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The impact of the complete atrioventricular block on in-hospital and long-term mortality in patients treated with primary percutaneous coronary intervention

Uticaj kompletnog atrioventrikularnog bloka na intrahospitalni i dugoročni mortalitet bolesnika lečenih primarnom perkutanom koronarnom intervencijom

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Abstract

Background/Aim. The prognostic impact of complete atrioventricular (AV) block on the long-term prognosis of patients with ST-elevation myocardial infarction (STEMI) has not been fully determined. The aim of the study was to analyze the incidence and prognostic impact of complete AV block on in-hospital mortality (IHM) and 6-year mortality in STEMI patients treated with primary percutaneous coronary intervention. **Methods**. The study included 3,044 consecutive STEMI patients. **Results.** Complete AV block was registered only on admission in 144 (4.73%) patients; 125 (86.8%) patients with complete AV block had inferior infarction. A temporary pacemaker was implanted in 72 (50%) patients with complete AV block. No patient underwent permanent pacemaker implantation. IHM was significantly higher in patients with complete AV block than in patients without complete AV block: 17.9% vs. 3.6%, respectively, $p < 0.001$. In patients with heart block and inferior infarction, IHM was 13%, whereas IHM was 53% in patients with heart block and anterior infarction. When we analyzed patients discharged alive from the hospital, we also found a significantly higher long-term (6-year) mortality rate in those with complete AV block vs. patients without AV block: 7.8% vs. 3.4%, respectively, $p < 0.001$. Complete AV block was an independent predictor for IHM and 6-year mortality: IHM [odds ratio (OR) 2.94 95%, confidence interval (CI) 1.23–5.22; 6-year mortality hazard ratio (HR) 1.61, 95%, CI 1.10–2.37]. When subanalysis was performed in patients with inferior STEMI, complete AV block was an independent predictor of IHM and 6-year mortality, while in patients with anterior STEMI, complete AV block was an independent predictor of IHM. **Conclusion.** In analyzed STEMI patients, complete AV block was transitory and was registered only on hospital admission. Although transitory, complete AV block remained a strong independent predictor of IHM and long-term mortality.

Key words:
atrioventricular block; mortality; percutaneous coronary intervention; prognosis; st elevation myocardial infarction.

Apstrakt

Uvod/Cilj. Uticaj kompletnog atrioventrikularnog (AV) bloka na dugoročnu prognozu bolesnika sa infarktom miokarda sa elevacijom ST segmenta (ST-*elevation myocardial infarction* – STEMI) nije utvrđen u potpunosti. Cilj rada bio je da se analiziraju incidenca i prognostički uticaj AV bloka na intrahospitalni mortalitet (IHM) i 6-godišnji mortalitet bolesnika sa STEMI, lečenih primarnom perkutanom koronarnom intervencijom. **Metode.** Studijom su bila obuhvaćena 3 044 konsekutivna bolesnika sa STEMI. **Rezultat.** Kompletan AV blok registrovan je kod 144 (4,73%) bolesnika samo pri prijemu u bolnicu; 125 (86,8%) bolesnika sa kompletnim AV blokom imalo je infarkt donjeg zida. Privremeni pejsmejker ugrađen je kod 72 (50%) bolesnika sa kompletnim AV blokom. Stalni pejsmejker nije ugrađen ni jednom bolesniku. Kod bolesnika sa kompletnim AV blokom, IHM je bio značajno viši u poređenju sa IHM bolesnika bez kompletnog AV bloka: 17,9% vs. 3,6%, $p < 0,001$. Kod bolesnika sa infarktom donjeg zida i kompletnim AV blokom IHM je iznosio 13%, dok je kod bolesnika sa infarktom prednjeg zida i kompletnim AV blokom IHM iznosio 53%. Analizom rezultata bolesnika otpuštenih iz bolnice, utvrđen je značajno viši dugoročni (6-godšnji) mortalitet kod bolesnika sa kompletnim AV blokom u

