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American Journal of Emergency Medicine 60 (2022) 189–192

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

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

A new dimension to the STEMI-related mortality risk seen in the COVID-19 pandemic era

Clodfelder et al. hypothesised that prehospital delays in care in myocardial infarct patients resulted in increased mortality despite the standard of care being unchanged [1]. An important dimension to this hypothesis is that, in the era of the COVID-19 pandemic, increased mortality might, in part, be attributable to the fact that prehospital delays have generated a resurgence of potentially lethal mechanical complications of ST elevation myocardial infarction (STEMI) suc h as ventricular septal rupture (VSR), left ventricular aneurysm (An) or pseudoaneurysm (PSA), left ventricular free wall rupture (LVFWR), and papillary muscle rupture (PMR), which had previously lapsed into relative obscurity following the use of myocardial reperfusion as the standard of care in STEMI. For example, notwithstanding the fact that meta analysis of data from 3,082,655 hospitalizations with STEMI over the period 2003–2015 (well within the myocardial reperfusion era) showed that the prevalence of VSR among STEMI patients had fallen to 0.21% [2], the subsequent development of the COVID-19 pandemic has generated a resurgence of STEMI-related VSR, with the consequence that a prevalence of VSR amounting to 0.36% was documented in a retrospective survey of 6185 consecutive STEMI patients admitted to hospital within 48 h of symptom onset. The survey covered the period March 1st 2019 to May 31st 2020 during which the rate of mechanical complications, namely, VSR, LVFWR, and PMR, among the study subjects significantly ($p < 0.001$) increased in parallel with increasing duration of prehospital delay. A manifestation of this phenomenon was that the rate of mechanical complication amounted to 0.82% for the time period 0–12 h, 1.435 for the period 12–24 h, 1.24% for the time period 24–36 h, and 5.07% during the time period 36–48 h.. A similar trend was noted for VSR although, in that specific instance, it did not reach statistical significance. Furthermore, in that review, the mortality rate for VSR was as high as 54.6% [3]. A comparable trend was demonstrated by data from another institution, whereby, with the onset of the COVID-19 pandemic, the average number of operations for VSR increased to 4 cases/year, having been as low as 1.9 cases/year in previous years [4].

Through the medium of Googlescholar and Pubmed, and through the use of the search terms"ventricular septal rupture or ventricular septal defect and ST elevation myocardial infarction" and "ventricular septal rupture and myocardial infarction and papillary muscle rupture", and "ventriculoseptal rupture and ST elevation myocardial infarction and left ventricular rupture", I have compiled a list of 62 anecdotal reports of the association of STEMI and VSR in which patients had delayed attending hospital (so-called pre-hospital delay) for myocardial infarction-related symptoms. These were reports published from January 2019 onwards. Excluded from this review were case reports where it was specified that the manuscript had been submitted to the relevant journal before January 2019 even though the publication date was 2019. Although only thirteen patients had expressly declared that fear of COVID 19 was the reason for the pre-hospital delay, a substantial degree of pre-hospital delay did take place during that period. The 62 cases of pre-hospital delay were subdivided into 42 in whom recognition of VSR coincided with electrocardiographic (ECG) recognition of STEMI, and 20 in whom there was an interval of a few hours or more between ECG recognition of STEMI and clinical as well as echocardiographic recognition of VSR.

1. Results

Clinical and echocardiographic recognition of VSR coinciding with electrocardiographic recognition of STEMI (Table 1). In this category there were 42 cases [5-41] (28 males) of mean age 67. The period of pre-hospital delay ranged from 6 h to 3 months. Twelve cases had a pre-hospital delay of 7 days or more [30-40].

Table 1 depicts the entire spectrum of pre-hospital delay in 39 cases in whom pre-hospital delay could be ascertained with some precision. Excluded from Table 1 are 3 cases in whom precise details of pre-hospital delay could not be given. These 3 cases had been characterised as "late presentation" [24,41] or delayed presentation [15].

