

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. Contents lists available at ScienceDirect



American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Potential role of telemedicine in solving ST-segment elevation dilemmas in remote areas during the COVID-19 pandemic

A recent report showed that ST-segment elevation myocardial infarction (STEMI) may be the first clinical manifestation in COVID-19 patients, with no culprit lesions identifiable in approximately 40% of patients [1]. This could pose a problem in remote areas, especially water-locked areas, in which referral should be considered wisely. The authors are currently based in Indonesia, an archipelago spanning over 17 thousand islands, with challenges due to its geography and uneven distribution of health workers. Some areas have limited medical equipment and are several hours/days travel from the nearest capable hospital. In line with current guidelines the maximum delay from STEMI diagnosis to reperfusion of 120 min should remain the goal for reperfusion therapy if primary PCI is feasible within this time frame and performed in facilities approved for the treatment of COVID-19 patients in a safe manner. Primary PCI pathways may be delayed during the pandemic up to 60 min due to delays in the delivery of care and the implementation of protective measures. Such problems may also be found in other island countries.

Previously, the authors experienced a similar dilemma during their time serving in rural areas, albeit within a reasonable distance to a referral center, which does not require water-based transportation. On that occasion, a particular patient was admitted with de Winter T-Wave Electrocardiography (ECG) which is frequently regarded as a "STEMI Equivalent" [2]. By then, the facility did not have the luxury of a cardiac catheterization laboratory, on the other hand, administering thrombolytics may pose unnecessary bleeding risk for the patient, and the referral can take hours. The authors decided to go through with conservative treatment since there was no recommendation for fibrinolytics for de Winter ECG in the guidelines, and apparently, the patient refused to be transferred to another hospital. A serial ECG 3 h later was taken, revealing a progression into anterior STEMI in which we pursued thrombolytic therapy [2].

Extrapolating that experience to the current situation, physicians in remote areas that require hours or days of land or water-based transportation may face the same predicament. As ST-segment elevation on ECG may be incited by both STEMI and COVID-19-induced myocarditis, the diagnosis is uncertain, and biomarkers such as troponin may be elevated in both conditions [3,4]. As mentioned earlier, ST elevation ECG with non-obstructed coronary arteries may be the first presentation of COVID-19. This may cause a dilemma on whether we should prepare reperfusion therapies and treat the patient for STEMI or not. Moreover, we see a shift in epidemiological patterns of up to 40% "missing" STEMI incidence, while the incidence of COVID-19 is increasing exponentially; hence, educated guesses through statistical bases are not advised. Cardiovascular risk factors and comorbidities are associated with increased

mortality and severity in COVID-19 [5-8]; hence, acute patients with cardiovascular risk factors are not equivalent to acute coronary syndrome (ACS). The simple solution is to perform coronary angiography, which is unavailable in remote areas. If there is no interventional option with on-site stenting, thrombolysis is a useful option in patients with STEMI. Failing to provide reperfusion in STEMI patients may lead to suboptimal outcomes, and incorrect administration of thrombolysis to myocarditis patients may prove detrimental. Patients with STEMI and simultaneous COVID-19 with myocarditis may benefit particularly from thrombolytic therapy because COVID-19 is associated with hypercoagulability and micro/macro thromboembolism. However, as of today, we are not aware of such studies. Thrombolysis in COVID-19 myocarditis without obstruction of the coronary arteries is associated with disadvantages and a higher complication rate for those patients. Thus, telemedicine for remote areas may make a major contribution to clarifying this important question.

Therefore, we must stratify patients based on indirect findings. Although ECG changes and troponin elevation in STEMI and COVID-19 myocarditis as well as in Takotsubo cardiomyopathy may look very similar, there are some notable differences. Troponin elevation in COVID-19 myocarditis and other myocarditis such as Takotsubo syndrome and Kawasaki disease, are modest compared to STEMI [9-11]. Bangalore et al. demonstrated that the median peak troponin T level in patients with culprit lesions was 6.3 ng/mL compared to 0.02 ng/mL in patients without culprit lesions. We expect that serial measurement of troponin T will show a continuous and stronger increase in STEMI compared to COVID-19 myocarditis.