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poređenju sa bolesnicima bez AV bloka: 7,8% vs. 3,4%, $p < 0,001$. Kompletan AV blok bio je nezavisan prediktor IHM i dugoročnog, 6-godišnjeg mortaliteta: IHM [*odds ratio* (OR) 2,94 95%, *confidence interval* (CI) 1,23–5,22; 6-godišnji mortalitet *hazard ratio* (HR) 1,61, 95%, CI 1,10–2,37]. Dodatnom analizom je utvrđeno da je kod bolesnika sa infarktom donjeg zida kompletan AV blok bio nezavisan prediktor IHM i 6-godišnjeg mortaliteta, dok je kod bolesnika sa infarktom prednjeg zida kompletan AV blok bio nezavisan prediktor samo IHM. **Zaključak.** Kod analiziranih bolesnika sa STEMI, kompletan AV blok bio je prolazan i registrovan je samo pri prijemu u bolnicu. Iako tranzitoran, kompletni AV blok bio je snažan nezavisni prediktor IHM i dugoročnog mortaliteta.

Ključne reči:
srce, blok; mortalitet; perkutana koronarna intervencija; prognoza; infarkt miokarda sa st elevacijom.

Introduction

The incidence of high-degree atrioventricular (AV) block (HAVB) in patients with ST-elevation myocardial infarction (MI) – STEMI is 3–14%. Complete AV block is the most common and severe conduction disorder in these patients [1]. Complete AV block is registered two to four times more frequently in patients with STEMI of the inferior wall than in patients with different STEMI localization. According to data found in the literature, around 28% of inferior wall STEMIs are complicated by complete AV blocks [2–6]. It is well known that complete AV block complicating STEMI is associated with less favorable in-hospital outcomes, regardless of the location of the MI [1, 2, 5, 7, 8]. The prognostic impact of complete AV block on the long-term prognosis of patients with STEMI has not been determined with certainty, and individual authors state that it bears a greater significance in patients with anterior wall infarction than in patients with infarction localized elsewhere [1, 3]. Bearing in mind that the introduction of primary percutaneous coronary intervention (pPCI), as well as its perfecting, has improved the prognosis of patients with STEMI compared to thrombolysis treatment [9], it is important that the authors of this paper analyze whether this contemporary therapeutic approach has influenced the incidence and the prognostic impact of complete AV block in STEMI patients in short-term and long-term follow-up [1, 2, 3, 10].

The aim of this study was to analyze the incidence and prognostic impact of complete AV block on in-hospital and 6-year all-cause mortality in STEMI patients treated with pPCI.

Methods

Study population, data collection, and definitions

The present study enrolled 3,044 consecutive patients hospitalized between February 2006 and December 2012. The patients were included in the prospective STEMI Register at the University Clinical Center of Serbia. The purpose and objective of the STEMI Register have been previously published [11, 12]. The study protocol was approved by the local research Ethics Committee (No 470/II-4, from February 21, 2008). All consecutive patients with STEMI aged 18 or above, admitted to the Coronary Care Unit after undergoing pPCI in the Center, were included in the Register. Coronary angiography was performed via the femoral approach. More detail about primary PCI and stenting of the infarct-related artery (IRA), the therapy administered to all eligible patients before pPCI (aspirin, 300 mg, and clopidogrel, 600 mg) and to the ones with visible intracoronary thrombi (GP IIb/IIIa receptor inhibitor during pPCI), has been available in previously published study [12]. Flow grades were assessed according to Thrombolysis in Myocardial infarction (TIMI) criteria. After pPCI, patients were treated according to current guidelines [11, 12]. A temporary transvenous pacemaker was implanted during pPCI if hemodynamic instability (hypotension or shock) and bradycardia with a low escape rhythm (heart rate < 40 beats/min) were present.

