High Degree Atrioventricular Block Complicating Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention: Incidence, Predictors and Outcomes

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ABSTRACT: **Background:** In the era of primary percutaneous coronary intervention (PPCI), information on the incidence and prognostic significance of high degree atrioventricular block (AVB) in ST elevation myocardial infarction (STEMI) patients is limited.

Objectives: To assess the incidence, time of onset, predictors and prognostic significance of high degree AVB in a large cohort of consecutive STEMI patients undergoing PPCI.

Methods: We retrospectively studied 1244 consecutive STEMI patients undergoing PPCI. Patient records were reviewed for the presence of high degree AVB, its time of occurrence and relation to in-hospital complications, as well as long-term mortality over a 5 year period.

Results: High degree AVB was present in 33 patients (3.0%), in 25 (76%) of whom the conduction disorder occurred prior to PPCI. Twelve patients (36%) required temporary pacing, all prior to or during coronary intervention, and all AVB resolved spontaneously before hospital discharge. AVB was associated with a significantly higher 30 day (15% vs. 2.0%, $P = 0.001$) and long-term mortality rate (30% vs. 6.0%, $P < 0.001$). Time of AVB had no effect on mortality. In a multivariate regression model, AVB emerged as an independent predictor for long-term mortality (hazard ratio 2.8, 95% confidence interval 1.20–6.44, $P = 0.001$).

Conclusions: High degree AVB remains a significant prognostic marker in STEMI patients in the PPCI era, albeit transient.

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KEY WORDS: myocardial infarction (MI), atrioventricular block (AVB), primary percutaneous coronary intervention (PPCI)

High degree atrioventricular block (AVB) is a common complication of acute ST elevation myocardial infarction (STEMI). The incidence of AVB among STEMI patients in the pre-thrombolytic era ranged from 2% to 13% and was as high as 28% in patients with inferior STEMI [1-4]. While the initiation of thrombolytic therapy substantially decreased the mortality rate associated with acute MI, the incidence of associated AVB, particularly in the setting of inferior MI, remained high [5-8]. Several clinical and demographic patient characteristics have been identified in the past as predictors of high degree AVB development in STEMI patients, such as advanced age, female gender, inferior infarct location, prior infarction, smoking, hypertension and diabetes [5,9,10]. Although most patients presenting with acute STEMI are currently treated with primary percutaneous coronary intervention (PPCI), information on the incidence and clinical implications of high degree AVB in the PPCI era is scarce. We investigated the incidence, predictors, as well as the short- and long-term mortality rates of high degree AVB in a large cohort of STEMI patients undergoing PPCI.

PATIENTS AND METHODS

We performed a retrospective, single-center observational study at the Tel Aviv Sourasky Medical Center, a tertiary referral hospital providing a round-the-clock PPCI service [11,12]. We included all 1335 consecutive patients admitted to the cardiac intensive care unit during the period January 2008 to July 2013 with the diagnosis of acute STEMI. Excluded were 28 patients who were treated either conservatively or with thrombolysis, and 63 patients whose final diagnosis on discharge was other than STEMI (e.g., myocarditis or Takotusubo cardiomyopathy). The final study population comprised 1244 patients whose baseline demographic, cardiovascular history, clinical risk factors, electrocardiographic (ECG) features, treatment characteristics and laboratory results were retrieved from their medical files.

The diagnosis of STEMI was established by a typical history of chest pain, diagnostic ECG changes, and serial elevation of serum cardiac biomarkers [13]. PPCI was performed in patients with symptoms ≤ 12 hours in duration as well as in patients with symptoms lasting 12–24 hours in duration if the symptoms continued to persist at the time of admission. Following PPCI, left ventricular ejection fraction (LVEF) was measured by bedside echocardiography in all patients within the first 48 hours of admission. Patient records were evaluated for the documentation of high degree AVB defined as Mobitz type II second-degree AVB and third-degree AVB [14] that occurred during the index hospitalization. The patients only