Five patients had coexisting VSR and left ventricular aneurysm [10,11,13,36,40],. Two patients had coexisting VSR and left ventricular pseudo aneurysm [32,41]. One patient had coexisting VSR and papillary muscle rupture [20]. On case had VSR and severe tricuspid valve regurgitation [30]. Two patients had coexisting VSR and left ventricular free wall rupture [6,34]. Among 28 patients in whom a systolic murmur was actively sought the murmur was deemed to be present in 25. Two of the three patients in whom auscultation did not detect a murmur were hypotensive, with blood pressures of 90/56 mmHg [5] and 70/50 mmHg [8], respectively. In the third patient with undetectable murmur, no mention was made of blood pressure [12]. In 14 other patients there was no record of auscultation for the systolic murmur. ST segment elevation involved the inferior leads in 19 patients (including 2 of the patients listed outside Table 1) [15,24], inferolateral leads in 3 cases, and inferior-posterior leads in one case. The rest (19 cases) had ST elevation in the anterior or anterolateral leads.

Among the 35 patients with published angiographic data there were 14 with multivessel disease. One patient had STEMI characterised by myocardial infarction and non obstructive coronary artery (MINOCA) disease [14].

Repair of the VSR was undertaken in 31 cases (including 3 cases outside Table 1). Heart transplant was undertaken in 3 cases. Six patients (including 2 patients referred to the palliative care team) did not have operative intervention. Relevant details were not available in one instance.

Fifteen patients (36% of the total of 42 cases) died, including the two patients with left ventricular free wall rupture and the patient with papillary muscle rupture and the patient with severe tricuspid valve regurgitation.

Delay between electrocardiographic documentation of STEMI and subsequent development of VSR (Table 2). Twenty patients (13 male)

https://doi.org/10.1016/j.ajem.2022.06.028

Table 1
Clinical and echocardiographic recognition of VSR coinciding with electrocardiographic recognition of STEMI.

Author (ref)	Age	Sex	Pre-hospital symptoms		STEMI subtype	VSR subtype	Mur	Repair	Outcome
			CP	SOB					
Mukherjee [5]	55	M	6 h	–	Inferior	VSR	N	Y	died
Fan [6]	68	F	6 h	–	anterior	VSR/LVFWR	NA	N	died
Bachini [7]	57	F	7 h	–	Anterior	VSR	Y	Y	died
Joshi* [8]	72	F	14 h	–	inferior	VSR	N	N	died
Yamamoto [9]	84	F	1d	–	anterior	VSR	Y	Y	died
Sejati [10]	67	M	1d	1d	anterior	VSR/An	Y	N	NA
Oman [11]	71	M	1d	–	anterolateral	VSR/An	NA	Y	died
Dewaswala [12]	54	M	1d	–	inferolateral	VSR	N	NA	NA
Song [13]	61	M	2d	–	anterior	VSR/An	NA	Y	recovered
Petrov [14]	78	F	2d		anterior	VSR	Y	Y	recovered
Gong [15]	50s	M	2d	–	anterior	VSR	Y	Y	NA
Ishiyama [16]	78	F	2d	–	anterior	VSR	NA	Y	recovered
Obagi [17]	64	M	few	–	inferior	VSR	Y	Y	recovered
Conti [18]	74	M	Anorexia for 3 days		Inferior	VSR	Y	Y	recovered
Purkayastha* [19]	86	F	3d	–	anterior	VSR	Y	N	palliation
Shah [20]	52	M	3d	3d	inferior	VSR/PMR	Y	Y	NA
Sutherland* [21]	73	M	3d	–	inferior	VSR	Y	N	died
Adhikari [22]	60	M	3d	–	anterior	VSR	Y	Y	died
Ishizuka [23]	68	M	–	3d	Inferior	VSR	Y	Y	recovered
Hildick-Smith [24]	82	F	4d	–	anterior	VSR	NA	Y	died
Via [25]	86	M	4d	4d	Inferior	VSR	NA	Y	recovered
Alsidawi* [26]	62	F	4d	4d	anterior	VSR	Y	N	palliation
Qureshi [27]	72	F	–	4d	anterolateral	VSR	Y	Y	died
Via [25]	76	F	–	5d	Anterior	VSR	NA	Y	recovered
Qureshi [27]	53	M	5d	5d	inferior	VSR	Y	Y	died
Bakhshi [28]	56	M	–	5d	anterolateral	VSR	Y	trans plant	recovered
Amorosi [29]	77	M	–	6d	inferior	VSR	Y	Y	recovered
Dawood [30]	75	F	7d	–	anterior	VSR/TR	Y	N	died
Bakhshi [28]	53	M	–	7d	anterolateral	VSR	NA	trans plant	recovered
Portuguesi [31]	61	M	7d	–	inferior	VSR	Y	Y	recovered
Shah [32]	75	M	7d	–	inferolateral	VSR/PSA	NA	Y	NA
Ahmed* [33]	65	M	7d	3d	inferior	VSR	Y	Y	recovered
Rigueira [34]	80	F	7d	–	inferolateral	VSR/LVFWR	NA	Y	died
Khorolsky [35]	58	M	8d	–	inferior	VSR	Y	trans plant	recovered
Patel* [36]	53	M	–	10d	inferior	VSR/An	Y	Y	recovered
Ch hetry* [37]	71	M	–	14d	inferior	VSR	Y	Y	recovered
Aykent* [38]	60	M	14d	7d	inferior	VSR	Y	Y	died
Jabri [39]	70	M	14d	–	anterior	VSR	NA	Y	NA
Goraya* [40]	53	M	–	3mo	inferior	VSR/An	NA	Y	recovered

