






COVID-19 Induced Acute Pancreatitis in a Malagasy Woman Patient: Case Report and Literature Review

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Background: SARS-CoV-2 has been described as a respiratory tropic virus since its emergence in December 2019. During the course of the disease, other extra-pulmonary manifestations have been reported in the literature including pancreatic involvement such as acute pancreatitis. This phenomenon linking COVID-19 and acute pancreatitis has been reported by several case reports and cohort studies. No cases had been reported in sub-Saharan Africa and Madagascar. We report one more case Of COVID-19 induced acute pancreatitis in a Malagasy woman patient without risk factors, further consolidating the existing evidence.

Case Presentation: A 44-year-old woman was diagnosed with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and had a favorable course under home isolation and drug treatments. One week later, the patient was admitted to hospital with severe acute abdominal pain. Acute pancreatitis was considered according to the revised Atlanta criteria with the presence of the three criteria. Other etiologies of acute pancreatitis (lithiasis, alcohol, hypercalcemia, hypertriglyceridemia, tumor, trauma, surgery) were excluded. Ultimately, a COVID-19 induced acute pancreatitis was retained. The outcome was favorable under symptomatic medical treatment (fluid resuscitation, bowel rest, management of pain and vomiting, and early oral feeding). The patient was discharged after one week of hospitalization.

Conclusion: COVID-19 is a possible etiology of acute pancreatitis. Acute pancreatitis should be routinely ruled out in a patient with COVID-19 infection with acute abdominal pain.

Keywords: acute pancreatitis, COVID-19, Madagascar

Background

The current coronavirus disease 2019 (COVID-19) originated in Wuhan, China in December 2019. COVID-19 disease causes severe acute respiratory syndrome.¹ In November 2021, more than 250 million people have been infected worldwide and more than 5 million deaths have occurred.² Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a respiratory-tropic virus with manifestations such as cough, dyspnea and fever.³ Over time, atypical presentations of the disease including cardiac, hepatic, renal, musculoskeletal, gastrointestinal and neurological manifestations have been identified.¹ However, gastrointestinal (GI) manifestations of COVID-19 are currently drawn significant attention. GI manifestations are reported in 11.4–61.1% of individuals with COVID-19, with variable onset and severity.³ The majority of COVID-19 associated GI symptoms are mild and self-limiting and include anorexia, diarrhea, nausea, vomiting and abdominal pain.^{3–5} Abdominal pain is less common than the other symptoms. However, a minority of patients with acute abdominal pain had a real abdominal cause; such as acute pancreatitis (AP), acute appendicitis, intestinal obstruction, bowel ischemia, hemoperitoneum, etc.^{3,6}

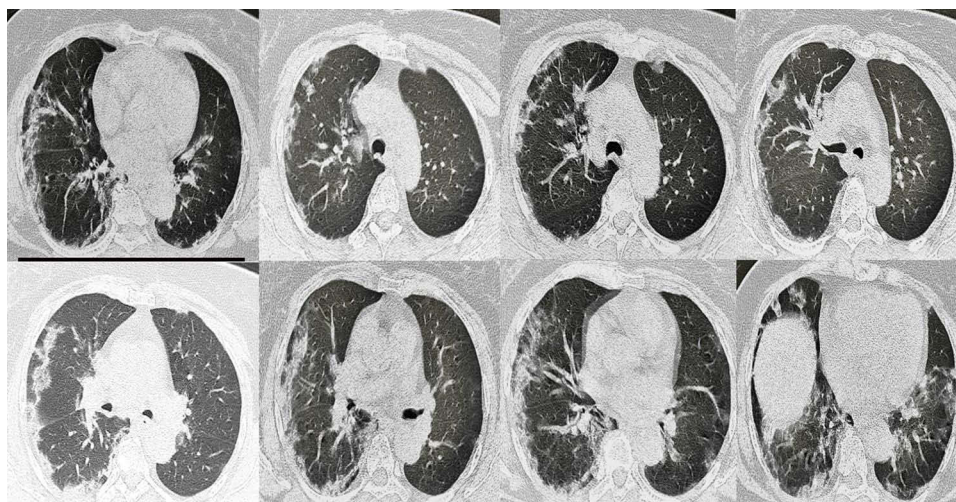


Figure 1 Chest computed tomography in a 44-year-old woman showing bilateral ground glass opacities.