received a final diagnosis of AVB if ECG documentation was available, or if the attending physician confirmed the diagnosis in the clinical charts. Additional parameters evaluated were the timing of AVB occurrence (before or after PPCI), the need for temporary pacemaker implantation (due to hemodynamic instability), and the course of the conduction disorder during hospitalization and up to hospital discharge. In-hospital mortality and complications occurring during the hospitalization were also assessed. These included cardiogenic shock or the need for intra-aortic balloon counter-pulsation (IABC) treatment, the need for emergent coronary artery bypass graft (CABG) surgery, mechanical ventilation, heart failure episodes treated conservatively, clinically relevant ventricular tachyarrhythmias, and atrial fibrillation. Mortality was assessed over a median period of 1526 ± 298 days (range 2–2130 days) until 1 August 2013. Assessment of survival after hospital discharge was determined from computerized records of the population registry bureau. The study protocol was approved by the local institutional ethics committee.

All data were summarized and displayed as mean (± standard deviation) or median (25–75%) for continuous variables and as number (percentage) of patients in each group for categorical variables. The *P* values for the chi-square test were calculated with Fisher's exact test. Continuous variables were compared using the independent sample *t*-test or the Mann-Whitney test. A multivariate binary logistic regression model was fitted at the enter mode to evaluate the association between baseline demographic, clinical characteristics and high degree AVB as the dependent variable. We adjusted for age, gender, hypertension, diabetes mellitus, multiple coronary artery disease (defined as coronary disease > 1 vessel), LVEF, time to coronary reperfusion (defined as the time from symptom onset, usually chest pain or discomfort recorded upon admission, to the restoration of flow in the infarct artery, as reported in the catheterization laboratory report), and peak creatine phosphokinase (CK) levels. Similarly, a multivariate Cox regression model was used to evaluate the association between AVB, age, gender, hypertension, diabetes mellitus, smoking, LVEF, peak CK levels, time to coronary reperfusion, the infarct-related artery and long-term mortality as the dependent variable. A two-tailed *P* value < 0.05 was considered significant for all analyses. All analyses were performed with the SPSS 20.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

The study population consisted of 1244 patients (80% males) with a mean age of 62 ± 13 years. High degree AVB occurred in 33 patients (3%), in 25 (76%) of whom it occurred prior to PPCI, while in another 8 patients high degree AVB (24%) occurred following the interventional procedure. Among the patients with AVB, only 12 patients (36%) required temporary pacing, all prior to or during PPCI, and all high degree AVB resolved spontaneously before hospital discharge. The culprit artery was the right coronary artery in 31 cases (94%) and left circumflex in the remaining 2 (6%). No AVB occurred among patients with an anterior wall myocardial infarction. Baseline clinical characteristics of patients with and without high degree AVB are listed in Table 1. Patients with AVB were more likely to be older, diabetic and to have longer hospitalization time. High degree AVB was associated with more in-hospital complications, and higher 30 day mortality (15% vs. 2%, $P = 0.001$) [Table 2]. Despite that, patients with AVB had similar ischemia time, LVEF, and peak CK.

A multivariate regression model was performed to elucidate the risk factors predicting the development of high degree AVB

Table 1. Baseline characteristics

	High degree atrioventricular block		
	No (n=1211)	Yes (n=33)	*P* value
Age (yr)	61 ± 13	68 ± 13	0.004
Male	977 (81%)	25 (76%)	0503
Diabetes mellitus	247 (20%)	12 (36%)	0.047
Dyslipidemia	571 (47%)	13 (39%)	0.480
Hypertension	527 (43%)	16 (48%)	0.597
Smoking history	604 (50%)	15 (45%)	0.725
Family history of CAD	190 (16%)	4 (12%)	0.808
Prior MI	116 (10%)	8 (8%)	0.763
No. of narrowed coronary arteries 1 2 3	 533 (44%) 362 (30%) 313 (26%)	 13 (39%) 12 (36%) 8 (25%)	0.815
Time to ED (min)	393 ± 664	464 ± 600	0.805
Door to balloon time (min) Duration of hospitalization (days) Peak CPK (U/L) LV ejection fraction	43 ± 38 5.5 ± 2.9 1178 ± 1379 48 ± 8	42 ± 14 6.2 ± 4.5 1106 ± 1133 49 ± 6	0.891 0. 01 0.717 0.466

