Clinical paper
Conduction disorders in bradyasystolic out-of-hospital cardiac arrest

Michiel Hulleman*, Hanne Mes, Marieke T. Blom, Rudolph W. Koster

Academic Medical Center – Department of Cardiology, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands

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A B S T R A C T

Aims: Bradyasystolic heart rhythms are often recorded in out-of-hospital cardiac arrest (OHCA). Atrioven-
tricular (AV) conduction disorders might lead to OHCA, but the prevalence of AV-conduction disorders and other bradyasystolic rhythms in OHCA is unknown. These patients might benefit from pre-hospital pacing. We aimed to determine the prevalence of different types of bradyasystolic heart rhythms in OHCA, including third degree AV-block, and document survival rates.

Methods: We used data from the ARREST-registry of OHCA in the Netherlands. Patients with bradyasys-
tolic OHCA in 2006–2012 were included. ECGs were classified according to the presence of P-waves and QRS complexes in five rhythm groups. Differences in survival to discharge in relation to resuscitation characteristics, rhythm and pacing were tested using Chi-Square test and multivariate regression analysis.

Results: We included 2333 patients with a bradyasystolic rhythm; 371 patients (16%) presented with a third degree AV-block. In total 45 patients (1.9%, 95%-CI 1.4–2.5%) survived. A third degree AV-block (adjusted OR 0.86, 95%-CI 0.38–1.96) or pacing (adjusted OR 0.89, 95%-CI 0.21–3.78) was not associated with survival. Pacing was initiated in 110 patients (4.7%), after a long delay (median 18.7 min). The strongest association with survival was found for the presence of a bradycardia (vs. asystole) (adjusted OR 4.20, 95%-CI 1.79–9.83); bystander witnessed (OR 4.13, 95%-CI 1.45–11.8) and EMS witnessed collapse (OR 5.18, 95%-CI 2.77–9.67).

Conclusion: In bradyasystolic OHCA, 16% of all patients present with third degree AV-block, but survival for these and other bradyasystolic patients remains poor. Pacing is seldom initiated, often delayed, and rarely beneficial.

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Introduction

In the last decades, the incidence of non-shockable heart rhythms (asystole or pulseless electrical activity [PEA]) as initial recorded rhythm in out-of-hospital cardiac arrest (OHCA) increased.1,2 The prognosis of survival of patients with a non-shockable heart rhythm remains very poor, with survival to discharge rates not exceeding 3% for asystole and 10% for PEA, without a tendency to improve over years.3−8 Non-shockable rhythms consist of multiple different rhythms such as sinus bradycardia, junctional/idiowentricular rhythms, third degree atrioventricular (AV)-block or asystole. Most of these rhythms are of bradyasystolic origin, a ventricular rate below 60 beats per minute or asystole.9 Despite their heterogeneous origin, all non-shockable rhythms are managed with one treatment algorithm with limited effect on survival, if no treatable causes can be identified. Generally, no other treatment besides high quality cardiopulmonary resuscitation (CPR), administration of intravenous vasopressors and transcutaneous pacing is available for these patients.

In a non-OHCA setting a symptomatic third degree AV-block is a Class I indication for pacing,10 but it is unknown if patients in true cardiac arrest caused by a third degree AV-block will benefit equally from pacing. Current evidence suggests that in OHCA pacing by any means (transcutaneous, transvenous or transmyocardial) does not improve short- or long-term survival, and since 2005 resuscitation guidelines do not encourage pacing for routine use in OHCA.11,12 However, it is not clear if different origins of bradyasystole, such as a third degree AV-block, have been identified in studies investigating pacing in OHCA.

The prevalence of the various different bradyasystolic heart rhythms is unknown. As an increasing number of non-shockable OHCA cases are observed worldwide, it is important to identify...
the electrocardiographically different rhythms, and to know their associated outcomes. We aimed to determine the prevalence of these bradyasystolic heart rhythms in a large cohort of consecutive OHCA patients, with an emphasis on identifying patients with AV-conduction disorders, and document the current resuscitation treatment practice and outcomes in these patients. We hypothesize that AV-conduction disorders are relatively common, but that pacing is often not initiated and is not associated with better survival.