COVID-19 has been reported by a number of authors as a possible etiology of AP.^{1,7–36} Although viral AP has been described in other infections, evidence of pancreatic involvement induced by SARS-CoV-2 infection remains limited. Clinicians involved in the management of AP should be aware of its existence in the context of COVID-19.¹⁰ Moreover, no cases

Table 1 Laboratory Results

Laboratory Tests	Value	Normal Range
Leukocytes (cells/L)	15.6×10^9	$4\text{--}10 \times 10^9$ cells/L
Neutrophil (cells/L)	13.7×10^9	$1.3\text{--}75 \times 10^9$ cells/L
Lymphocyte (cells/L)	1.3×10^9	$1.5\text{--}4 \times 10^9$ cells/L
Hemoglobin (g/dL)	14.5	12–16 g/dL
Platelet count (cells/L)	331	$150\text{--}450 \times 10^9$ cells/L
Hematocrit (%)	44.7	37–47%
C-reactive protein (mg/L)	25	0–6 mg/L
Aspartate aminotransferase (U/L)	41	5–34 U/L
Alanine aminotransferase (U/L)	196	0–55 U/L
Total bilirubin ($\mu\text{mol/L}$)	4.4	0–20 $\mu\text{mol/L}$
Gamma-lutamyl transpeptidase (U/L)	249	9–36 U/L
Alkaline phosphatase (U/L)	73	42–98 U/L
Serum lipase level (U/L)	301	0–60 U/L
Blood sodium level (mmol/L)	139	136–145 mmol/L
Blood potassium level (mmol/L)	4.8	3.5–5.1 mmol/L
Serum calcium level (mmol/L)	2.2	2.1–2.55 mmol/L
Serum triglyceride level (g/L)	2.1	0–1.99 g/L
Serum creatinine level ($\mu\text{mol/L}$)	54	49–90 $\mu\text{mol/L}$
Fasting blood glucose (mmol/L)	6.9	4.1–5.6 mmol/L
HbA1c (glycated Hemoglobin) (%)	6.6	4–6%
D-dimer (ng/mL)	805	0–500 ng/mL
COVID-19 RT-PCR of nasopharyngeal swabs	Positive	–
Hepatitis B surface ntigen	Negative	–
Hepatitis C antibody	Negative	–
Hepatitis A antibody type IgM	Negative	–
Human immunodeficiency virus serology	Negative	–

have been reported in Madagascar or even in sub-Saharan Africa. We report one more case of SARS-CoV-2 infection induced AP in a Malagasy woman patient without risk factors, further consolidating the existing evidence.

Case Presentation

A 44-year-old woman was admitted to hospital during the 2nd wave of the COVID-19 pandemic in Madagascar (April 2021), for severe epigastric pain. She was neither an alcoholic nor a smoker. The patient did not report a history of trauma or recent surgery. The patient presented a week earlier with asthenia, myalgia, dry cough, a few episodes of difficulty breathing and fever. The Chest computed tomography scan showed bilateral ground glass opacities (Figure 1). COVID-19 reverse transcription polymerase chain reaction (RT-PCR) of nasopharyngeal swabs was positive. A moderate COVID-19 was retained. The patient had a favorable evolution with home isolation and drug management (paracetamol, aspirin, atorvastatin, amoxicillin-clavulanic acid, enoxaparin preventive dose). One week later, severe epigastric pain (visual analog scale 9/10), associated with nausea and vomiting (3–4 times) suddenly appeared, leading to hospitalization. General examination reported a Body mass index of 28.5 kg/m^2 , a blood pressure of 100/70 mmHg, a heart rate of 64 bpm, a respiratory rate of 26/min and an oxygen saturation of 94%. Physical examination on admission showed epigastric tenderness and abdominal bloating. Laboratory tests reported a serum lipase level at 301 U/L ($> 3 \times$ Upper limit of normal), C-reactive protein at 25 mg/L, serum calcium level at 2.2 mmol/L, serum triglyceride level at 2.1 g/L, D-dimer at 805 ng/mL. The other laboratory tests are reported in Table 1. Abdominal ultrasound showed no extrahepatic or intrahepatic lithiasis. The Abdominal computed tomography scan showed a benign edematous pancreatitis with no evidence of gallstones (Figure 2). The outcome was favorable under symptomatic medical treatment associating fluid resuscitation, bowel rest, management of pain and vomiting, preventive dose of enoxaparin and early oral feeding upon pain resolution. The patient was discharged after one week of hospitalization. We ultimately retained the diagnosis of SARS-CoV-2 infection induced AP in a woman patient without risk factors.