NS = non-significant, SD = standard deviation, CAD = coronary artery disease, MI = myocardial infarction, ED = emergency department, CPK = creatine phosphokinase, LV = left ventricle

Table 2. In-hospital complications

	High degree atrioventricular block		
	No (n=1211)	Yes (n=33)	*P* value
Cardiogenic shock/Need for IABC	44 (4%)	5 (15%)	0.008
Mechanical ventilation	45 (4%)	4 (12%)	0.037
Heart failure	98 (8%)	6 (18%)	0.051
Ventricular fibrillation/tachycardia	64 (5%)	3 (9%)	0.418
Atrial fibrillation	44 (4%)	2 (6%)	0.612
30 day mortality	24 (2%)	5 (15%)	0.001

IABC = intra-aortic balloon counter-pulsation

Table 3. Binary logistic regression model for predicting high degree AVB

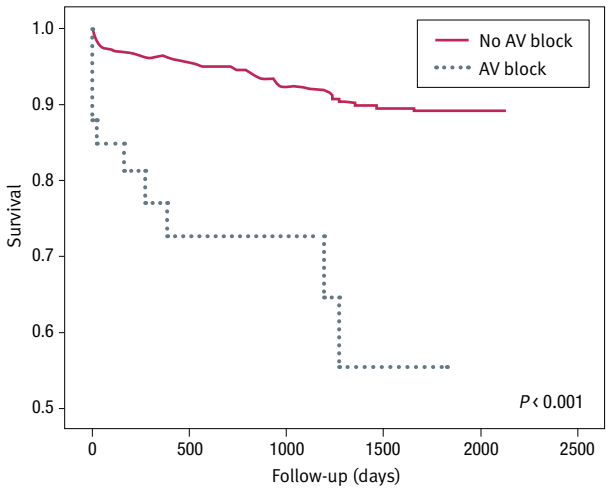
Correlates	OR	95%CI	*P* value
Age (yr)	1.038	1.00–1.07	0.018
Male gender	1.06	0.45–2.51	0.895
Diabetes mellitus	1.985	0.91–4.34	0.085
Hypertension	0.825	1.55–4.31	0.629
Time to reperfusion	1.000	1.00–1.01	0.901
LV ejection fraction	1.032	0.38–1.79	0.196
Peak CPK	1.000	1.00–1.00	0.513
CAD extent	1.014	0.65–1.57	0.952

LV = left ventricle, CPK = creatine phosphokinase, CAD = coronary artery disease, OR = odds ratio

[Table 3]. The major risk factor found for AVB-complicated STEMI was advanced age [odds ratio (OR) 1.04, 95% confidence interval (CI) 1.0–1.07, $P = 0.018$) and a strong trend for diabetes (OR 1.98, 95%CI 0.90–4.33, $P = 0.08$).

As all patients with AVB had non-anterior STEMI, mortality was compared in this subpopulation only. Over a mean period of 2.7 ± 1.6 years (range 1– 5 years), 62 patients (7.3%) died. Mortality was significantly higher among those with high degree AVB than those without AVB (30% vs. 6.0%, $P < 0.001$). The time of AVB occurrence had no significant impact on 30 day mortality (16% vs. 27%, $P = 0.81$) or long-term mortality (27% vs. 45%, $P = 0.61$). Therefore, we combined the AVB before and after PPCI into one group. Kaplan-Meier survival curve for long-term survival in those with and without AVB is shown in Figure 1. In a multivariate regression model, AVB emerged as an independent predictor for both 30 day (hazard ratio 3.75, 95%CI 1.48–9.49, $P = 0.005$) and long-term mortality (hazard ratio 2.8, 95%CI 1.20–6.44, $P = 0.01$).

