Atrioventricular and intraventricular blocks in the setting of acute coronary syndromes: a narrative review

Marco Schiavone1,*,†, Federica Sabato1,†, Cecilia Gobbi2, Marialessia Denora1, Lucrezia Zanchi1, Alessio Gasperetti1,3, Giovanni B. Forleo1

1 Cardiology Unit, ASST Fatebenefratelli Sacco - Luigi Sacco University Hospital, 20157 Milan, Italy
2 Department of Cardiology, Saint Martin Private Hospital Center, 14000 Caen, France
3 Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, MD 21205, USA

*Correspondence: marco.schiavone1@gmail.com (Marco Schiavone)
† These authors contributed equally.

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Acute coronary syndromes (ACS) might be complicated by atrioventricular (AV) and intraventricular (IV) blocks in a significant number of cases, and often represent a diagnostic and a therapeutic challenge. These conduction disturbances are predictors of adverse prognosis, with complete AV blocks presenting the most severe outcomes, showing an increased in-hospital mortality. With the advent of emergency percutaneous coronary intervention (PCI) and the end of the thrombolysis era, the incidence of both AV and IV blocks has surely decreased, but their prognosis in this setting still remains a matter of debate. The aim of this review is to evaluate the current knowledge on AV and IV blocks in the AMI setting, with or without ST segment elevation.

Keywords
Atrioventricular blocks, Intraventricular blocks, Acute coronary syndrome, Acute myocardial infarction, Review

1. Introduction

Acute myocardial infarction (AMI) is a life-threatening condition that needs to be diagnosed without delay. In this clinical scenario, especially when a ST-segment elevation MI (STEMI) is suspected, a 12-lead electrocardiogram (ECG) needs to be collected within 10 min after the first medical contact. Indeed, the electrocardiographic evaluation is mandatory not only to analyze the ischemic findings, but also to evaluate the presence of different conduction disturbances that may arise in the context of acute coronary syndromes (ACS). Thus, AMIs could be complicated by atrioventricular (AV) and intraventricular (IV) blocks in a significant number of cases, and often represent a diagnostic and a therapeutic challenge. These conduction disturbances are predictors of adverse prognosis, with complete AV blocks presenting the most severe outcomes, showing an increased in-hospital mortality. With the advent of emergency percutaneous coronary intervention (PCI) and the end of the thrombolysis era, the incidence of both AV and IV blocks has surely decreased, but the true prognosis of AV and IV blocks still remains a matter of debate. Fig. 1 summarizes different AMI types in relation to the onset of AV and IV blocks. The aim of this review is to evaluate the current knowledge on AV and IV blocks in the AMI setting, with or without ST segment elevation.

2. Atrioventricular blocks
2.1 Pathophysiology of atrioventricular blocks during acute coronary syndromes

High-degree atrioventricular block (HAVB), defined as second-degree type 2 or third-degree AV block, is an alarming finding in patients with AMI, especially in patients with STEMI, that is generally characterized by an occlusion of the culprit artery [1, 2]. Specifically, inferior wall MI, deriving from a thrombotic occlusion of the dominant coronary artery, can result in a supra-hisian AV block in 90% of patients, while patients presenting with an anterior MI usually develop infra-hisian HAVB, involving both bundle branches, below the AV node. Developing AV blocks in the setting of AMI is specifically related to an involvement of the AV nodal branch, that supplies the AV node. This branch might show significant variations in its origin: in 85–90% of individuals it arises from the right coronary artery (RCA), either from the proximal posterolateral branch (77%), or from the distal posterolateral branch (2%), or directly from the distal RCA (10% of cases) [3, 4]. In a lower number of patients (about 6–7%) it may originate from the posterior descending artery (branch of the RCA or of the left coronary artery, LCA) or from the distal circumflex branch of the LCA (approximately 3–4%) [3]. It should be specified that in cases of codominance (balanced coronary system, 10–20% of individuals), both the RCA and the left circumflex artery supply the posterior descending artery, and thereby the risk of inferior MI resulting in HAVBs is lower than in patients with right dominance (80–90%). Finally, in about 2–3% of people, the AV nodal branch may arise from both the RCA and the left circumflex artery [5]. Indeed, a dual blood supply to the AV node has often been postulated, since it has been reported that patients
with inferior MI and left anterior descending (LAD) artery obstruction may have a significantly higher risk of developing complete AV block than patients with inferior MI without LAD obstruction [6].

