transmission, clinical presentation, treatment, and vaccination have revealed new aspects of this viral syndrome. COVID-19 is commonly transmitted as droplet infection and sometimes as airborne. There are sporadic cases where fecal–oral transmission was considered as the mode of transmission.3 Although COVID-19 infection affects primarily respiratory systems, cardiovascular and gastrointestinal (GI) system involvement has been reported in the recent literature.4–6 COVID-19 infection has not only impacted public health and economics but also the management of acute and chronic medical conditions. Elective ambulatory visits and surgeries have been cancelled to mitigate the risk of infection transmission and to enable healthcare systems to facilitate large volumes of COVID-19 infected patients. Telehealth has played important role in this situation,7 providing convenience, patient and provider satisfaction, and decreased healthcare costs.8 There are lack of standardized guidelines to manage acute and chronic medical conditions and confusion exists in the medical community.

Anorectal diseases are common and can impact the quality of life. The disease spectrum ranges...
from benign conditions such as hemorrhoids to malignant conditions such as cancers. A National Health Service study has predicted poor outcomes of colorectal cancer in future because of delays in detection and treatment of these cancers during the pandemic. Information on management of anorectal disease during this pandemic is scarce. In this review article, we explore the impact of the COVID-19 pandemic on the management of anorectal disease.

Literature search
We searched PubMed, Medline, and Google scholar from 1 December 2019 to 31 March 2021 with following search terms ‘COVID-19 infections and lower gastrointestinal tract manifestations’, ‘mechanism of gastrointestinal presentation in COVID-19’, ‘fecal excretion of COVID-19’, ‘fecal transmission of COVID-19’, ‘anorectal emergencies, rectal varices, perianal abscess, obstructive anorectal cancer, acute hemorrhoid thrombosis or strangulation and COVID-19’, ‘benign anorectal disease, hemorrhoids, anal fissure, anal fistula, anal warts and COVID-19’, ‘anorectal cancers management, anorectal cancer screening and COVID-19’, ‘telehealth during coronavirus pandemic and anorectal diseases’, ‘COVID-19 vaccination and management of anorectal diseases’ and ‘surgical practice during COVID-19’. All types of articles including reviews, case studies, observational studies and correspondences were considered. In addition, we searched the references of the selected articles to find related articles that were not identified by the electronic searches. Pertinent studies were initially searched based on the title and the abstract, then full text was read to verify the relevance.

Lower GI manifestations of COVID-19
COVID-19 commonly presents with GI symptoms. The SARS-CoV-2 virus binds to angiotensin converting enzyme receptor 2 (ACE-2) to enter host cells. The ACE-2 receptor is widely expressed in the human body including in alveolar type 2 cells, kidneys, adipose tissue, colon, and the central nervous system. In fact, the ACE-2 receptor is highly prevalent in the colon. Another host cell protein transmembrane serine protease 2 (TMPRSS2) assists in trafficking of the SARS-CoV2 virus to host cells. This protein is found in the ileum and colon (Figure 1). In an in vitro study of human gut enterocytes, there was evidence of invasion and proliferation in the enterocytes. Fortunately, the virus is deactivated at gastric pH; however, patients on proton pump inhibitors have been found to be at increased risk of SARS-CoV2 infection.
not seen with H₂-blockers. Rather, famotidine was shown to improve the clinical outcomes in one study. The common lower GI symptoms observed in observational studies included abdominal pain and diarrhea. Diarrhea as a presenting symptom for COVID-19 infection is observed in 2–50% patients whereas abdominal pain is observed in 4–26%. These symptoms are non-specific and could be side effects of the empirical treatments used for COVID-19 infection.

