



MAIN TEXT

Extracorporeal life support in mitral papillary muscle rupture: Outcome of multicenter study

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Abstract

Background: Post-acute myocardial infarction papillary muscle rupture (post-AMI PMR) may present variable clinical scenarios and degree of emergency due to result of cardiogenic shock. Veno-arterial extracorporeal life support (V-A ECLS) has been proposed to improve extremely poor pre- or postoperative conditions. Information in this respect is scarce.

Methods: From the CAUTION (meChanical complicAtion of acUte myocardial infarcTion: an InternatiONal multiceNter cohort study) database (16 different Centers, data from 2001 to 2018), we extracted adult patients who were surgically treated for post-AMI PMR and underwent pre- or/and postoperative V-A ECLS support. The end-points of this study were in-hospital survival and ECLS complications.

Results: From a total of 214 post-AMI PMR patients submitted to surgery, V-A ECLS was instituted in 23 (11%) patients. The median age was 61.7 years (range 46–81 years). Preoperatively, ECLS was commenced in 10 patients (43.5%), whereas intra/postoperative in the remaining 13. The most common V-A ECLS indication was post-cardiotomy shock, followed by preoperative cardiogenic shock and cardiac arrest. The median duration of V-A ECLS was 4 days. V-A ECLS complications occurred in more than half of the patients. Overall, in-hospital mortality was 39.2% (9/23), compared to 22% (42/219) for the non-ECLS group.

Conclusions: In post-AMI PMR patients, V-A ECLS was used in almost 10% of the patients either to promote bridge to surgery or as postoperative support. Further investigations are required to better evaluate a potential for increased use and its effects of V-A ECLS in such a context based on the still high perioperative mortality.

KEYWORDS

acute myocardial infarction, mitral regurgitation, papillary muscle rupture

1 | INTRODUCTION

Post-acute myocardial infarction papillary muscle rupture (post-AMI PMR) occurs in 0.05% to 0.26% of patients with ischemic myocardial injury.¹ It usually develops within a week from the acute event, especially as an evolution of inferior AMI.^{1,2} The acute mitral regurgitation related to post-AMI PMR may suddenly evolve into hemodynamic deterioration, leading to pulmonary edema and cardiogenic shock, or even cardiac arrest. In this setting, prompt hemodynamic stabilization followed by surgical intervention usually represent the standard of care. However, immediate surgical correction, in the presence of extremely poor clinical conditions, may be associated with high perioperative morbidity and mortality rates.^{3,4} The use of mechanical circulatory support (MCS) to improve preoperative patient conditions and bridge the patients to definitive correction in more favorable hemodynamic as well as

metabolic conditions has been proposed.^{1,4} The most recent ESC/EACTS Guidelines on myocardial revascularization allocate ECLS support, in the presence of post-AMI mechanical complications (MCs), in class of recommendation IIb, level of evidence C.^{5,6} However, specific investigation of experiences related to V-A ECLS in the presence of post-AMI PMR has been limitedly reported.⁶ To our knowledge, this is the first international study reporting the in-hospital outcomes of patients with post-AMI PMR who required pre- or intra/postoperative V-A ECLS.

2 | PATIENTS AND METHODS

2.1 | Patient population and study design

The study cohort consisted of patients retrieved from the database of the CAUTION study (“Mechanical



Complications of Acute myocardial Infarction: An International Multicenter Cohort Study”). The CAUTION study (trial registration: [Clinicaltrials.gov](https://clinicaltrials.gov), NCT03848429) is a retrospective, international, multicenter, observational trial aimed at evaluating the postoperative outcomes of patients surgically treated for post-AMI MCs. The patient population of this CAUTION sub-study consisted of the adult patients (>18 years old) who were surgically treated for post-AMI PMR, between January 2001 and December 2018 at 16 different centers, and submitted to V-A ECLS support. Detailed information about demographics, preoperative risk factors, operative details, postoperative hospital course, morbidity, and mortality of this patient cohort were analyzed. The study was conducted in accordance with the guidelines of the Declaration of Helsinki, and the related protocol was authorized by the local ethical committee of the leading center (Maastricht University Medical Centre METC 2018–0924) and thereafter by the ethical committees of each of the involved centers.