One of the distinguishing features is diffuse ST-segment changes and PR depression associated with myocarditis; however, it may be misinterpreted by untrained eyes. Cardiologists are usually stationed in cities and are unable to provide direct services. Hence, the tele-ECG service may be useful in these scenarios. A one-time or serial ECG consult with a cardiologist may increase the probability of distinguishing the pathologies. Tele-ECG itself has been shown to be successful and can improve the case-resolving capacity concurrent with overcoming geographical limitations to provide specialized healthcare [16]. Furthermore, a report has shown that some COVID-19 patients present with segmental ST elevation typical of STEMI, and trigger catheterization laboratory activations only to show normal or non-obstructive coronary angiography [10]. In light of such cases, tele-ECG is not foolproof.

Echocardiography can be helpful for differential diagnosis; however, this requires an experienced echocardiographer onsite, who often may not be available. Echocardiography may provide clues for distinguishing between the two conditions by observing characteristic regional wall-motion abnormalities (RWMA) and other features, such as a decrease in the ventricular ejection fraction. Stefanini et al. reported that among 11 patients without culprit lesions, two had no wall motion abnormalities while two others did [1]. On the other hand, 16 out of 17 patients with culprit lesions had RMWA and one patient had diffuse wall motion abnormalities. Bangalore et al. reported that RMWA is present in 6 out of 8 patients with identifiable culprit lesions and 0 out of 9

patients without culprit lesions [10]. Hence, echocardiography is a potential tool to rule out true STEMI; nevertheless, a larger sample size is needed and additional parameters may be required to increase its sensitivity. Moreover, echocardiography seems to be a promising diagnostic noninvasive tool to detect coronary artery abnormalities [12], especially in this era where Kawasaki-like disease in the pediatric population has been reported [13]. However, echocardiography is more difficult to operate and limited in availability compared to ECG so a possible solution may be remote echocardiography. A study in Brazil indicated that echocardiography with remote interpretation is feasible. The authors trained non-physicians to aid in performing echocardiography, which was then transmitted to the experts. The program has been shown to improve early diagnosis and referral [14]. To add a "layer" to tele-ECG and risk factor-based considerations, tele-echocardiography can be performed to increase the accuracy and distinguish whether patients are at a high probability of true STEMI, COVID-19 myocarditis, or cardiac injury to guide efficient treatment and patient transfer. The development of a more complex scoring system or artificial intelligence [15] integrating other variables such as clinical history, risk factors, chest X-ray, and laboratory markers can provide a better prediction for ST elevation ECG in COVID-19 patients. Nevertheless, the distribution of echocardiography machines and establishment of telecardiology care can provide a lasting foundation beyond the COVID-19 era. This may be the impetus to integrate tele-cardiology into the healthcare system and improve diagnosis and referral of patients with heart disease in underserved areas. It is an investment that cannot go wrong. Although there is no formal scoring available to distinguish STEMI from COVID-19 myocarditis, several features such as troponin, ECG, and echocardiographic findings may help to differentiate them. However, these facilities/human resources may not be present in remote areas. Thus, the more widespread use of telemedicine should be encouraged for remote areas and may make a major contribution to filling this gap.

Funding

None.

Declaration of competing interest

None.

Acknowledgement

None.

References

- Stefanini GG, Montorfano M, Trabattoni D, et al. ST-elevation myocardial infarction in patients with COVID-19: clinical and angiographic outcomes. Circulation. 2020. https://doi.org/10.1161/CIRCULATIONAHA.120.047525 April. CIRCULATIONAHA.120.047525.
- [2] Pranata R, Huang I, Damay V. Should de Winter T-wave electrocardiography pattern be treated as ST-segment elevation myocardial infarction equivalent with consequent reperfusion? A dilemmatic experience in rural area of Indonesia. Case Rep Cardiol. 2018;2018:1–4. https://doi.org/10.1155/2018/6868204.
- [3] Santoso A, Pranata R, Wibowo A, Al-Farabi MJ, Huang I, Antariksa B. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: a meta-analysis. Am J Emerg Med. 2020. https://doi.org/10.1016/j.ajem.2020.04.052 April.
- [4] Pranata R, Huang I, Lukito AA, Raharjo SB. Elevated N-terminal pro-brain natriuretic peptide is associated with increased mortality in patients with COVID-19 – systematic review and meta-analysis. Postgrad Med J. 2020. https://doi.org/10.1136/ postgradmedj-2020-137884.
- [5] Pranata R, Lim MA, Huang I, Raharjo SB, Lukito AA. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis and meta-regression. J Renin Angiotensin Aldosterone Syst. 2020;21(2):147032032092689. https://doi.org/10.1177/1470320320926899.
- [6] Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – a systematic review, meta-

analysis, and meta-regression. Diabetes Metab Syndr Clin Res Rev. 2020;14(4): 395–403. https://doi.org/10.1016/j.dsx.2020.04.018.