One study had shown that patients with GI symptoms had a longer time from disease onset to the hospital admission as compared with patients without GI symptoms (16 versus 11.6 days). This was reproduced in another multicenter study (9 versus 7.3 days). This could be because patients with GI symptoms were diagnosed late because of atypical presentation. GI symptoms should increase the index of suspicion to test for COVID-19 infection. A few studies have also shown increased disease severity and poor disease course associated with GI symptoms. The mortality of patients with GI symptoms is similar to those without GI symptoms (0.4% versus 2.1%, p = 0.15). The literature has shown sporadic cases of acute abdomen, colonic ileus, colitis. Fecal transmission

Fecal excretion of the SARS-CoV-2 and its ability to stay viable can potentially cause fecal–oral transmission. A meta-analysis of 17 studies including Asian and North American data showed a 43% virus detection rate in fecal specimens. This rate was higher in patients with GI symptoms and severe disease. Stool samples can stay positive for the virus when it is not detectable in the respiratory tract. One meta-analysis with several observational studies showed that 48% of patients had positive stool PCR, and the majority of these stayed positive after the respiratory tract PCR (RT-PCR) was negative. The presence of the virus in stool explains the GI involvement and the risk of fecal–oral transmission persist for several days even after clinical recovery. In some countries outside the United States (US), patients were kept in hospital until their stool samples became negative. It took an average of 11.2 days to become stool RNA negative after a negative respiratory tract sample. There is a recommendation to screen stool donors for symptoms and travel and additionally with RT-PCR in order to prevent transmission with feces.

Inflammatory bowel disease

Patients with inflammatory bowel disease (IBD) who are taking treatment are considered immunocompromised patients. This could be a concern for developing severe COVID-19 infection in these patients. Active IBD, advanced age, and comorbidities are associated with poor outcomes. As the screening endoscopy for colon cancer screening in IBD patients is delayed during COVID-19 pandemic, alternative tests as biomarkers, imaging, and symptoms assessment should be done.

The American Gastroenterology Association recommends that patients who test negative for SARS-CoV-2 can continue the appropriate treatments; those patients with positive tests should consider holding thiopurines, methotrexate, and tofacitinib, tapering systemic steroids or switch to budesonide, and delaying biologics by 2 weeks. Amino salicylates and rectal therapies can be continued. Treatment decisions can be altered based on risk and benefits assessments. IBD patients with anorectal involvement should also follow the same guidelines.

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Hemorrhoids and anal fissure

The COVID-19 has resulted in delay for elective procedures. This can impact proctological management of advanced hemorrhoids. Telemedicine can be a possible alternative in this situation. The traditional risk factors for the hemorrhoids include constipation, obesity, and sedentary lifestyle. These risk factors have increased during the COVID-19 pandemic. This will add to the physical and psychological problems of this population.
Hemorrhoid is a benign condition and mostly improves with conservative management. Some cases require surgical intervention. If the surgery is delayed in these cases, it can lead to progression of disease and complications such as bleeding and pain. Traditionally, hemorrhoids are treated with office procedures including rubber band ligation, sclerotherapy, and infrared coagulation, and operating room procedures such as hemorrhoidectomy and stapled hemorrhoidopexy for advanced hemorrhoids. The emergent hemorrhoidectomy is recommended for cases with acute thrombosis and strangulation.43 There are no disease-specific guidelines for the management of hemorrhoids. All office and elective procedures should be rescheduled during the pandemic. A recent study has shown that patients with a diagnosis of chronic hemorrhoids before the pandemic had worsening of symptoms during the pandemic as compared with recently diagnosed cases. Patients were reasonably satisfied with the implementation of telemedicine. Lifestyle changes, including physical activity and weight loss, have led to improvement in hemorrhoid severity score.44 Preventive measures can reduce the incidence of hemorrhoids and hence reduce the burden on the health system. Patients should be advised to increase physical activity, increase fluid intake, consume a high fiber diet, and avoid straining; actively treating constipation will also help in preventing hemorrhoids.45