According to the presence of a complete AV block, patients were divided into two groups: patients with complete AV block and patients without complete AV block. Demographic, baseline clinical, angiographic, and procedural data were collected and analyzed. An echocardiographic examination was performed within the first 3 days after pPCI. The central measure of left ventricular systolic function – left ventricle ejection fraction (LVEF) was assessed according to the biplane Simpson method in classical two- and four-chamber apical projections. In 10% of patients, the data about LVEF was missing. The missing data were imputed via the single imputation method. Kidney function was assessed by estimating creatinine clearance (CrCl) on admission using the Cockroft-Gault formula.

Patients were followed up for 6 years after enrolment. Follow-up data were obtained by scheduled telephone interviews and outpatient visits.

Statistical analysis

Categorical variables were expressed as frequency and percentage, while the continuous variables were expressed as the median (med) with the 25th and 75th quartiles (IQR). Analysis for the normality of data was performed using the Kolmogorov-Smirnov test. Baseline differences between groups were analyzed using the Mann-Whitney test for continuous variables and Pearson's chi-squared test for categorical variables. The Kaplan-Meier method was used for constructing the probability curves for 6-year survival, while the difference between patients, with and without complete AV block, was tested with the log-rank test. A 30-day landmark analysis was also performed. Multiple logistic regression was used to define independent predictors of in-hospital mortality (IHM) (backward method, with $p < 0.10$ for entrance into the model). Multiple Cox analysis (backward method, with $p <$

0.10 for entrance into the model) was used for identifying independent risk factors for the occurrence of 6-year all-cause mortality. The value of $p < 0.05$ was considered significant. The SPSS statistical software, version 19, was applied (SPSS Inc, Chicago, IL).

Results

Complete AV block was registered in 144 (4.73%) patients on admission; among patients with complete AV block, 125 (86.80%) had inferior infarction. No patient developed a complete post-procedural (post pPCI) AV block. Demographic, baseline clinical, laboratory, and angiographic characteristics, as well as ejection fraction (EF) in patients with and without complete AV block, are shown in Table 1.

As compared to patients without complete AV block, patients with complete AV block were older and, to a greater percentage, female. A higher percentage of these patients had cardiac insufficiency, lower systolic pressure, and lower values of CrCl on admission. Moreover, patients with complete AV block had a higher incidence of multivessel coronary disease (MVD) and a higher incidence of pre-procedural occlusion of the IRA (TIMI flow grade 0). Additionally, the value of post-procedural TIMI flow grade in the IRA in these patients was more frequently below 3 than in patients without complete AV block. Patients with complete AV block had a lower value of EF and, on average, a higher maximum value of creatine kinase. There was no significant difference in the duration of chest pain amongst the analyzed patients, but syncope prior to first medical contact was more frequently registered in patients with complete AV block. A temporary pacemaker was implanted in 72 (50%) patients with complete AV block. None of the patients underwent permanent pacemaker implantation.

IHM was significantly higher in patients with complete AV block than in patients without complete AV block: 17.9% vs. 3.6%, respectively, $p < 0.001$. In patients with complete AV block and inferior infarction, IHM was 13%, whereas, in patients with complete AV block and anterior infarction, IHM was 53%, $p < 0.001$. When 30-day landmark analysis was performed, a significantly higher 6-year mortality rate in patients with complete AV block vs. patients without complete AV block was found: 7.8% vs. 3.4%, respectively, $p < 0.001$. There was no difference in 6-year mortality between patients with complete AV block and inferior vs. anterior infarction: 10.3% vs. 15.32%, p = 0.210. In-hospital and long-term mortality in patients with and without complete AV block is shown in Figure 1.

The causes of death after hospital discharge in all patients with complete AV block were heart-related, e.g., sudden death, reinfarction, or worsening of heart failure.

Complete AV block was an independent predictor for in-hospital and 6-year mortality in the analyzed patients, as shown in Tables 2 and 3.