2.2 | Definitions and main goals

Rupture of the whole papillary muscle (body) was defined as “complete” or “total”; a rupture involving one of the heads of the papillary muscle was considered “partial.” Cardiogenic shock was defined as with reduction in cardiac index ($<1.8\text{ L}/\text{min}/\text{m}^2$) and/or systolic blood pressure $<90\text{ mm Hg}$, mean arterial pressure $<65\text{ mm Hg}$, despite maximal conservative treatment. Pre-emptive V-A ECLS implantation was considered when implanted preoperatively in case of hemodynamic instability at risk of evolution to cardiogenic shock or cardiac arrest. Urgent surgery was defined as surgery required during the same hospitalization for patients who have not been admitted in elective regimen. Emergent surgery was considered an operation that occurred within 24 h after admission, whereas salvage surgery when patients required cardiopulmonary resuscitation en route to the operating room. V-A ECLS central cannulation was defined as cannulation of the ascending aorta for arterial blood inflow and the right atrium for drainage outflow; peripheral cannulation was considered the femoral or axillary artery for patients' arterial blood inflow and the femoral vein for venous drainage (bi-caval single drainage cannula). Post-cardiotomy ECLS (PC-ECLS) was considered as a tool to rescue patients in refractory cardio-circulatory failure, with or without respiratory dysfunction, in various circumstances following cardiac surgery that otherwise would almost certainly lead to death.⁷ Primary end-points of the analysis were in-hospital survival and prevalence, as well as type, of ECLS complications. We also assessed in-hospital survival for

the non-ECLS group of patients for its comparison with the counterpart (ECLS subgroup). In-hospital survival was defined as hospital discharge or transfer to another facility from the ECLS center.

2.3 | Statistical analysis

Only a descriptive analysis with pooled prevalence rates was carried out, considering the restricted number of ECLS patients and the quality of data available. Variables are expressed as a count (with percentage) for categorical variables and the mean (\pm standard deviation) for normally distributed continuous variables or median (interquartile range, IQR) for those with non-normal distribution. Comparison between groups (before and after conversion) was performed using the Mann–Whitney U test or t-test whichever appropriate for the continuous variables and Pearson's χ^2 test for categorical variables. A two-tailed p -value of <0.05 was considered significant. Analyses were performed with STATA (StataCorp, 2022, version 17, TX, USA).

3 | RESULTS

From the 214 post-AMI PMR patients enrolled in the CAUTION_{PMR} study, there were 23 post-AMI PMR patients who underwent V-A ECLS support (10.7%; 23/214). All these subjects developed acute and severe (3+ or 4+) mitral regurgitation due to the rupture of the papillary muscle. The median age was 61.7 years (range 46–81 years), with predominance of male gender (86.2%; 19/23). Hypertension and smoking were the most frequent cardiovascular risk factors (52.2%; 12/23 and 43.5%; 10/23, respectively). Demographics and clinical characteristics of the ECLS patients are reported in [Table 1](#). More than two thirds of the subjects had posteromedial PMR and complete PMR. The rupture occurred after ST segment elevation MI in approximately 80% (18/23) of cases. On echocardiographic evaluation, more than half of patients reported preoperative depression of the left ventricle ejection function (LVEF below 45%) ([Table 2](#)). Cardiogenic shock and acute pulmonary edema rates were 73.9% (17/23) and 43.5% (10/23), respectively. Inotropic support was required in 86.9% (20/23) of cases.