Anorectal warts
Human papilloma virus (HPV) is the most common sexually transmitted infection in US, with estimate of 5.5 million cases per year.46 This can infect the anus due to anal receptive intercourse or direct spread from the genital area.57 Clinically, HPV can present as warts (condyloma acuminata) and/or dysplastic lesions (anal intraepithelial neoplasia). The dysplastic lesions are precursors of the invasive squamous cell cancer.48 An immunocompromised state is established risk factor for progression of HPV infection. The literature shows an interesting case of a patient with a history of renal transplant who demonstrated spontaneous regression of warts during COVID-19 infection. This can be explained by manipulation of immunosuppression medications or induction of innate and adaptive immune responses.49 There is limited data regarding management of anal warts during the COVID-19 era. A delay in surgical treatment is expected. The authors suggest that topical medical treatments, such as trichloroacetic acid, imiquimod, podophyllotoxin, 5-flouracil (5-FU), and interferon, should be considered for condyloma acuminata if surgical treatment is not available. Although these agents are associated with high recurrence and local irritation, they show decent clearance rates.48 The medical management of warts does not allow tissue diagnosis. In cases with initial lesion, intolerance to medical treatment and giant lesion surgical treatments should be considered. Surgical resection should be considered in patients with extensive dysplastic lesions and high grade squamous intraepithelial lesions (HSIL). Individuals with low grade squamous intraepithelial lesions (LSIL) require 4–6 months follow up to monitor disease progression. Topical agents such as imiquimod and 5-FU may show benefit in LSIL or as an adjunct treatment for HSIL.38,50,51 The implementation of preventive measures such as vaccination in young adults (9–26 years) and use of condoms during sexual activity can reduce disease burden during the COVID-19 era.

Anal fistula
Cryptoglandular infection, trauma, radiation, and IBD can lead to epithelialized tract from the anal canal to perianal skin. It is considered complex fistula if the area affected is more than 30% of the external sphincter (transsphincteric), extrasphincteric or suprasphincteric.52 The standard management is surgical treatment, including fistulotomy with or without seton placement, fibrin plug, ligation of intersphincteric fistula tract, and endorectal advancement flap.53 A delay in the treatment of anal fistula is expected during the COVID-19 pandemic and will increase, to the discomfort of patients. Outpatient exploration with proctoscopy, and seton placement, are options based on a previous study in Crohn’s disease patients.38

Rectal cancer
COVID-19 has disrupted the management of rectal cancers.54 An earlier study from Wuhan had shown that cancer patients had higher susceptibility to succumb to COVID-19 infection. This can be explained due to immunocompromised state of these patients.55 This led to
hospital-based policies and fear among patient populations, which caused a reduction in treatment and follow-up visits. Consultation rates from primary providers dropped to 30% during the pandemic, and most consultations were conducted virtually. In some cases, patients chose to avoid visiting healthcare facilities and preferred to monitor symptoms at home. The delay in the surgery for early-stage rectal cancer will lead to progression to advanced cancer.56 COVID-19 infection in the cancer patient is potentially fatal. Cancer care and mitigation of the pandemic can impact on each other and a balance between cancer management delay and COVID-19 exposure prevention is required.57

Total meso-rectal excision without chemoradiation is considered as the standard of care treatment for early-stage rectal cancer. The excision is combined with radiation or chemoradiation therapy if complete excision is not certain (intermediate stage cancer). The National Institute for Health and Care Excellence (NICE) guideline does not recommend radiation therapy for localized early-stage cancer.58 The role of adjuvant chemotherapy for localized rectal cancer is limited.59 The European Society for Medical Oncology (ESMO) has recommended the management of rectal cancer during the COVID-19 pandemic. According to this expert consensus statement, neoadjuvant short- or long-course radiation therapy for locally advanced but operable cancers is recommended during the pandemic (Figure 2).60 In cases where surgeries are delayed due to cancellation of elective surgeries, total neoadjuvant chemo and radiation therapy (CRT) has shown safety data.60,61 The utilization of short course radiation therapy was increased in early stage and locally advanced rectal cancer.54 Short course radiation therapy can delay the progression of the disease and serve as a bridge to surgery. As a previous trial had shown non inferiority of intermittent chemotherapy for advanced rectal cancer as compared with continuous chemotherapy, this can lead to reduced chemotherapy time, fewer side effects, and better quality of life.62 This approach can be used during the COVID-19 pandemic for metastatic rectal cancer.