Fig. 1. Atrioventricular and intraventricular blocks in the AMI setting.
Ischemia of the AV nodal branch may result in HAVB, with supraventricular blocks in case of inferior MI or infranodal blocks in case of anterior MI. Bundle branches ischemia may derive from LAD or RCA involvement, resulting in LBBB or RBBB. Abbreviations: AV, atrioventricular; HAVB, high-degree atrioventricular block; LBBB, left bundle branch block; LAD, left anterior descending; MI, myocardial infarction; RBBB, right bundle branch block; RCA, right coronary artery.

Besides a pure ischemic damage of the AV node, additional mechanisms may result in transient AV block during inferior MI, such as the cardiodepressor Bezold–Jarisch reflex. Indeed, experimental and early clinical reports have shown that this parasympathetic response may arise suddenly after the occlusion and the recanalization of the RCA [7, 8]. Later studies have reported how this reflex response has progressively been deemed as an indicator of successful thrombolysis [9–11]. Although the exact mechanisms underlying this neurologic phenomenon remain partially unknown, a stimulation of the vagal afferents in response to sympathetic overactivity inducing bradycardia, hypotension and vasodilatation, mostly due to early coronary artery reperfusion, has been identified as the major determinant of this reflex [11].

2.2 Incidence and prognosis of high-degree AV blocks in the AMI setting
Several reports have shown how that the incidence of HAVB may range from 3% to 14% in different clinical settings, and especially in inferior or anterior STEMI patients, more than in non-STEMI cases [12–19]. Although the incidence of HAVB has decreased after the thrombolytic era from 5–7% to 3% [12], specific risk factors such as older age, hypertension, diabetes, female sex, worse Killip class at presentation and tobacco use, still represent independent predictors that may predispose to AVB in this setting [20]. More importantly, as described in a meta-analysis from Meine et al. [21], HAVB represented a major predictor of mortality in the thrombolytic era especially when considering in-hospital mortality as the endpoint (nearly 3 to 5-fold higher), while instead their occurrence does not seem to impact long-term mortality. More recently, Auffret et al. [22] highlighted how, although patients with HAVB had a higher mortality rate than patients without it, HAVB was not an independent predictor of in-hospital mortality. This finding might be likely related to the progress that has been made in managing AMI during the last decade. Nevertheless, in another study conducted during PCI era, including also NSTEMI patients, patients with HAVB showed eight-fold higher mortality rates, especially when considering patients with anterior MI [23].

Moreover, in this study, there was no significant difference in mortality at one-year follow-up between patients with or without HAVB [23]. A recent Danish registry including 2073 STEMI patients treated with primary PCI had shown how, although the incidence has been reduced compared with earlier reports, HAVB remains a severe prognostic marker in the AMI setting [hazard ratio = 3.14 95% confidence interval (CI), 2.04–4.84, P < 0.001], significantly increasing the mortality rate within the first 30 days from occurrence [24].

Thus, in this report, HAVB patients who were discharged showed a similar prognosis when compared to patients who have not developed HAVB. More importantly, Gang et al. [24] evaluated how, apart from well-known risk factors, such as age >65 years, female gender, hypertension, and diabetes, also RCA occlusion may predispose to develop HAVB in this scenario.