Discussion and Conclusions

AP appears to be an uncommon complication or association of COVID-19.³⁷ A retrospective American study had objectified a point prevalence of AP of 0.27% (32 patients) out of 11,883 hospitalized COVID-19 patients.³⁸ We report

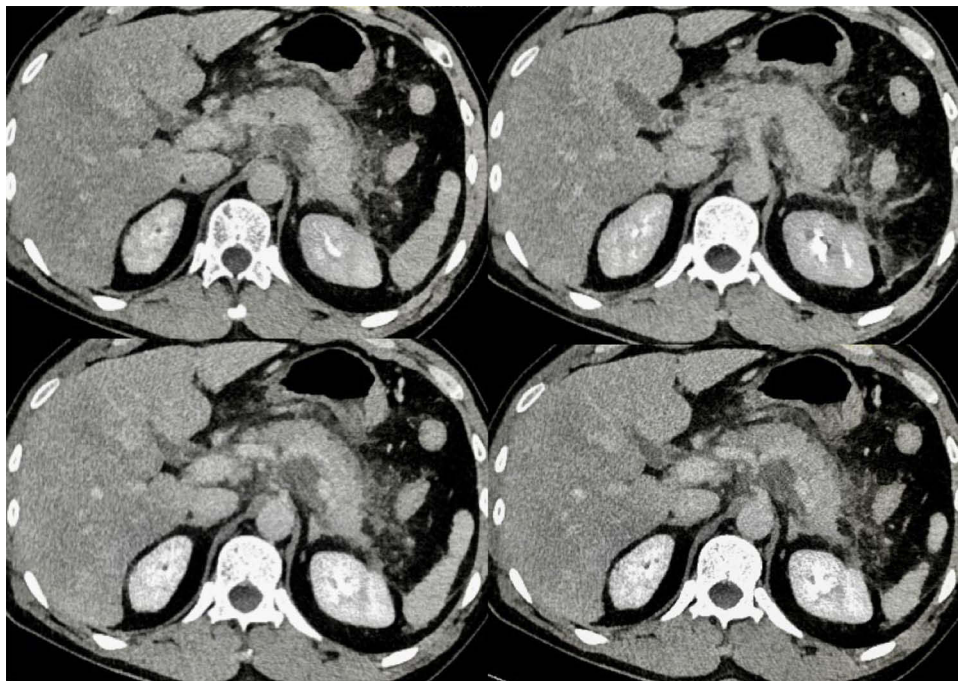


Figure 2 Abdominal computed tomography in a 44-year-old woman showing interstitial edema of the pancreas with the homogeneous enhancement of the pancreatic suggesting benign edematous pancreatitis with no evidence of gallstones.

Table 2 A Few Reported Cases of COVID-19 Induced Acute Pancreatitis (2020–2021)^{1,7–36}