The American College of Surgeons recommends up to 3 months deferral of elective surgeries for benign conditions such as small asymptomatic rectal carcinoid and malignant polyp. Urgent intervention is indicated for cancers requiring multiple transfusions, near obstructions, cancers which do not respond to neoadjuvant treatments, cancers with concerns of sepsis and local perforation, and early cancers where adjuvant therapy has a limited role.63 These patients should undergo appropriate surgery as soon as is feasible, likely within days. Recent data have shown increased emergency presentation of colorectal cancer patients with bleeding, obstruction, peritonitis, and colon perforation, which reflects the delay in urgent surgeries.64 The survey from Italy demonstrated that non-traumatic abdominal emergencies were delayed.65 The increase in emergency cases and complicated cases is
expected to increase because of the delay in urgent and elective surgeries during the COVID-19 pandemic.

**Anal cancer**
The standard treatment for anal cancer is chemoradiation therapy and this has proven curative potential. Management of these patients during the COVID-19 pandemic stays the same and CRT is recommended. The mitomycin and capecitabine chemotherapy (MMC) can cause hematologic toxicities (HT) including neutropenia and leukopenia. Cisplatin-based therapy has fewer incidences of HT. Cisplatin-based therapy should be considered during the COVID-19 pandemic to limit the immunocompromised state in these patients.

**Disruption of colorectal cancer screening tests**
In the beginning of the COVID-19 pandemic, public health and professional organizations recommended postponing non-urgent procedures, including cancer screening. Colorectal cancer screening is delayed and, in some cases, not performed during the COVID-19 pandemic. The decreased screening tests for rectal cancers during COVID-19 raises an important concern. These patients will present late or with emergency presentation, causing increased burden on the health system. It is challenging to prioritize the control of future risks by implementing screening tests over the current pandemic.

The National Cancer Institute Population-based Research to Optimize the Screening Process (PROSPR) consortium recommend to implement fecal immunohistochemical testing to limit exposure to COVID-19, screening populations at high cancer risk, with infection control by pre-procedure COVID-19 testing (subjective and objective) and customization of screening based on geographic virus prevalence.

The future of colorectal cancer screening during the pandemic will likely be a two-step procedure, noninvasive or biochemical testing with either fecal immunohistochemical testing (FIT) or multitarget DNA/FIT test followed by colonoscopy if initial tests are positive. FIT is commonly utilized as a remote test to screen patients for colorectal cancers. Many patients have had a delay in colonoscopies after positive FIT or guaiac testing. A delay in colonoscopy of >9 months after a positive FIT test increased the risk of colorectal cancer and advanced stage cancer. Patients with a positive FIT test should be prioritized for colonoscopy.

**Anorectal emergencies**
The American College of Surgeons recognize acute hemorrhoidal thrombosis/necrosis, perianal/perirectal abscess, and Fournier gangrene (perineal necrotizing fasciitis) as surgical emergencies during the COVID-19 pandemic. The conditions should be managed with emergency surgery as there is no substitute treatment, and any delay in the procedure will increase hospital stay, morbidity, and mortality. If there are limited resources in hospital during the pandemic, then these cases should be transferred early to facilities with the capacity to perform emergency surgery.

Other notable emergent conditions are bleeding rectal varices, foreign body, and rectal obstruction with cancers. The management of these conditions should not deviate from standard treatments.

Urgent hemorrhoidectomy is recommended for acute hemorrhoid thrombosis and strangulation. The perianal/perirectal abscess should be drained in the operating theater if the abscess is deep. If the operating room is unavailable then outpatient percutaneous drainage should be considered. Early surgical debridement with intravenous hydration and antibiotics are the standard treatment for perineal necrotizing fasciitis. Diversion colostomy is required in few cases to avoid fecal contamination.