When subanalysis related to the localization of the infarction was carried out, it was found that complete AV block was an independent predictor of in-hospital [hazard ratio (HR) 2.51, 95% confidence interval (CI) 1.41–4.81, $p = 0.001$)] and 6-year (HR 2.52, 95% CI 1.43–3.89, $p < 0.001$) mortality in patients with inferior STEMI, while in patients

Table 1

Demographic, baseline clinical, laboratory, angiographic, procedural characteristics and left ventricular ejection fraction of the study patients according to the presence of complete atrioventricular (AV) block on admission

Characteristics	Complete AV block n=144	No complete AV block n=2,900	*p*-value
Age, years, med (IQR)	64.5 (59.2,75)	60 (51,69)	< 0.001
Female, n (%)	55 (38.2)	805 (27.75)	0.011
Previous MI, n (%)	18 (12.5)	309 (10.65)	0.122
Diabetes mellitus, n (%)	35 (24.31)	575 (19.83)	0.144
Hypertension, n (%)	99 (68.75)	1999 (68.93)	0.888
HLP, n (%)	67 (46.53)	1823 (62.86)	< 0.001
Smoking, n (%)	75 (52.08)	1581 (54.51)	0.145
Pain duration, hrs, med (IQR)	3 (1,41)	3 (2,4.5)	0.658
Syncope, n (%)	8 (5.55)	37 (1.27)	< 0.001
Killip II and III on admission, n (%)	37 (88.92)	354 (12.21)	< 0.001
Killip IV on admission, n (%)	10 (6.91)	56 (1.93)	< 0.001
Systolic BP (mmHg) on admission, med (IQR)	110 (90,130)	140 (120,150)	< 0.001
Inferior infarction, n (%)	125 (86.80)	1,283 (44.24)	< 0.001
Anterior infarction, n (%)	17 (11.80)	1,230 (42.41)	0.154
Right ventricular MI, n (%)	71 (49.30)	371 (12.79)	< 0.001
3-vessel disease, n (%)	45 (31.25)	792 (27.31)	0.225
Pre-procedural flow TIMI 0, n (%)	122 (84.72)	2,225 (76.78)	0.001
Post-procedural flow TIMI < 3, n (%)	14 (9.72)	132 (4.55)	0.001
Troponin T, med (IQR)	355 (101,970)	309 (89,888)	0.971
Hemoglobin g/L, med (IQR)	136 (124,142)	142 (131,153)	< 0.001
Glucose on admission, med (IQR)	8.2 (6.6,11.2)	7 (5.9, 9.1)	< 0.001
CrCl < 60 mL/min/m^2, n (%)	54 (37.5)	435 (15)	< 0.001
LVEF (%), med (IQR)	45 (35,50)	50 (40,55)	< 0.001

Med – median; IQR – interquartile range; MI – myocardial infarction; HLP – hyperlipidemia; HF – heart failure; BP – arterial blood pressure; CrCl – creatinine clearance; TIMI – thrombolysis in myocardial infarction; LVEF – left ventricle ejection fraction.