Concerning the operative procedure, patients underwent salvage/emergent surgery in the majority of cases (74%; 17/23). Mitral valve replacement (MVR) was performed in 20 patients, while mitral valve repair (MVR) in the remaining three. Concomitant coronary artery bypass grafting (CABG) was performed in 14 patients (60.9%). [Table 3](#) lists the V-A ECLS details; in 10 patients V-A ECLS



TABLE 1 Demographics and clinical characteristics.

	V-A ECLS cohort (n = 23)	Non-ECLS cohort (n = 191)
Mean age (years)	61.7 (range 46–81)	66.5 (range 29–86)
Gender		
Male	19 (82.6%)	137 (71.7%)
Female	4 (17.4%)	54 (28.3%)
BMI (Kg/m ²)	26.4 ± 3	26.3 ± 3
Hypertension	12 (52.2%)	120 (62.8%)
Diabetes mellitus	6 (26.1%)	42 (21.9%)
Dyslipidemia	7 (30.4%)	71 (37.2%)
Stroke/TIA	3 (13.1%)	15 (7.8%)
Smoking	10 (43.5%)	79 (41.4%)
COPD	4 (17.4%)	42 (21.9%)
Chronic kidney disease	4 (17.4%)	36 (18.8%)
Peripheral vascular disease	2 (8.7%)	38 (19.9%)
Atrial fibrillation	3 (13.1%)	44 (23%)
History of CAD or AMI	7 (30.4%)	61 (31.9%)
Previous PCI	4 (14.4%)	31 (16.2%)

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ECLS, extracorporeal life support; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; V-A, veno-arterial.

was implanted before surgery; cardiogenic shock and extracorporeal cardiopulmonary resuscitation (ECPR) for cardiac arrest were the indications. In the remaining subjects, ECLS support was applied for post-cardiotomy cardiogenic shock syndrome. More than two third of the patients underwent peripheral cannulation (femoral artery/femoral vein), while central cannulation strategy (ascending aorta/right atrium) was reported in 6 individuals (all central ones were intra/postoperative implant).

Intra-aortic balloon pump was inserted in 15 patients (65.2%) as LV unloading strategy. The use of Impella, as LV unloading strategy ECLS cohort was not reported. The mean duration of V-A ECLS was 4 days (range 1–15). All the V-A ECLS weaning attempts were undertaken after surgery. Overall, in-hospital mortality rate was 39.2% (9/23 patients), higher than the non-ECLS patients (22%; 42/191) (Figure 1). In the V-A ECLS cohort, there were no death in the preoperative subgroup, when concomitant LV unloading was performed, while in the postoperative V-A ECLS implant subgroup mortality was 60% (3/5) with concomitant LV unloading and 40% (2/5) without it. Complications occurred in 70% of the ECLS patients. Cardiovascular and renal complications were the most frequent ones in the overall V-A ECLS group and

TABLE 2 Cardiovascular characteristics.

	V-A ECLS cohort (n = 23)	Non-ECLS cohort (n = 191)
Papillary muscle rupture		
Antero-lateral ^a	3 (18.7%)	52 (28.8%)
Postero-medial ^a	13 (81.3%)	128 (71.1%)
Partial	5 (31.2%)	65 (36.9%)
Complete	11 (68.8%)	133 (75.6%)
STEMI	18 (78.3%)	128 (67%)
Cardiogenic shock	17 (73.9%)	102 (53.4%)
Cardiac arrest	4 (17.4%)	15 (7.8%)
Acute pulmonary edema	10 (43.5%)	85 (44.5%)
Cardiac tamponade	4 (17.4%)	1 (0.5%)
Chest pain	9 (39.1%)	91 (47.6%)
Dyspnea	10 (43.5%)	105 (55%)
Preoperative LVEF <45%	15 (65.2%)	88 (46.1%)
PAPS >50 mm Hg at rest	6 (26.1%)	28 (14.6%)
Preoperative PCI	2 (8.7%)	33 (17.3%)
IABP implant	15 (65.2%)	141 (73.8%)
Preoperative	12 (80%)	116 (82.3%)
Postoperative	3 (20%)	25 (17.7%)
Inotropes	20 (86.9%)	134 (70.1%)
Late hospitalization (>7 days from MI symptoms)	1 (4.3%)	18 (9.4%)

Abbreviations: ECLS, extracorporeal life support; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PAPS, pulmonary artery systolic pressure; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; V-A, veno-arterial.