Rectal varices can sometimes present with massive lower GI bleeding, requiring emergent volume resuscitation, correction of coagulopathy, and blood transfusion. The endoscopic management of rectal varices can be challenging, and is usually done with band ligation or sclerotherapy with high recurrence rate. The trans-jugular intrahepatic portosystemic shunt (TIPSS) procedure is considered in severe cases to decrease portal pressure.

The rectal foreign body is also seen as a traumatic rectal emergency. It can be caused due to accident, sexual pleasure, and/or assault. Diagnosis can be difficult as sometimes patients do not
provide the complete history. It can complicate to rectal perforation, infection, pain, and bleeding. Rectal examination and radiology testing can be helpful. The foreign body should be removed trans-anally, endoscopically, or surgically with goal of minimizing trauma.72,77

The rise of telehealth
The major preventive strategy to prevent COVID-19 transmission is social distancing.78 Telehealth is defined as communication between patients and providers using telecommunication modalities including telephone and video calls.78 Suspected or confirmed cases of viral infection can be assessed remotely, thus minimizing disease spread. This technology also serves as convenient access to healthcare for patients who are not infected but are at high risk of developing the infection (advanced age and history of comorbid conditions).79 Telehealth can decrease cost, travel time, and missing days due to physician appointments and switching providers. Hence, a recent survey demonstrated high acceptance and satisfaction among patients.80 Established patients with limited disease are suitable for this technology. Telehealth can be used to manage patients who had cancelled elective procedures with alternative non-surgical options. This forum can be utilized as an opportunity to educate patients about the current pandemic and the preventive measures. Providers who are quarantined can also utilize telehealth to continue the care of their patients.81 Patients who have possible exposure or confirmed cases of COVID-19 should be offered a telehealth option. This limits disease spread and delays the management of medical issues.

Acute care surgery availability via telehealth can reduce unnecessary emergency or ambulatory clinic visits and non-complicated colorectal problems can be managed non-operatively. Although laparoscopic surgery is the treatment of choice for acute appendicitis, cases of mild appendicitis can be managed non-operatively with antibiotics when surgery cannot be performed during COVID. The non-operative management of emergency cases can reduce the healthcare burden.82,83

Surgical practice during the COVID-19 era
In this health crisis, the worldwide surgical community has had to make necessary changes to continue uninterrupted emergency and oncologic surgeries. The ProctoLock Survey Study showed high prevalence of positive SARS-CoV-2 in providers (11%) and relatively low availability of personal protective equipment (PPE) (71%), ranging from <33% in Africa and >80% in North America). A good number of providers use PPE for COVID-19 positive patients, whereas only 53% used PPE for COVID-19 negative patients. Surgical teams had reduced the workforce and elective procedures had been cancelled. There has been a large reduction in non-oncological procedures, emergency surgeries, and new cancer diagnosis. Among non-oncological procedures, 42% were performed in the office setting. The study also shows fear among the population, with 36% patients having refused surgeries.84

Extensive departmental and scheduling changes have taken place. Restrictions were implemented for all visits to admitted patients, and families were updated about the patient's conditions via phone calls. Separate operating room and recovery areas were specified for suspected or confirmed COVID-19 patients. Telephone or online approaches were utilized for surgical follow up. All patients were screened using symptoms questionnaire and were give a PCR test to rule out COVID-19. Necessary operating room apparatus included plastic wrappings and single-use equipment, and proper disposal of PPE after surgery on COVID-19 patient was practiced.85,86

Current PPE recommendations for the operating room staff include contact, droplet, and airborne precautions. Standard surgical PPE includes googles, N95 masks, powered-air-purifying-respirators (PAPR), face shield, double gloves, protective gowns, and shoe cover.86 Although the utilization of standard PPE will ensure better outcomes and improve confidence of surgeons due to lower chances of viral transmission, it may cause discomfort for the surgeon. An international survey demonstrated that the PPE use can increase fatigue, communication problems, and reduce visibility.87 A checklist protocol in operating rooms and training sessions for adequate doffing and donning techniques are recommended to avoid viral self-contamination and transmission.88