Figure 1. Cumulative survival rates for 1244 patients with ST elevation myocardial infarction based on the presence of high degree atrioventricular block (AVB), $P < 0.001$



DISCUSSION

In this large cohort of consecutive STEMI patients undergoing PPCI, high degree AVB was associated with increased short- and long-term mortality.

The etiology of AVB in the setting of STEMI is thought to be multifactorial and dependent on the location of the culprit lesion [15-18]. The AV nodal artery normally arises from the right coronary artery [19] and the ischemic insult caused by STEMI is thought to be sufficient to cause a transient dysfunction of the conduction fibers. The conduction tissue of the AV node is usually resistant to permanent damage from ischemia due to the high intracellular contents of glycogen, the rich complex arterial blood supply, and the capability of nutrient and oxygen absorption by diffusion from surrounding venous sinusoids [16]. In addition, AVB is thought to be provoked by enhanced parasympathetic tone or local release of potassium or adenosine [20]. These mechanistic considerations contribute to our understanding of the transiency of the majority of AVB events, as demonstrated in our study.

In the thrombolytic era, it was shown that thrombolytic therapy may paradoxically precipitate the development of AVB [1,9]. It was suggested that the reperfusion of the obstructed coronary artery induces a surge of afferent vagal activity that in turn induced a transient AVB. Similarly, almost a quarter of the patients in our cohort developed AVB following PPCI, thus it appears that reperfusion by coronary stenting may occasionally have a similar effect. In the present study there was a lower incidence of high degree AVB compared with reports from the thrombolytic era. Despite the low incidence and the fact that all cases in our cohort resolved prior to discharge, high degree AVB was associated with a significantly increased risk of both short- and long-term mortality, independently of other clinically important confounders. High degree AVB has consistently been found to mark an adverse short-term mortality, whereas the long-term impact remained questionable [3,5,9,10]. Gang et al. [21] investigated the incidence and outcomes associated with high degree AVB in a large cohort of STEMI patients treated with PPCI [21]. In that cohort the incidence of AVB was 3%, similar to our results; however, 20% of AVB were related to left anterior descending artery lesions, while no such lesions were found in our cohort. In addition, there were missing data regarding LVEF and peak CK in the patient groups. Moreover, while in the report by Gang et al. AVB was associated with adverse 30 day outcomes with no significant effect on long-term mortality beyond that period, our results show an increased short- and long-term mortality up to 5 years of follow-up among patients with high degree AVB. Contrary to previous reports [9,10,21], none of the patients with AVB had an anterior STEMI. In patients with an anterior infarction, AVB is a consequence of extensive septal necrosis that involves the bundle branches. In this population damage to the His-Purkinje system

often leads to unstable escape rhythms with wide QRS complexes and frequent ventricular asystole. It is possible, therefore, that AVB in patients with an anterior infarction takes longer to develop and that the implementation of early reperfusion using PPCI can help prevent this complication.

The current study suggests some important clinical implications. Patients with AVB complicating STEMI require special attention and monitoring throughout the hospitalization course, even after resolution of the conduction disturbance. The fact that AVB patients had a similar ischemia time, LVEF and peak CK as STEMI patients without AVB might suggest that the enhanced mortality may not be related to worse cardiac function as previously proposed. Furthermore, since AVB was associated with higher long-term mortality, it should be regularly reported as part of the in-hospital course, even if transient and with no hemodynamic consequences.

Our study bears some notable limitations. This was a single-center retrospective observational study, and as such may have been subject to bias, even though we included consecutive patients and attempted to adjust for confounding factors using the multivariate Cox regression model. Second, all registries have an innate risk of under-reporting, which could lead to underestimation of the reported AVB incidence. Lastly, we had no information on the rates of right ventricular infarction. Right ventricular infarction often coincides with AVB and thus may substantially influence mortality.

We conclude that although high degree AVB complicating STEMI is much less frequent and often transient in the PPCI era, its occurrence is still associated with high risk of both short- and long-term mortality.

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"Spend the afternoon. You can't take it with you"

Annie Dillard (born 1945), American author

"I have lived in this world just long enough to look carefully the second time into things that I am most certain of the first time"

Josh Billings (1818-1885), American humorist