These findings have been further confirmed by Singh et al. [25], analyzing the Global Registry of Acute Coronary Events (GRACE), including a total of 59229 patients with ACS between 1999 and 2007 and providing what seems to be a robust evidence on this topic. In particular, a total of 2.9% of patients had developed HAVB at any point during hospitalization, 22.7% of whom dying during in-hospital admission [adjusted odds ratio = 4.2, 95% confidence interval (CI), 3.6–4.9, P < 0.001]. Importantly, in this registry, the ACS subtype determined a different association between HAVB and in-hospital mortality, conferring a different risk profile [OR: ST-segment elevation myocardial infarction (STEMI) = 3.0; non-STEMI = 6.4; unstable angina = 8.2, P for interaction <0.001]. Although this finding may appear counterintuitive, patients with NSTEMI or unstable angina (UA) might show a higher risk due to multi-vessel ischemia, potentially compromising primary and collateral blood flow supplying the AV node and thereby resulting in more advanced conduction impairment. Instead, HAVB in STEMI patients is usually related to a single vessel occlusion, resulting in a less severe conduction system compromise, especially when the vessel is rapidly reperfused, as commonly expected in the primary
PCI era. Another interesting finding of this summary was that HAVB already present at the time of hospital presentation, as well as early (<12 h) PCI or fibrinolysis, were all associated with improved in-hospital survival, whereas temporary pacemaker insertion was not. Indeed, according to the 2017 ESC guidelines for the management of STEMI patients [26], a temporary pacemaker (PM) is only indicated in case of sinus bradycardia with hemodynamic intolerance or HAVB without stable escape rhythm and in cases of failure to respond to positive chronotrophic medication (class I, level of evidence C). HAVB in this setting usually resolves within a few days, and a PM implantation is usually not needed, as well as not affecting prognosis [27, 28]. Indeed, it has been estimated that only 9% of patients require permanent PM implantation [24], since a prompt coronary intervention is generally sufficient to restore blood supply to the AV node and resolve HAVB once the acute phase is ended. Interestingly, Singh et al. [25] showed a significant linear decline in the rate of HAVB in general (0.02%/year; P for trend < 0.001), both at presentation (0.05%/year; P for trend = 0.02) and in the hospital setting (0.2%/year; P for trend < 0.001), in either temporary (0.2%/year; P for trend < 0.001) or permanent PM use (0.06%/year; P for trend < 0.001), as well as in in-hospital mortality in patients with ACS and without HAVB (0.2%/year; P for trend < 0.001). However, a significant linear decline was not observed for in-hospital mortality associated with HAVB (P for trend = 0.62) regardless of the time HAVB occurred (at presentation; P for trend = 0.33 vs. inhospital; P for trend = 0.58). In this study, temporary pacemaker use was even higher in HAVB patients who died in hospital (52 vs. 30%, P < 0.001), whereas, in survivors, permanent PM implantation rate was higher (7.1 vs. 1.8%, P < 0.001). At univariate analysis, patients with HAVB at presentation, or who underwent PCI or fibrinolysis within 12 h of hospitalization, and permanent PM implant were more likely to survive in-hospital, while a prior history of heart failure, chronic renal disease, and the use of a temporary PM were associated with higher risk of in-hospital death. Nevertheless, patients with HAVB who survived the initial hospital admission and received a permanent PM, showed elevated odds of death at 6 months (adjusted OR = 2.4, 95% CI, 1.2–5.1). In conclusion, despite the incidence of HAVB is decreasing in hospital (52 vs. 30%, P < 0.001), whereasthepatients, per- manent PM implantation, has been recently reported [24], since a prompt coronary intervention is generally sufficient to restore blood supply to the AV node and resolve HAVB once the acute phase is ended. Interestingly, Singh et al. [25] showed a significant linear decline in the rate of HAVB in general (0.02%/year; P for trend < 0.001), both at presentation (0.05%/year; P for trend = 0.02) and in the hospital setting (0.2%/year; P for trend < 0.001), in either temporary (0.2%/year; P for trend < 0.001) or permanent PM use (0.06%/year; P for trend < 0.001), as well as in in-hospital mortality in patients with ACS and without HAVB (0.2%/year; P for trend < 0.001). However, a significant linear decline was not observed for in-hospital mortality associated with HAVB (P for trend = 0.62) regardless of the time HAVB occurred (at presentation; P for trend = 0.33 vs. in-hospital; P for trend = 0.58). In this study, temporary pacemaker use was even higher in HAVB patients who died in hospital (52 vs. 30%, P < 0.001), whereas, in survivors, permanent PM implantation rate was higher (7.1 vs. 1.8%, P < 0.001). At univariate analysis, patients with HAVB at presentation, or who underwent PCI or fibrinolysis within 12 h of hospitalization, and permanent PM implant were more likely to survive in-hospital, while a prior history of heart failure, chronic renal disease, and the use of a temporary PM were associated with higher risk of in-hospital death. Nevertheless, patients with HAVB who survived the initial hospital admission and received a permanent PM, showed elevated odds of death at 6 months (adjusted OR = 2.4, 95% CI, 1.2–5.1). In conclusion, despite the incidence of HAVB is decreasing in the PCI era and their new-onset is overall low, this conduct disturbance continues to result into a higher risk of in-hospital death. Table 1 (Ref. [12–20, 22–25, 29, 30]) summarizes the prevalence and related outcomes of HAVB and complete AV blocks in the AMI setting.