Theoretically, laparoscopic surgery has a higher potential for spread of the virus via aerosol exposure due to surgical smoke or artificial pneumoperitoneum. Maneuvers such as desufflation can
be utilized to limit the spread of virus. In patients with peritonitis along with colorectal pathology, exploratory laparotomy could be the preferred treatment with less risk of virus transmission.89 Since the risk of infectivity is not clearly defined, the European societies recommend standard laparoscopic surgeries with caution. The benefits of this minimally invasive surgery can balance the risk of virus spread.82

Surgical procedures for anorectal cancers can be prioritized following the available data on colorectal surgeries. Patients with early stage and less aggressive lesions can be managed pharmacologically or with radiation therapy, and surgery can be deferred for over 2 months. Those with moderate priority cases and patients with cancers that can be cured only with surgery should undergo treatment within 2 months. The patients with cancer-related emergencies including bleeding and obstruction that are not manageable with non-surgical treatments or endoscopy should undergo surgery within 2 weeks.90

**COVID-19 vaccination**

COVID-19 vaccination has been introduced recently based on promising data. The notable technologies utilized are mRNA) viral vectors, inactivated virus, and protein subunits. Both mRNA vaccines, including BNT162b2 and mRNA-1273, have shown up to 95% efficacy with minimal adverse effects. This has raised enthusiasm among the public and medical community to supply vaccine globally.91,92 The vaccination program is actively vaccinating vulnerable populations, including healthcare providers, patients with high work-related risk, the elderly, and patients with comorbid conditions. There is no established test to determine immunogenicity after the infection and vaccine. The Centers for Disease Control (CDC) recommends a wait time

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**Figure 3.** Severe acute respiratory syndrome coronavirus 2 and anorectal disease management.
of at least 90 days after recent infection before receiving the vaccine. A recent study has shown that the vaccine has potential beneficial effects on the infection rate, hospitalizations, and deaths. Anorectal disease does not pose any contraindication to the COVID-19 vaccine. Patients with cancer should also receive this vaccine as these are a vulnerable population. There are some safety concerns, especially in patients on cancer treatments, but the benefits from the vaccine outweigh these risks. Most cancer treatments will not prevent immunogenicity. The vaccination program should extend to close contacts of high-risk populations.

The authors expect that the exceptional efforts towards vaccination will lower the burden on health care. Fear among patient populations seeking medical attention will be lowered. This will lead to normalization of routine clinical practice and elective procedures. Non-pharmacological preventive measures including facial masks, hand sanitization, and social distancing should be continued during this period because there is no data showing that vaccination reduces transmission from asymptomatic individuals.

In summary, coronavirus disease 2019 had impacted health care and disrupted the management of all acute and chronic diseases (Figure 3). Although COVID-19 presents predominantly with respiratory symptoms, many patients present with pre-existing anorectal disease or develop new lower GI symptoms. Patients with GI manifestations have delayed diagnosis and potentially severe disease. The literature about the management of anorectal diseases during the pandemic is limited. Telemedicine can play vital role in educating patients about risk factor mitigation and provide information about warning signs. Improvement in PPE availability, maneuvers to remove surgical smoke during laparoscopic procedures, and noninvasive management of mild emergency conditions, can all help limit the virus spread. Emergency anorectal conditions, including acute hemorrhoidal thrombosis, with or without prolapse, anorectal abscess and bleeding rectal varices, foreign body, and obstructed cancers require prompt surgery or transfer to a facility with appropriate capacity. Cancer management is delayed during the pandemic, which will increase disease burden and patient discomfort in future. Anorectal cancer screening and treatment recommendations need to be re-defined based on large multicenter studies, which will guide patients and clinicians to optimize care.

Contributions
WQ contributed to the manuscript concept. WA, RH, and WQ drafted the article. WA and AM revised the manuscript. WQ did the critical review. All authors approved the final version.

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