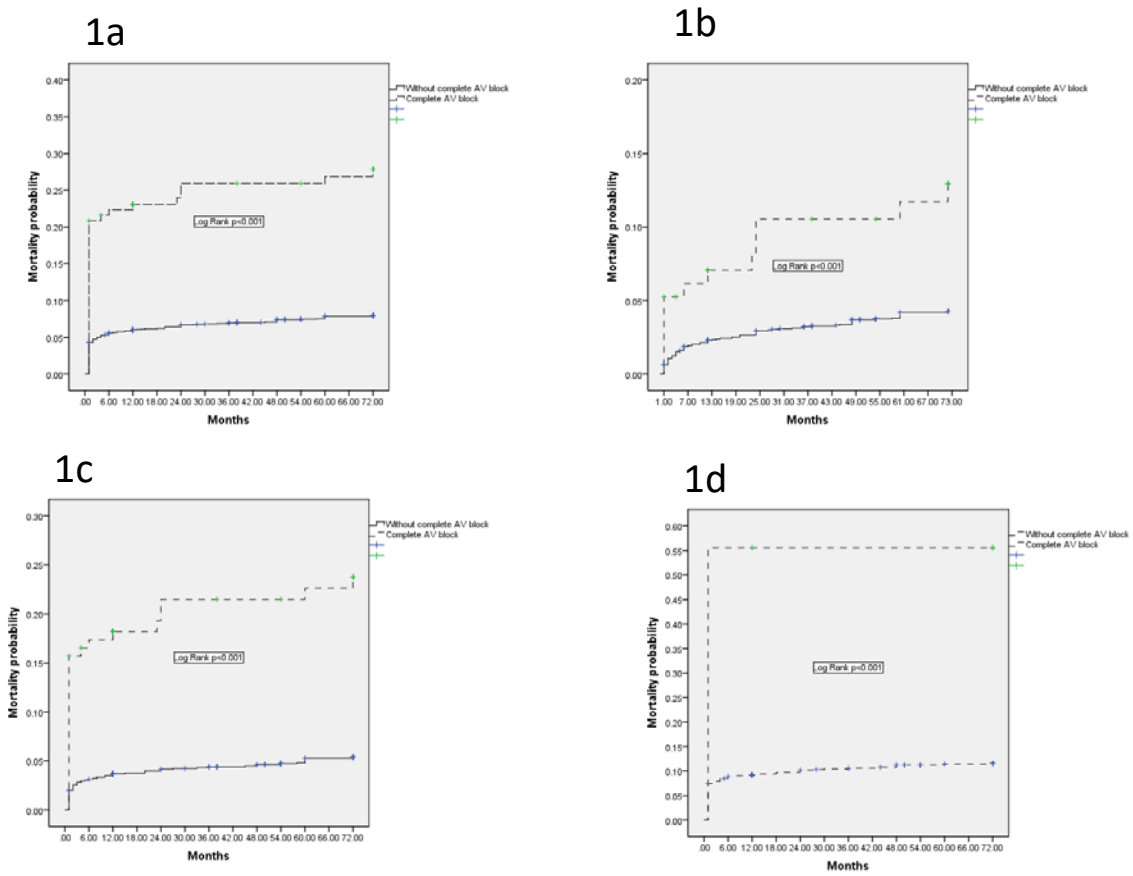

Fig. 1 – Kaplan-Meier curves estimating the probability of 6-year mortality: a) during the entire 6-year period (in-hospital + follow-up); b) in those who survived hospitalization; c) patients with inferior myocardial infarction (MI); d) patients with anterior MI.
AV – atrioventricular.

Table 2

Independent predictors for in-hospital mortality

Variable	OR	95% CI	*p*-value
Age, years	1.04	1.02–1.07	< 0.001
Post-procedural flow TIMI < 3	3.72	2.04–6.79	< 0.001
Killip class > 1 on admission	3.04	1.83–5.05	< 0.001
Complete AV block	2.94	1.23–5.22	0.011
CrCl < 60 mL/min on admission	1.96	1.09–3.53	0.024
Previous infarction	1.72	1.02–3.19	0.056
LVEF (%)	0.84	0.81–0.86	< 0.001

TIMI – thrombolysis in myocardial infarction; AV – atrioventricular; CrCl – creatinine clearance; LVEF – left ventricle ejection fraction; OR – odds ratio; CI – confidence interval.

Table 3

Independent predictors for 6-year mortality

Variable	HR	95% CI	*p*-value
Age, years	1.04	1.03–1.06	< 0.001
Post-procedural flow TIMI < 3	1.99	1.40–2.81	< 0.001
Killip class > 1 on admission	1.82	1.33–2.49	< 0.001
Complete AV block	1.61	1.10–2.37	0.017
CrCl < 60 mL/min on admission	1.45	1.04–2.02	0.028
LVEF (%)	0.92	9.90–0.93	< 0.001

TIMI – thrombolysis in myocardial infarction; AV – atrioventricular; CrCl – creatinine clearance; LVEF – left ventricle ejection fraction; HR – hazard ratio; CI – confidence interval.

with anterior STEMI, complete AV block was an independent predictor of only IHM (HR 4.43, 95% CI 1.05–13.77, $p < 0.001$), but not of 6-year mortality.