^aData concerning 16/23 pts in V-A ECLS Cohort = 69.5% of cohort and 180/191 pts in Non-ECLS Cohort = 94.2%.

pre- and intra/postoperative subgroups. One patient was re-explored due to cardiac tamponade. Detailed information, about V-A ECLS cohort are reported in Table 3. Compared to non-ECLS group, cardiovascular, renal, and hemorrhagic complication were higher in the V-A ECLS group (Figure 2).

4 | COMMENT

Despite the experience and related management of V-A ECLS has been improving in the last two decades, a recent analysis of the Nationwide Inpatient Sample from 2002 to 2014 reported that V-A ECLS was used only in 5% of the entire cohort of post-AMI PMR patients enrolled.⁸ Furthermore, its implantation, as a method of resuscitation and cardiovascular support in post-AMI mechanical complications, has shown no significant temporal trend changes over time.² First experiences reporting V-A ECLS



TABLE 3 V-A ECLS cohort details.

	Overall (n = 23)	Preoperative implant ^c (n = 10)	Intra/ postoperative implant (n = 13)
Indication			
Cardiac arrest (eCPR)	4 (17.4%)	4 (40%)	–
Pre-emptive	2 (8.7%)	2 (20%)	–
Cardiogenic shock	17 (73.9%)	4 (40%)	13 (100%)
Duration (days)			
Whole cohort	4 (range 1–15)	4 (range 2–7)	4 (range 1–15)
Survivors only ^a	4 (range 1–5)	5 (range 4–6)	4 (range 1–5)
Cannulation strategy ^b			
Central	6 (30%)	–	6 (46%)
Peripheral	14 (70%)	10 (100%)	7 (54%)
Complication			
Bleeding	7 (30.4%)	1 (10%)	6 (46%)
Neurological	2 (8.7%)	1 (10%)	1 (7.7%)
Renal	13 (56.5%)	5 (50%)	7 (53.8%)
Cardiovascular	14 (60.9%)	7 (70%)	7 (53.8%)
Pulmonary	8 (34.8%)	5 (50%)	3 (23.1%)
Sepsis	5 (21.7%)	1 (10%)	4 (30.8%)
Outcome			
In-hospital mortality (%)	9 (39.9%)	4 (40%)	5 (38.5%)
With LV unloading	3 (33.3%)	0 (%)	3 (60%)
Without LV unloading	6 (66.7%)	4 (100%)	2 (40%)

Abbreviations: ECLS, extracorporeal life support; eCPR, extracorporeal cardiopulmonary resuscitation; LV, left ventricle; RV, right ventricle; V-A, veno-arterial.

^aData concerning overall survived patients 14/23 = 60.1%.

^bData concerning 20/23 pts = 87% of cohort.

^cAll the preoperative V-A ECMO implant were weaned in the postoperative period.

support in post-AMI PMR individuals undergoing surgery, suggested a more conservative approach in these patients, advising it only for younger subjects with minimal comorbidity, to reduce the additional risk of ECLS-related complications such as neurological complication or bleeding.⁹ Nowadays, in recent updated studies focused on trends and outcomes, the use of V-A ECLS in complex post-AMI MCs has shown promising results, acting as a bridge to surgery in the context of extreme hemodynamic compromise, like cardiac arrest or refractory cardiogenic shock.^{2,6} Despite these limited case reports and few observational studies most of them provided limited information on indications and results of V-A ECLS support in this setting.^{6,9–14}