Auteurs, Years [Ref]	Country	Age (Years)	Sex	Clinical Manifestations	COVID-19 PCR	Severity of COVID	Lipase and Amylase	Severity of AP	Treatments	Outcomes
Acherjya GK et al, 2020 ¹	Bangladesh	57	F	Arthralgia, generalized aching, then abdominal pain on the 5th day	P	Moderate	L: 8352 U/L A: 80 U/L	Benign	Symptomatic medical treatment	Favorable
Eldaly AS et al, 2021 ⁷	Egypt	44	M	Abdominal pain, vomiting, no respiratory symptoms	P	Asymptomatic	L: 286 U/L A: 773 U/L	Benign	Symptomatic medical treatment	Favorable
Wifi MN et al, 2021 ⁸	Egypt	72	F	Coughing, sneezing, abdominal pain, vomiting	P	Mild	L: 710 U/L A: 1667 U/L	Benign	Symptomatic medical treatment	Favorable
da Costa Ferreira et al, 2021 ⁹	Brazil	35	M	Epigastric pain, dyspnea, nausea, vomiting	P	Severe	A: 1669 U/L	Severe	Symptomatic medical treatment	Favorable
Kandasamy S, 2020 ¹⁰	India	45	F	Intense epigastric pain, nausea, vomiting, then dyspnea 1 week later	P	Moderate	L: 294 U/L A: 364 U/L	Benign	Symptomatic medical treatment	Favorable
Cheung S, et al, 2020 ¹¹	USA	38	M	Severe epigastric pain, vomiting, fever	P	Asymptomatic	L: 20,320 ukat/L A: N/A	Benign	Symptomatic medical treatment	Favorable
Kumaran NK, et al, 2020 ¹²	United Kingdom	67	F	Epigastric pain, diarrhea, vomiting	P	Severe	L: N/A A: 1483 U/L	Severe (necrotizing), sepsis	Symptomatic medical treatment, antibiotic therapy	Favorable
Arbati MM, et al, 2021 ¹³	Iran	28	M	Dyspnea, cough, myalgia, fever, severe epigastric pain, nausea, vomiting	P	Severe	L: 759 U/L A: 1273 U/L	Severe (necrotizing)	Symptomatic medical treatment, antibiotic therapy	Favorable
AlHarmi RAR et al, 2021 ¹⁴	Bahrain	52	F	Cough, fever, dyspnea, then abdominal pain days later	P	Moderate	L: N/A A: N/A	Benign	Symptomatic medical treatment	Favorable
Brikman S et al, 2020 ¹⁵	Israel	61	M	Fever, cough, dyspnea then abdominal pain at the 14th day of evolution	P	Severe	L: 203 U/L A: 142 U/L	Benign	Symptomatic medical treatment	Favorable

Kataria S et al, 2020 ¹⁶	USA	42	F	Fever and cough then abdominal pain 2nd day	P	Moderate	L: 1541 U/L A: 501 U/L	Benign	Symptomatic medical treatment	Favorable
Purayil et al, 2020 ¹⁷	Qatar	58	M	Fever, vomiting, epigastric pain, no respiratory symptoms	P	Asymptomatic	L: > 600 U/L A: 249 U/L	Benign	Symptomatic medical treatment	Favorable
Lakshmanan et al, 2020 ¹⁸	USA	68	M	Anorexia, nausea then persistent nausea, vomiting several weeks later, no abdominal pain	P	Asymptomatic	L: 1030 U/L A: 2035 U/L	Benign	Symptomatic medical treatment	Favorable
Alwaeli H et al, 2020 ¹⁹	USA	30	M	Abdominal pain, vomiting, diarrhea, dyspnea	P	Mild	L: 1022 U/L A: 151 U/L	Severe	Symptomatic medical treatment	Favorable
Sandhu et al, 2021 ²⁰	India	25	F	Abdominal pain, fever and shortness of breath	P	Severe	L: 35.6 U/L A: 350 U/L	Severe	Symptomatic medical treatment, intubation, mechanical ventilation	Death
Gupta A et al, 2021 ²¹	India	25	F	Fever, headache, ageusia, then abdominal pain on 8 days later	P	Severe	L: 2052.61 U/L A: 1814 U/L	Benign	Symptomatic medical treatment, antibiotic therapy, oxygenation	Favorable
Rabice SR et al, 2020 ²²	USA	36	F (Pregnant)	Cough, fever, then abdominal pain 2 days later	P	Moderate	L: 875 U/L A: 88 U/L	Benign	Symptomatic medical treatment, then cesarean section at 38 week and 2 days of gestation	Favorable with alive baby
Alves AM et al, 2020 ²³	Brazil	56	F	Cough, dyspnea, general malaise and abdominal pain	P	Severe	L: 2993 U/L A: 544 U/L	Benign	Mechanical ventilation, antibiotic therapy, symptomatic medical treatment	Favorable
Karimzadeh et al, 2020 ²⁴	India	65	F	Abdominal pain, nausea, chills, myalgia	P	Severe	L: 283 U/L A: 192 U/L	Benign	Symptomatic medical treatment, antibiotics, hydroxychloroquine, antivirals	Favorable

(Continued)

Table 2 (Continued).