Discussion

The results of the present study have shown that transient complete AV block on hospital admission was present in 4.73% of analyzed patients with STEMI. Complete AV block on admission was a strong independent predictor of in-hospital and 6-year mortality in the analyzed patients. When patients were analyzed according to the localization of the infarction, complete AV block was an independent predictor of in-hospital and long-term mortality in patients with inferior STEMI, while in patients with anterior STEMI, it was an independent predictor of only in-hospital but not of long-term mortality.

The incidence of complete AV block, the clinical characteristics of the patients, and the percentage of patients with an implanted temporary pacemaker (PM) are in line with the findings obtained in the literature relating to patients treated with pPCI [1, 2, 6, 13]. Complete AV block complicating STEMI in the pPCI era is most commonly registered on admission as a part of acute ischemia. The most common mechanism of the occurrence of complete AV block in patients with MI is AV nodal ischemia. The nodal artery most commonly stems from the right coronary artery (RCA), which explains why complete AV block complicates inferior STEMI much more frequently than anterior STEMI. However, the AV node also receives blood from the collateral vessels and the septal branches stemming from the left anterior descendent coronary artery (LAD), which is why patients with complete AV block more commonly suffer from MVD compared to patients without complete (or high degree) AV block [1], which was also the case with the patients in the present study. In RCA occlusion, ischemia is most commonly above the His bundle, resulting in a satisfactory escape rhythm, which is why, in most cases, these patients do not need a temporary PM. Upon opening the RCA, AV conduction in these patients usually normalizes. In patients with LAD occlusion, ischemia is usually infra-Hisian, and the escape rhythm is usually unstable, which is why implanting a temporary PM is necessary for these patients [2, 3, 4, 6, 14–18]. In the present study, all patients with anterior STEMI and complete AV block had a temporary pacemaker implanted. The Bezold–Jarisch reflex is a less significant mechanism in the occurrence of complete AV block and is mostly seen in patients with inferior STEMI [2, 18].

A full withdrawal of complete AV block after the opening of an infarcted artery, which has been noted in the present study, can also be found in literature analyzing patients treated with pPCI [14]. AV node cells have a high intracellular glycogen content making them ‘resistant’ to ischemia, which explains the transitory character of complete AV block in patients with STEMI and the normalization of AV conduction upon timely opening of the IRA [1, 18]. However, there are also studies showing that complete AV block did not withdraw in all patients after opening the IRA. In a study by Gang et al. [2], which analyzes the occurrence of HAVB complicating STEMI in the pPCI era, 9% of patients developed HAVB 48 hrs upon admission to the hospital, while persistent AV conduction disorder remained in 9% of patients with HAVB, and they had a permanent PM implanted. Furthermore, in a study by Gómez-Talavera et al. [10], 3.9% of the patients had persistent complete AV block upon pPCI.

The results of the present study have shown that complete AV block remains an independent predictor of mortality even after the treatment with (contemporary) pPCI. When subanalysis in relation to the localization of the infarction was performed in the subgroup of patients with inferior MI, complete AV block remained an independent predictor of short-term and 6-year mortality. In the subgroup of patients with anterior MI, complete AV block was not an independent predictor of 6-year mortality. That can be explained by the small number of patients with anterior MI complicated by AV block released from the hospital alive. However, patients with anterior MI and complete AV block have a significantly higher 6-year mortality compared to patients with anterior MI who did not have complete AV block. It is a common finding in literature for complete AV block to be a predictor of IHM, while its effect on long-term mortality depends on the localization of the infarction and/or the patient population being analyzed. In a study by Aguiar Rosa et al. [1], complete AV block was an independent predictor only of in-hospital but not of 1-year mortality in patients with MI. In this study, just like in the present study, a significantly higher IHM was registered in patients with anterior STEMI compared to patients with inferior STEMI. IHM in this study was four times higher in patients with complete AV block, while in the present study, it was 2.54 times higher. Opposed to the present study, the one by Aguiar Rosa et al. [1] analyzed STEMI and non-STEMI patients. Amongst the patients with STEMI, there were those treated by thrombolysis, which can explain the higher risk of IHM. On the other hand, in a study by Shacham et al. [15], complete AV block complicating STEMI treated with pPCI was an independent predictor of 30-day and 5-year mortality. In this study, there were no patients with complete AV block with anterior STEMI. In a study by Kim et al. [3], it was found that complete AV block was an independent predictor of long-term mortality only in patients with anterior STEMI but not in patients with inferior STEMI. The same finding can be seen in the study by Kawamura et al. [4]. In a study by Gang et al. [2], it was found that overall long-term mortality was significantly higher in patients with HAVB compared to patients without HABV. However, when landmark analysis was performed and patients deceased within the first 30 days were excluded, mortality between the two analyzed groups did not display significant differences. In the present study, the highest mortality was registered in the first month. However, after the 30-day landmark analysis, long-term mortality was significantly higher in patients with complete AV block compared to patients without AV block. In a study by Kosmidou et al. [13], after a 30-day landmark analysis, mortality was higher in patients with HAVB compared to patients without HAVB. However, the difference disappeared after a year, which is