The infarcted myocardial area may directly involve a PM or extend beyond the infarct-related artery (IRA) usually generating a sudden acute mitral valve regurgitation due to either chordae tethering, or partial/total PMR, often leading to hemodynamic instability or frank

cardiogenic shock. This cardio-circulatory compromise might be refractory to conventional drug therapy or intra-aortic balloon implant, justifying the need for preoperative V-A ECLS. In our study cohort, the incidence of STEMI, reduced LVEF, as well as complete PMR were the more frequent characteristics reported in the patients who required preoperative cardiocirculatory support. Complete PMR, rather than partial one, is usually associated with more severe mitral regurgitation, with ‘flailing’ of both leaflets and a larger coaptation gap. Due to the high risk of a worsened evolution to cardiogenic shock and subsequent multi-organ failure as well as possible death, an early diagnosis and a timely treatment are extremely important in post-AMI PMR patients. However, we recently highlighted that even if surgery is promptly performed, in-hospital mortality of PMR patients undergoing surgery remains high, most likely due to poor preoperative cardio-circulatory and respiratory conditions or complicated postoperative



course, particularly by low cardiac output syndrome.¹⁵ It is, therefore, likely that even if surgery remains the cornerstone of treatment for patients with PMR, a more aggressive use of MCS might be taken into timely consideration. V-A ECLS, or alternative temporary cardio-circulatory assist devices, may constitute a safe bridging to operative room as soon as hemodynamic stability is obtained, or enhance the patient management in the perioperative phase which is usually characterized by critical cardio-circulatory conditions secondary to the AMI and subsequent surgery. The precarious hemodynamic state in post-AMI PMR patients, and the difficult reconstruction of the MV due to infarcted and compromised PM, often translates into a MVR as the procedure of choice in order to reduce the aortic clamping times, duration of the CPB support, and its related effects.¹⁵ Percutaneous catheter-based treatment has

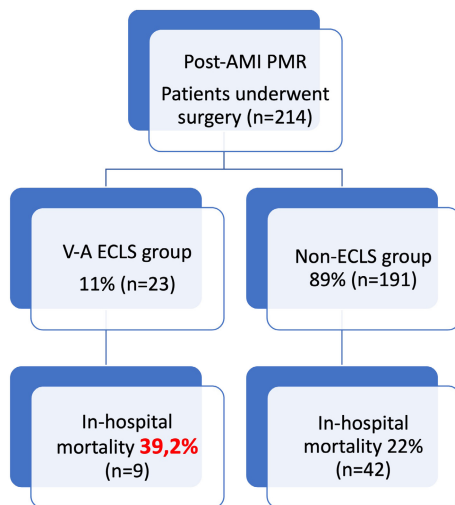


FIGURE 1 V-A ECLS group versus Non-ECLS group from CAUTION_{PMR} study.

been recently proposed as a bridge-to-surgery management or even as an alternative in inoperable patients. In the V-A ECLS cohort, MVR was the most frequent procedure, and more than half of the patients underwent concomitant surgical revascularization. The benefit of concomitant CABG and reperfusion to necrotic tissue, in terms of early postoperative mortality, is still controversial.^{16,17} One limitation of preoperative use of V-A ECLS strategy in post-AMI PMR is the increase in LV afterload related to the retrograde aortic blood flow generated by the extracorporeal life support, that could be deleterious in PMR, increasing the mitral regurgitation and favoring pulmonary edema occurrence. An unloading strategy of the LV, if preoperative V-A ECLS is started, should be considered in the management strategy to prevent LV distention and blood stasis, improving cardio-circulatory and respiratory blood congestion. Accordingly, in our study there was no mortality in preoperative ECLS combined to LV unloading strategy. We might hypothesize that the LV unloading strategy should be standardized concomitantly to preoperative ECLS approach in post-AMI PMR patients. Different approaches to LV-unloading have been proposed. Usually, inodilators and IABP are the first choice, thanks to their easy availability and readiness. In our cohort, IABP was the only LV-unloading strategy reported and applied in most than half of patients. The ECPELLA experience with V-A ECLS combined to Impella CP (Abiomed, Danvers, MA) was reported in only few cases.¹³ Its safety and efficacy need to be established in further research, in particular, to define the potential correlated risk of trans-aortic axial pump malfunction due to intra-device suction of cardiac necrotic tissue derived from the ruptured PM and its possible systemic dissemination.