Auteurs, Years [Ref]	Country	Age (Years)	Sex	Clinical Manifestations	COVID-19 PCR	Severity of COVID	Lipase and Amylase	Severity of AP	Treatments	Outcomes
Alloway BC et al, 2020 ²⁵	USA	7	F	Abdominal pain, anorexia, fever	P	Mild	L: 676 puis 1672 U/L A: N/A	severe (necrotizing)	Symptomatic medical treatment, antibiotic therapy	Favorable
Bokhari SMM et al, 2020 ²⁶	Pakistan	32	M	Recurrent fever, myalgia, cough, diarrhea, then severe abdominal pain one week later	P	Mild	L: 721 U/L A: 672 U/L	Benign	Symptomatic medical treatment, antibiotic therapy	Favorable
Simou EM et al, 2020 ²⁷	Morocco	67	-	Dyspnea, fever, myalgia, arthralgia then deterioration with sepsis at 5th day	P	Severe	L: 576 U/L A: N/A	Grave (stage C)	Symptomatic medical treatment, antibiotic therapy	Death
Sudarsanam et al, 2021 ²⁸	India	35	M	Abdominal pain, fever, cough	P	Mild	L: 42 U/L A: 46 U/L	Grave (necrotizing)	Symptomatic medical treatment, antibiotic therapy	Favorable
Kopiczko N, et al, 2021 ²⁹	Poland	6	F	Epigastric pain, vomiting	P	-	L: 4159 U/L A: 910 U/L	Benign	Symptomatic medical treatment	Favorable
Sanchez RE et al, 2020 ³⁰	Colombia	16	M	Nausea, vomiting, epigastric pain	P	Moderate	L: 961 U/L A: N/A	Benign	Symptomatic medical treatment, oxygenation, remdesivir	Favorable
Basukala S et al, 2021 ³¹	Nepal	49	F	Severe abdominal pain, fever, shortness of breath	P	Severe	L: 568 U/L A: 1563 U/L	Severe (necrotic and hemorrhagic), sepsis	Surgery, symptomatic medical treatment, antibiotics	Death
Mazrouei et al, 2020 ³²	United Arab Emirates	20	M	Epigastric pain, nausea, diarrhea	P	Mild	L: 578 U/L A: 391 U/L	Benign	Symptomatic medical treatment	Favorable
Ghosh A et al, 2020 ³³	India	63	M	Fever, shortness of breath, cough, no digestive signs, hypoglycemia	P	Moderate	L: 412 U/L A: 58 U/L	Severe (necrotizing)	Symptomatic medical treatment	Favorable

Berrichi S et al, 2021 ³⁴	Morocco	36	F	Cough, shortness of breath, headache, then a week later, dyspnea and abdominal pain	P	Severe	L: 2570 U/L A: N/A	Benign	VV-ECMO, symptomatic medical treatment, plasmapheresis	Death
		51	F	Severe epigastric pain, nausea, vomiting, shortness of breath	P	Moderate	L: 676 U/L A: N/A	Benign	Oxygenation, corticosteroid therapy, symptomatic medical treatment	Favorable
Higgins JS et al, 2021 ³⁵	Malta	63	F	Intermittent epigastric pain, nausea, no respiratory signs	P	Asymptomatic	L: N/A A: 1079 U/L	Benign	Symptomatic medical treatment	Favorable
		87	F	Diffuse abdominal pain, nausea, vomiting	P	Asymptomatic	L: N/A A: 499 U/L	Benign	Symptomatic medical treatment	Favorable
		64	F	Severe abdominal pain, nausea, vomiting	P	Asymptomatic	L: N/A A: 2141 U/L	Benign	Symptomatic medical treatment	Favorable
Aday U et al, 2021 ³⁶	Korea	32	M	Sudden-onset abdominal pain, nausea	P	asymptomatic	L: 1236 U/L A: 738 U/L	Necrotizing pancreatitis	Surgery, symptomatic medical treatment, antibiotics	Favorable