why there was no difference in the mortality between the analyzed groups between year one and year three of the follow-up. Although most studies indicate that, in the pPCI era, complete AV block predominantly affects intrahospital mortality in patients with STEMI, in a study by Chera et al. [6], complete AV block was not found to be an independent predictor of IHM. A similar finding can be seen in a study by Lee et al., where the prognostic impact of complete AV block in patients with STEMI was analyzed, and it was not found that complete AV block influenced IHM [14]. The findings of the two previously cited studies may be explained by the fact that the studies were performed on a small number of patients. In addition, there is a smaller number of papers showing that complete AV does not affect mortality. In a study by Auffret et al. [9], HAVB was not an independent predictor of either short-term or long-term mortality. However, the authors of that study believe that a complete AV block in their patients was a surrogate marker for a more massive infarction. The results of a study by Kim et al. [19]. also showed that complete AV block was not an independent predictor of 30-day adverse cardiovascular events in patients with MI. In fact, the presence of LAD as the infarcted artery was an independent predictor for the occurrence of 30-day major adverse cardiovascular events in patients with complete AV block. In the patients from the present study, complete AV block remained an independent predictor of mortality, along with cardiac insufficiency and lower EF of the left ventricle, as "stronger" markers indicating extensive necrosis of the myocardium, i.e., a more massive infarction.

The data shown in our study represent an addition to the existing knowledge on the unfavorable prognostic influence of complete AV block in patients with STEMI. At this moment, there is no ideal therapeutic strategy that would improve the prognosis of patients with STEMI and complete AV block. In the current absence of new knowledge and therapy options, patients with STEMI and complete AV block require special attention during hospitalization, more frequent check-ups after hospital discharge, and more "aggressive" secondary prevention of coronary artery disease.

Study limitations

The limitations of the present study need to be acknowledged. The study is observational, but it is controlled, prospective, and has included consecutive patients, thus limiting possible selection bias. In the present study, patients were treated with clopidogrel. No patients were treated with more recently developed antiplatelet drugs (prasugrel and/or ticagrelor), and pPCI was predominantly performed using bare metal stents. Ticagrelor, prasugrel, and/or the new generation of drug-eluting stents or biodegradable polymers were not available for routine administration to patients at the time of their enrollment into the Register, which may have influenced the prognosis of the analyzed patients. The study was not designed to evaluate whether changing any treatment strategy would impact the short- and long-term outcomes of the patients analyzed.

Conclusion

In STEMI patients treated with contemporary pPCI, complete AV block was transitory and was registered only on hospital admission. In-hospital and 6-year mortality was significantly higher in patients with complete AV block compared to patients without complete AV block. Although transitory, complete AV block was a strong independent predictor of in-hospital and long-term mortality in the analyzed patients.

Disclosure statement

The authors report no financial relationships or conflicts of interest regarding the content herein.

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