Abbreviations: Y = yes; N = no; h = hours; d = days; mo = months; NA = not available; * = fear of Covid; CP = chest pain; SOB = shortness of breath; VSR = ventricular septal rupture; An = aneurysm; PSA = pseudo-aneurysm; LVFWR = left ventricular free wall rupture; PMR = Papillary muscle rupture; Mur = murmur; TR = Tricuspid Regurgitation

belonged to this category [41-60]. Their mean age was 66. The admission ECG showed ST segment elevation in the inferior leads in 12 cases, both anterior and inferior leads in 2 cases, inferolateral in 1 case, and inferior/posterior leads in 1 patient. Four patients had ST elevation in the anterior or anterolateral leads. Thirteen patients had multivessel disease. Two patients had coexisting left ventricular aneurysm [49,60], associated, in one patient, with non-fatal hemopericardium but without demonstrable left ventricular free wall rupture (LVFWR) [60]. Non-fatal hemopericardium was documented in one other patient who had neither left ventricular aneurysm nor demonstrable LVFWR [52].

A pansystolic murmur was documented in all 13 patients in whom that murmur was sought (ie 65% of the total of 20 patients), and this occurred at the onset of VSR symptoms. The interval between electrocardiographic documentation of STEMI and onset of VSR ranged from a few hours to 3 months. The total delay (comprising the pre hospital delay plus the delay between electrocardiographic documentation of STEMI and onset of VSR) ranged from 18 h to 3 months. In 5 cases this total delay amounted to 7 days or more. Repair of the VSR was undertaken in 17 cases. Three patients died, including one patient who died before surgical intervention could be undertaken and two patients who died in spite of operative intervention. One patient was referred to the palliative care team. One patient was managed conservatively. One other patient remains critically ill following operative intervention [26]. Fifteen patients had a successful outcome after operative intervention.

1.1. Range of manifestations of STEMI-related VSR in the COVID 19 era

These 62 cases were characterised by a mean age of 66 and a predominance of males. In some cases ECG documentation of STEMI coincided with recognition of VSR but, in others, there was an interval between the two events. In 60 cases symptoms of STEMI included either chest pain or breathlessness or both. Two patients had neither chest pain nor breathlessness. Instead, they presented with 3 days of persistent anorexia. In 9 cases VSR coexisted either with left ventricular aneurysm or pseudoaneurysm. In 2 cases VSR coexisted with left ventricular free wall rupture, in the absence of left ventricular aneurysm or pseudoaneurysm. In one instance VSR coexisted with PMR. In another instance VSR coexisted with severe tricuspid regurgitation. Among 54 subjects

Table 2
Delay between electrocardiographic documentation of STEMI and subsequent development of VSR.