Abbreviations: Ref, reference; F, female; M, male; P, positive; L, lipase, A, amylase; COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; AP, acute pancreatitis, N/A, not available; symptomatic medical treatment, fluid resuscitation, bowel rest, management of pain and nausea; USA, United States of America; VV-ECMO, veno-venous extra-corporeal membrane oxygenation.

this first case in sub-Saharan Africa of SARS-CoV-2 infection induced AP, to show the possibility of this association in the black African population. The association between COVID-19 and AP had already been reported by many North African authors (2 cases in Egypt, 4 cases in Morocco, 6 cases in Algeria).^{7,8,27,34,39}

The revised Atlanta criteria defines AP if at least 2 of the following 3 criteria are met: (1) severe abdominal pain; (2) serum lipase level (or amylase) more than 3 times the upper limit of normal (ULN); (3) radiological features compatible with AP.⁴⁰ Our case fulfilled all 3 criteria, allowing us to definitely retain the diagnosis of AP.

The causes of AP are dominated by lithiasis and alcoholic causes (>80%).^{40,41} But, about 10% of AP cases are directly caused by infectious microorganisms such as parasites, bacteria, and viruses.⁴¹ Viral AP has been widely reported in the medical literature. The main viruses reported were cytomegalovirus, Epstein Barr virus, mumps, hepatitis A, B and E viruses, herpes simplex virus, varicella zona virus, coxsackie viruses, echo viruses and human immunodeficiency virus (HIV).^{7,9,12,14} Recently, COVID-19 has been identified as a possible viral cause of AP. The mechanism of the relationship between pancreatitis and COVID-19 infection remains unknown and multifactorial. Pancreatic injury could be explained by the expression of angiotensin-converting enzyme-2 (ACE-2) receptors on the pancreas, with subsequent injury to the islet of the pancreas with an elevation of serum amylase and lipase enzymes and risk of development of acute diabetes, as in our case.⁴² Several case reports on SARS-CoV-2 infection induced AP have been reported by numerous authors confirming this relationship between COVID-19 and AP.^{1,7-36} The description of these numerous case reports of COVID-19 induced AP is reported in Table 2.

However, in our clinical practice, further investigations should be conducted to exclude other causes in order to establish a correlation between the virus and AP, to avoid misdiagnosis and subsequent mismanagement of the disease. In addition, a retrospective cohort study conducted in 6 US centers had shown that approximately 48% of patients with lipase elevation above 3 x ULN were due to non-pancreatic etiologies.⁴³ Hence the importance of a radiological features in favor of AP and the elimination of all other possible causes of AP. In our case, the other causes of AP (gallstones, alcohol, hypercalcemia, hypertriglyceridemia, trauma, surgery, drugs, comorbidities) were ruled out, in order to retain COVID-19 as a possible origin of AP.

Abdominal pain is a classic gastrointestinal symptom of COVID-19, which may not alert clinicians to a possible AP.³⁻⁶ However, all reported cases of COVID-19-induced AP have reported the almost constant presence of abdominal pain, either concomitant or remote from the acute respiratory episode.^{1,7-36} Hence, the importance of routine pancreatic enzyme testing (Serum lipase and/or amylase level) in COVID-19 patients with abdominal pain.

The management of viral AP is no different from the treatment of AP due to other causes. Because COVID-19 AP is moderate in 70% of reported cases (23/33 of the cases described in Table 2, symptomatic medical treatment (fluid resuscitation, bowel rest, management of pain and vomiting, and early oral feeding) combined with adequate COVID-19 management was usually sufficient, such as our case.^{1,7-36}

The prognosis of COVID-19-related AP was favorable in the majority of reported cases, including our patient.^{1,7-36} Of the 33 case reports described in Table 2, we had listed 4 deaths, which were concomitantly related to the severity of the AP and the respiratory involvement of COVID-19.^{1,7-36}

In conclusion, SARS-CoV-2 infection is a possible etiology of AP. AP should be routinely ruled out in the presence of concomitant or delayed onset of acute abdominal pain in COVID-19 patients. The prognosis of COVID-19-induced AP remains favorable in the majority of cases.

Ethical Approval and Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. The publication of this case has been approved by the University Hospital Joseph Raseta Befelatanana Antananarivo Ethics Committee.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no conflicts of interest.

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