2.3 HAVB in the COVID-19 era: any role for undiagnosed ACS?

Several studies have reported the presence of a significant interaction between the cardiovascular system and Coronavirus disease (COVID-19), often sustained by macro- and microthrombosis, as well as a direct cardiac damage, that may lead to significant myocardial injury in different ways [31–38]. As highlighted in different reports, ACS and cardiac bradyarrhythmias and tachyarrhythmias are commonly reported complications in COVID-19 hospitalized patients, often impairing prognosis [39–45]. Specifically, an interesting case series from Dagher et al. [46] described 4 cases of COVID-19 patients, without previous history of arrhythmia, who developed a transient HAVB during the course of their hospitalization, not requiring permanent pacing. The authors hypothesized that a high systemic inflammatory burden, a direct viral injury to the myocardium, or a drug-related damage (e.g., hydroxychloroquine, which has however proven to be safe, though not effective [47–49]) could have induced HAVB in these patients, even if the exact underlying mechanism remained to be postulated. Another case of an infra-hisian block, otherwise requiring permanent PM implantation, has been recently reported [50]. Also in this case, a direct myocardial damage was hypothesized as the most likely cause. Indeed, as far as this can be reasonable, this panel of authors would suggest that also a transient vascular damage and/or a supply/demand imbalance resulting in myocardial ischemia, which is now regarded as the most important mechanism of cardiovascular damage in COVID-19, even in the absence of an overt AMI, may have played a significant role in these findings. However, specific data on HAVB and type 2 MI have not been investigated so far in other settings. Surely, further studies are needed to better characterize arrhythmias in COVID-19 patients and their potential links with myocardial ischemia, as well as specific studies focused on type 2 MI and its implication on transient HAVB, due do a consistent and durable supply/demand imbalance.

3. Intraventricular blocks

3.1 Pathophysiology of intraventricular blocks during ACS

Intraventricular (IV) conduction disturbances in the setting of ACS represent a significant diagnostic challenge, since the ECG interpretation becomes often difficult and may lead to a late recognition of a potentially life-threatening condition. Intraventricular conduction blocks, in addition to the extent of ST-segment deviations, are regarded to be related with a more severe ischemic damage and a more rapid progression of myocardial necrosis than ST-segment deviations alone [51, 52]. When considering the vascularization of the conduction system below the AV node, it should be noted that, as for the left bundle branch, the LAD and its septal branches supply blood to the anterior fascicle, and the posterior fascicle is perfused by the RCA, whereas the right bundle branch is entirely supplied LAD and/or its proximal septal branches [53]. Due to its dual blood supply, a left bundle branch block (LBBB) is caused mainly by sclerosis and fibrosis, more than by a massive myocardial infarction, while RBBB suggests a proximal occlusion of LAD, expressing a wider infarct size in anterior MI, thus being usually associated with a higher mortality rate (see after) [54, 55]. Moreover, in a minor report, some authors have suggested that RBBB could occur not only in anterior MI, but also during inferior MI, in relation to a concurrent right ventricular en-
Table 1. Main studies summarizing prevalence and related outcomes of complete atrioventricular blocks (CAVB) or high-degree atrioventricular blocks (HAVB) in the acute myocardial infarction (AMI) setting.

| Authors                 | Years          | Location       | Study type | Population | Inclusion criteria | Prevalence | Mortality                      |
|-------------------------|----------------|----------------|------------|------------|--------------------|------------|--------------------------------|
| Feigl et al. [29]       | 1972–1982      | Israel         | Prospective | n = 288    | HAVB               | 14%        | NA                             |
| Gang et al. [24]        | 2012           | Denmark        | Prospective | n = 2073   | HAVB               | 3.2%       | 37% (in-hospital)              |
| Nguyen et al. [12]      | 1975–2005      | U.S.           | Prospective | n = 13663  | CAVB               | 4%         | 43.2% (in-hospital)            |
| Singh et al. [25]       | 1999–2007      | International  | Prospective | n = 59229  | HAVB               | 2.9%       | 22.7% (in-hospital)            |
| Hashmi et al. [30]      | 2015–2016      | Pakistan       | Prospective | n = 179    | CAVB               | 7.3%       | NA                             |
| Meine et al. [20]       | 2005           | International  | Prospective | n = 75993  | HAVB               | 6.9%       | 23% in-hospital                 |
| Aguiar Rosa et al. [23] | 2005–2015      | Portugal       | Prospective | n = 4779   | CAVB               | 1.9%       | 28% (in-hospital)              |
| Auffret et al. [22]     | 2006–2013      | France         | Retrospective| n = 6662   | HAVB               | 3.5%       | 18.1% (on admission) 28.6% (in-hospital) |
| Aplin et al. [13]       | 1990–1992      | Denmark (TRACE trial) | Prospective | n = 6657   | CAVB               | 5%         | 31.6% (30-days) 21% (7-days) 35% (1-year) |
| Harpaz et al. [14]      | 1992–1996      | Israel         | Prospective | n = 3300   | CAVB               | 3.7%       | 29% (30-days)                 |
| Spencer et al. [15]     | 1975–1997      | USA            | Retrospective| n = 9082   | CAVB               | 5%         | 46.8% (in-hospital)            |
| Simons et al. [16]      | 1990–1993      | International  | Prospective | n = 40898  | CAVB               | 8.3%       | 21% (in-hospital)              |
| Goldberg et al. [17]    | 1975–1988      | USA            | Retrospective| n = 4762   | CAVB               | 5.8%       | 48.9% (in-hospital)            |
| Hreybe et al. [18]      | 1996–2003      | USA            | Retrospective| n = 21807  | CAVB               | 2.5%       | NA                             |
| Clemmensen et al. [19]  | 1985–1988      | International  | Prospective | n = 373    | CAVB               | 13%        | 20% (in-hospital)              |