Implantation of V-A ECLS in the intra/post-operative setting represents an invaluable support in case of

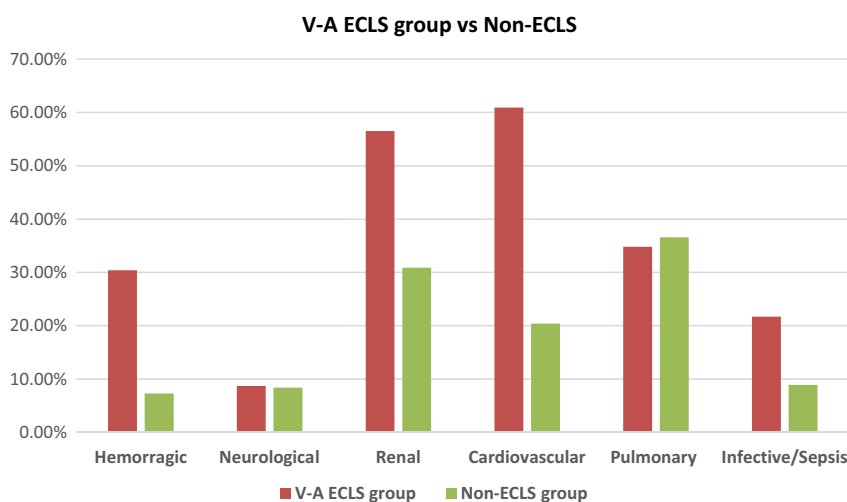


FIGURE 2 V-A ECLS group versus Non-ECLS group complications.



post-cardiotomy cardiogenic shock or cardiac arrest.⁷ LV, RV, or biventricular dysfunction related to the AMI-related injury or mechanical complications, potentially further exacerbated by the surgery-induced myocardial ischemia, may represent potential targets for such a cardio-circulatory support.⁷ However, despite this system may be life-saving, complications during ECLS support may occur. The complications rates and types in patients supported with V-A ECLS of our study are in accordance with ones described in the Extracorporeal Life Support Organization (ELSO) Registry.⁶ We only observed a higher rate of cardiovascular complications most likely related to the peculiar post-AMI setting and related surgery usually performed in emergency/urgency. Indeed, the current study is focused solely on post-AMI PMR patients while the ELSO Registry reported complications on a different, wider cohort that, however, included all types of post-AMI mechanical complications without specifying the frequency of complications in the individual subgroups. Nonetheless, these data are not surprising, taking into consideration the peculiar hemodynamic condition characterized by a huge acute left ventricular volume overload, the elevated wall shear stress and distention to which LV is subjected in post-AMI PMR due to the related acute mitral valve regurgitation. The incidence and the severity of some complications ECLS-related could be potentially influenced by the type of indication for ECLS application. In this way, pre-emptive ECLS might be associated to different incidence of complication, if compared to eCPR or ECLS in cardiogenic shock. *Actually*, no data were reported in literature in post-AMI PMR about it and further studies could be useful to understand this hypothesis.