- [7] Pranata R, Huang I, Lim MA, Wahjoepramono EJ, July J. Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19 – systematic review, meta-analysis, and meta-regression. J Stroke Cerebrovasc Dis. 2020:104949. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104949 May.
- [8] Pranata R, Soeroto AY, Ian H, et al. Effect of chronic obstructive pulmonary disease and smoking on the outcome of COVID-19. Int J Tuberc Lung Dis. 2020. https://doi. org/10.5588/ijtld.20.0278.
- [9] Pelliccia F, Kaski JC, Crea F, Camici PG. Pathophysiology of Takotsubo syndrome. Circulation. 2017;135(24):2426–41. https://doi.org/10.1161/CIRCULATIONAHA.116. 027121.
- [10] Bangalore S, Sharma A, Slotwiner A, et al. ST-segment elevation in patients with COVID-19 – a case series. N Engl J Med. 2020. https://doi.org/10.1056/ NEJMc2009020 April. NEJMc2009020.
- [11] Sato YZ, Molkara DP, Daniels LB, et al. Cardiovascular biomarkers in acute Kawasaki disease. Int J Cardiol. 2013;164(1):58–63. https://doi.org/10.1016/j.ijcard.2011.06. 065.
- [12] McCrindle BW, Cifra B. The role of echocardiography in Kawasaki disease. Int J Rheum Dis. 2018;21(1):50–5. https://doi.org/10.1111/1756-185X.13216.
- [13] Viner RM, Whittaker E. Comment Kawasaki-like disease: emerging complication during the COVID-19 pandemic. Lancet. 2020;6736(20):19–20. https://doi.org/10. 1016/S0140-6736(20)31129-6.
- [14] Nascimento BR, Beaton AZ, Nunes MCP, et al. Integration of echocardiographic screening by non-physicians with remote reading in primary care. Heart. 2019; 105(4):283–90. https://doi.org/10.1136/heartjnl-2018-313593.
- [15] Mehta S, Fernandez F, Villagrán C, et al. Enriching artificial intelligence ST-elevation myocardial infarction (STEMI) detection algorithms with differential diagnoses. J Am Coll Cardiol. 2020;75(11):3470. https://doi.org/10.1016/S0735-1097(20) 34097-3.
- [16] Soriano Marcolino M, Minelli Figueira R, Pereira Afonso Dos Santos J, Silva Cardoso C, Luiz Ribeiro A, Alkmim MB. The experience of a sustainable large scale Brazilian Telehealth Network. Telemed J E Health. 2016;22(11):899–908. https://doi.org/10. 1089/tmj.2015.0234.

Raymond Pranata MD

Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia Corresponding author at: Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Banten, Indonesia. *E-mail address:* raymond_pranata@hotmail.com.

Alexander Edo Tondas MD

Department of Cardiology and Vascular Medicine, Mohammad Hoesin General Hospital, Palembang, Sumatera Selatan, Indonesia Biomedicine Doctoral Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia E-mail address: edotondas@fk.unsri.ac.id.

Ian Huang MD

Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia Department of Internal Medicine, Hasan Sadikin General Hospital, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia

Michael Anthonius Lim MD Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Bambang Budi Siswanto MD, PhD

Department of Cardiology and Vascular Medicine, Faculty of Medicine Universitas Indonesia, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia

Markus Meyer MD, PhD Department of Cardiology and Vascular Medicine, Faculty of Medicine Universitas, Indonesia, Jakarta

Veselin Mitrovic MD, PhD Department of Cardiology, Kerckhoff-Klinik, Bad Nauheim, Germany E-mail address: v.mitrovic@kerckhoff-klinik.de.