Table 2. Main studies summarizing prevalence and related outcomes of right and left bundle branch block (RBBB - LBBB) in the acute myocardial infarction (AMI) setting.

| Authors                     | Years           | Location | Study type | Population | Inclusion criteria | Prevalence | Mortality                      |
|-----------------------------|-----------------|----------|------------|------------|--------------------|------------|--------------------------------|
| Melgarejo-Moreno et al. [62]| 1992–1994       | Spain    | Retrospective | n = 1238  | RBBB               | 10.9%      | - Early mortality: 43.1% (new-onset) - 15.5% (old) - 15.3% (indeterminate) |
| Iwasaki et al. [56]         | 1997–2006       | Japan    | Retrospective | n = 1265  | RBBB               | 11.50%     | - 1 year mortality: 58.8% (new-onset) - 35.5% (old) - 23% (indeterminate) |
| Tolppanen et al. [51]       | 2005–2012       | International | Prospective   | n = 199   | RBBB or LBBB       | 50% (37% transient) | 68% (1-year)—this study included only patients with cardiogenic shock 10.7% (1-year - RBBB) 7% (1-year - LBBB) |
| Neumann et al. [63]         | 2007–2008       | International | Prospective   | n = 4067  | RBBB or LBBB       | NA         |                                |
| Vivas et al. [61]           | 2004–2006       | Spain    | Retrospective | n = 913   | RBBB or LBBB       | RBBB: 13% (77% new-onset or indeterminate, 23% old) LBBB: 2% (62% new-onset or indeterminate, 38% old) | RBBB: 17% (in-hospital) LBBB: 29% (in-hospital) |
largement, thus representing an independent predictor of adverse outcome during hospitalization regardless of infarction location in their cohort [56].

3.2 Incidence and prognosis of intraventricular blocks in the AMI setting

Changes in QRS duration and pattern usually reflect severe ischemia in ACS, and when ventricular conduction blocks occur, they generally define a high-risk this scenario, although the evidence is inconclusive. Indeed, few studies suggested that patients presenting with bundle branch block (BBB) did not show higher in-hospital mortality [57] (although reflecting high-risk clinical characteristics), whereas in other studies, BBB—and especially right bundle branch block (RBBB)—has been linked with major adverse cardiovascular events (MACEs) during follow-up [58, 59]. Particular attention should be paid to the new-onset of a permanent BBB which appeared to be independently associated with a higher 30-day and 7-year all-cause mortality in different reports [60, 61]. Interestingly, even a transient ventricular conduction block has shown to be a strong independent predictor of 1-year mortality, maybe because developing a BBB (especially a RBBB) usually indicates a wider ischemia in this scenario [51]. Table 2 (Ref. [26, 56, 61–63]) summarizes the main studies focused on the prevalence and related outcomes of RBBB and LBBB in the AMI setting.