Also not surprisingly, the mortality rate of the ECLS group in the current study was higher than the non-ECLS counterpart (Figure 1). There are, however, inherent and significant differences in patients who were mechanically bridged to surgery, supported from the operating room, or postoperatively by ECLS, and those undergoing prompt surgery following PMR without mechanical support; with the former generally exhibiting extreme or higher surgical risks, often not immediately suitable for surgery at all due to extremely poor clinical conditions.⁴ Current data would seem to open a possible window in complex post-AMI PMR patients in terms of management (bridging to surgery or intra/postoperative support) and possible survival chance, when a V-A ECLS implant is considered as upgrading and supportive therapy. This strategy is meant to prophylactically enhance the preoperative and perioperative patient status to improve postoperative outcome in an otherwise extremely high-risk urgent/emergent cardiac surgical intervention and related course.

4.1 | Limitations

This study has several important limitations. Data in the CAUTION_{PMR} Study are submitted voluntarily; thus, the accuracy and level of selective reporting is unknown with high-volume centers more readily reporting on worse outcomes and low-volume centers not reporting fatal encounters at all. The mortality rates may, therefore, be underestimated and not translatable to “real world scenario.” The information, due to the retrospective nature of this study, could be subject to incomplete or missing reporting of events as well (as an example, missing data concerning timing from ECLS to surgery or different LV unloading strategy). We excluded from analysis variables with more than 20% missing values. A further limitation concerns the variability of protocols and policy for the use of MCS, because they are individualized in each single ECLS center. According to the definition of ‘ECLS complication’ as reported by ELSO, differentiation between complications intrinsically related to ECLS support and those occurring as a consequence of the pre-existing disease are not possible. Consequently, the recognition of complications might be misdiagnosis or inappropriate as assignment. As inherent to many databases, the presence of selection bias cannot be excluded also in our dataset.

5 | CONCLUSION

V-A ECLS has been proposed to improve extremely poor preoperative or intra/postoperative patient conditions in complex post-AMI PMR clinical scenarios. Despite the overall mortality remains high, its use might represent a “bail-out” option in terms of management and possible survival chances of the most critically ill patients affected by such a post-AMI mechanical complication. Despite the limited patient cohort, this study showed that the use of V-A ECLS has shown to be a potential tool to manage pre- and perioperative complex clinical/hemodynamic conditions and provide benefit in terms of early survival. Further clinical research and investigations are required to provide additional insight in such a challenging setting.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

GM: acquisition of data, analysis and interpretation of data, writing original draft and revising it, final approval and submission, MM: analysis and interpretation of data, revision of article and final approval, MDB: analysis of data, critical revision of article, and final approval, MK: conception



and design of the study, revision of article, and final approval, FF: acquisition of data, revision of article, and final approval, CFR: analysis and interpretation of data, critical revision of article, and final approval, SP: analysis and interpretation of data, critical revision of article, and final approval, IV: acquisition of data, revision of article and final approval, AC: acquisition of data, revision of article and final approval, GF: acquisition of data, revision of article and final approval, CT: acquisition of data, revision of article and final approval, MC: acquisition of data, revision of article and final approval, TF: acquisition of data, revision of article and final approval, GT: acquisition of data, revision of article and final approval, GAD: acquisition of data, revision of article and final approval, SDA: acquisition of data, PSN: acquisition of data, revision of article and final approval, VL: acquisition of data, revision of article and final approval, EV: acquisition of data, revision of article and final approval, SHS: acquisition of data, revision of article and final approval, RS: acquisition of data, revision of article and final approval, IB: acquisition of data, revision of article and final approval, JMK: acquisition of data, revision of article and final approval, MP: acquisition of data, revision of article and final approval, MT: acquisition of data, revision of article and final approval, BM: acquisition of data, revision of article and final approval, FAK: acquisition of data, revision of article and final approval, CF: acquisition of data, revision of article and final approval, CS: acquisition of data, revision of article and final approval, PS: acquisition of data, revision of article and final approval, AK: acquisition of data, revision of article and final approval, MAD: acquisition of data, revision of article and final approval, DR: acquisition and analysis of data, revision of article and final approval, RL: conception and design of the study, revision of article, and final approval.

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