Author (ref)	Age	Sex	Pre-hospital symptoms		STEMI subtype	STEMI – VSR interval	Mur	Repair	Outcome
			CP	SOB					
Hajsadeghi [42]	60	M	12 h	–	inferior	few hours	Y	Y	died
Coyan [43]*	64	M	5d	–	inferior	NA	NA	Y	recovered
Choi [44]	58	M	12 h	–	anterior	6 h	Y	Y	recovered
Sharma [45]	68	F	36 h	–	Inferior/ posterior	12 h	NA	Y	died
Masroor [46]	48	M	2d	–	inferolateral	overnight	Y	Y	recovered
Greco [47]	52	M	14d	–	inferior	overnight	NA	Y	recovered
Ferraioli [48]	85	F	1d	–	Inferior	1d	Y	Y	recovered
Tulun [49]	70	F	3d	3d	anterior	1d	NA	Y	recovered
Gadre [50]*	66	F	2d	–	inferior	1d	Y	N	palliation
Cohen [51]	70	M	7d	–	inferior	1d	Y	Y	recovered
Maidman [52]	65	M	3d	3d	inferior	2d	NA	Y	recovered
Gu [53]	65	F	12 h	–	anterolateral	2d	Y	Y	recovered
Suryono [54]	48	M	13 h	–	anterior/inferior	3d	Y	N	recovered
Arai [55]	89	M	anorexia for 3 days		anterior/inferior	3d	Y	Y	recovered
Saplaouras [56]	73	M	7d	–	inferior	3d	Y	N	died
Quast [57]	62	M	1d	–	inferior	4d	NA	Y	recovered
Alsidawi [26]*	67	F	14 h	–	inferior	8d	Y	Y	critical
Parsaee [58]	79	M	2d	–	inferior	1mo	Y	Y	recovered
Chadha [59]	69	M	8 h	–	inferior	2mo	Y	Y	recovered
Mahmoud [60]	62	F	1d	–	anterolateral	3mo	NA	Y	recovered

Abbreviations: Y = yes; N = no; h = hours; d = days; mo = months; NA = not available; * = fear of Covid; CP = chest pain; SOB = shortness of breath; Mur = murmur; STEMI = ST elevation myocardial infarction; VSR = ventricular septal rupture.

who had coronary angiography there were 27 with multivessel disease and one with MINOCA.

1.2. Comment

These reports highlight the need for a high index of suspicion for VSR and other mechanical complications when a patient presents with a history of delay in seeking medical attention for STEMI. The presence of a pansystolic murmur should be a "red flag" for VSR, and for the presence PMR, respectively, with the caveat that both VSR and PMR might be present in the same patient [20]. Conversely, in the presence of severe hypotension, the systolic murmur of VSR "may be difficult to identify because turbulent flow across the defect is reduced" [61], and the same might also be true of the systolic murmur of PMR [62]. Clinicians should also be especially vigilant for "stepwise" evolution of VSR [41-60], whereby a patient with delayed presentation of STEMI initially presents without clinical or echocardiographic stigmata of VSR but subsequently experiences hypotension and/or increasing breathlessness signalling onset of VSR [41-60]. The onset of VSR, in such cases, is typically associated with new-onset pansystolic murmur.

1.3. Recommendation for good practice

The evaluation of STEMI patients with prehospital delay should routinely include careful auscultation for a systolic murmur, and point-of care transthoracic echocardiography for the purpose of identifying mechanical complications such as VSR, PMR, left ventricular aneurysm, and LVFWR.

CRediT authorship contribution statement

Oscar M.P. Jolobe: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

I have no conflict of interest with regard to the manuscript with the above title.

Acknowledgment

I have no funding, and no conflict of interest.
I am indebted to Peter Laws for compilation of the tables.

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9 June 2022