3.3 Left bundle branch block (LBBB)

Recognition of MI in the context of a LBBB has always been a challenge in the emergency department (ED), since the ST-segment deviation is one of the fundamental features of LBBB. Over the years, many criteria have been proposed to help clinicians making a correct diagnosis in this setting, with the most well-known being the Sgarbossa criteria. The so-called Sgarbossa rule was first described in 1996 and it is still often used in the ED in its original version showing a high specificity, although a low sensitivity must be taken into account [64]. According to the original Sgarbossa rule, at least 3 points of the following criteria are needed to diagnose MI in the presence of LBBB: (1) ST-segment elevation of 1 mm concordant with the QRS in at least 1 lead = 5 points; (2) ST-segment depression of 1 mm in any leads V1–V3 = 3 points; (3) discordant ST-segment elevation in any lead >5 mm in at least 1 lead = 2 points. Subsequently, Smith et al. [65] modified Sgarbossa criteria aiming to increase both the sensitivity and the specificity of this rule to the 91% and 90%, respectively, by replacing absolute ST-segment elevation of 5 mm with a relative ST/S ratio less than 0.25. Sgarbossa and modified Sgarbossa criteria are summarized in Fig. 2. Even more recently, new different criteria, such the BARCELONA algorithm [66], have been proposed. The BARCELONA algorithm is capable to identify MI in the presence of LBBB with a sensitivity of 93–95% and a specificity of 89–94%. According to such algorithm, a discordant ST deviation ≥1 mm in any lead or a discordant ST deviation ≥1 mm in leads with max R or S wave voltage ≤6 mm, can appropriately predict MI. Lastly, as reported by the 2017 ESC guidelines for the management of STEMI patients, since all algorithms do not provide diagnostic certainty, the presence of concordant and marked ST-segment elevation appears to be the best indicator of ongoing MI and it may significantly help the diagnosis of STEMI in LBBB. However, whenever AMI is suspected in the presence of a new-onset or old LBBB, patients might need emergent or urgent coronary angiography, and they should be managed similarly to STEMI patients [26]. In this setting, besides an accurate clinical evaluation, a bedside echocardiogram evaluating new wall motion abnormalities is a useful tool to establish a differential diagnosis. On the other side, it should be noted that a new LBBB does not predict a MI and should not be considered as a STEMI equivalent if isolated according to ACCF/AHA Guidelines, as well as not predicting an MI per se [67, 68]. Indeed, further data showed how only 30% of patients presenting to the ED with LBBB and suspected MI where found to have ACS [55].

Fig. 2. Sgarbossa and modified Sgarbossa criteria. At least 3 points of the following criteria are needed to diagnose MI in the presence of LBBB, according to the original Sgarbossa rule: (1) ST-segment elevation of 1 mm concordant with the QRS in at least 1 lead = 5 points; (2) ST-segment depression of 1 mm in any leads V1–V3 = 3 points; (3) discordant ST-segment elevation in any lead >5 mm in at least 1 lead = 2 points. Smith et al. modified Sgarbossa criteria aiming to increase both the sensitivity and the specificity of this rule to the 91% and 90%, respectively, by replacing absolute ST-segment elevation of 5 mm with a relative ST/S ratio less then 0.25.

3.4 Right bundle branch block (RBBB)

The exact prevalence of patients presenting with RBBB in the setting of a MI is still not clear, representing about 3.1% of patients presenting to the ED with AMI [63]. The prognosis of these patients presenting with RBBB during MI is...
still debated, but as previously mentioned, patients with MI and RBBB generally show poor prognosis [69]. Since also in the presence of RBBB (and not only in the LBBB scenario) it might be difficult to detect transmural ischemia, potentially confounding a STEMI diagnosis, the 2017 ESC guidelines for the management of STEMI patients recommend considering an emergency activation of the catheterization laboratory when persistent ischemic symptoms occur in the presence of RBBB. A distinction should be made between permanent and transient new-onset RBBB, as well as with new-onset and previous RBBB. Indeed, in a recent review, transient RBBB appeared to be associated with a lower risk of short-term mortality, whereas patients with new-onset RBBB had higher risk when compared to those being admitted with a previous RBBB [70].

4. Conclusions

HAVB in the AMI setting has become less frequent in the PCI era, but there is still an association with an increased in-hospital mortality, although long-term mortality appears to be not affected. IV blocks represent a relevant diagnostic challenge, and specific attention should be paid to clinical presentation in order to avoid inadequate treatment delay. Mortality of patients with RBBB seems to be higher, being usually associated to a larger extent of the ischemic myocardial damage.

Author contributions

MS, FS, CG, and GBF conceived of this review. MS, FS, CG and AG structured and organized this review. MS, CG, FS, MD, LZ, revised the literature and synthesized study data. MS, FS, and CG wrote the original draft of this paper. MD and LZ updated this review by analyzing the latest published studies and reports. MS, FS, CG and AG organized study tables and images. AG and GBF revised and edited the original draft of this paper. GBF supervised the entire work as senior author. All authors have read and approved the submitted version.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

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