Methods

Study design and setting

ARREST is an ongoing prospective registry of all consecutive resuscitation attempts in North-Holland, the Netherlands (population 2.4 million). The organization of the emergency medical services (EMS) and data collection in the study region has been described previously. In short, for all suspected OHCA, two ambulances of a single tier are dispatched with defibrillators, all of which have pacing capability. Also, in a large part of the study region first responders (policemen, fire fighters and local lay rescuers) equipped with an automated external defibrillator (AED) are dispatched in case of a suspected OHCA. On-site AEDs are available and used in an increasing number of public places. The present study is a retrospective analysis of electrocardiographic data gathered in the ARREST study.

Selection of patients

The present investigation covered the period January 1, 2006–December 31, 2012. All patients on whom EMS personnel attempted resuscitation during OHCA with an electrocardiogram (ECG) documenting an initial bradyasystolic heart rhythm were included in the study. We excluded patients with a clear non-cardiac cause (e.g., trauma, drowning, respiratory, neurologic, suicide), patients of whom the resuscitation ECG could not be retrieved or with an inconclusive ECG, patients with unknown survival status and patients with a paced rhythm before cardiac arrest.

The Medical Ethics Review Board of the Academic Medical Center, Amsterdam, approved the ARREST data collection and gave a waiver for obtaining (written) informed consent.

Data collection and definitions

Data of 7925 EMS-attended OHCA cases was retrieved from dispatch centers, EMS personnel, first responders and hospital case files. All data was collected according to Utstein recommendations. All ambulance recordings of continuous single and 12-lead ECGs were digitally sent to the study center. If an AED was used, ARREST study personnel collected the stored continuous single lead ECG from the AED shortly after the resuscitation attempt. All manual defibrillator and AED clock times were synchronized to the dispatch center clock. The time stamp of EMS call and time of initial recorded rhythm from manual defibrillator or AED was used to calculate call-to-ECG delay.

In ARREST, the initial recorded rhythms of all ECGs from the AED or manual defibrillator, whichever was connected first, are categorized shortly after the OHCA by experienced research personnel in ventricular fibrillation (VF)/ventricular tachycardia (VT), supraventricular tachycardia, normal rhythm (frequency 60–100), bradycardia (defined as a ventricular rate of less than 60 beats per minute), asystole or undetermined rhythm. For the current analysis, all ECGs were reassessed by two researchers (M.H. and H.M) for the presence of p-waves, QRS complexes (with rate and QRS duration noted) and AV-conduction disorders (first, second and third degree AV-block). In case of disagreement, the rhythm was also interpreted by RWK to reach consensus. The presence of rapid irregular peak-to-peak baseline deviations of less than 100 μV (not related to deviations in the impedance signal) was considered secondary asystole (following VF dissolution). ECGs were classified in five different rhythm groups: asystole (absence of p-waves and QRS complexes and no or less than 100 μV baseline deviations), third degree AV-block without escape rhythm, third degree AV-block with escape rhythm, idioventricular/junctional rhythm and sinus bradycardia (Fig. 1). When EMS personnel initiated pacing, the rhythm immediately preceding pacing and the occurrence of electrical capture was also noted.

Neurological status at discharge was reviewed by research personnel from hospital patient charts using the Cerebral Performance Category (CPC) scale. A CPC score of 1 (normal cerebral performance) or 2 (moderate cerebral disability) at discharge was considered as survival with a favorable neurologic outcome.

Statistical analysis

Normally distributed continuous variables were presented as mean ± standard deviation (SD) and differences tested for significance with Student’s t-test and ANOVA. Time intervals were presented as median with interquartile range (IQR), differences tested using Mann–Whitney U and Kruskall–Wallis test. Differences between proportions were tested with Chi-Square test. Survival rates of the different rhythm groups were expressed as proportions with 95% confidence intervals (CI). Survival differences associated with demographic and resuscitation characteristics were calculated using logistic regression analysis, expressed as unadjusted odds ratio (OR) with 95%-CI. Survival differences in
relation to ECG characteristics and pacing were expressed as unadjusted and adjusted OR. Only demographic and resuscitation characteristics that had a univariate association with survival of $P<0.10$ were added to the multivariate model. Patients with any missing data were excluded from the logistic regression analysis. All statistical tests were two-tailed, and a $P$ of $<0.05$ was considered statistically significant. Statistics were performed in SPSS 20.0 for Mac (IBM SPSS, NY, USA).

**Results**

**Bradyasystolic rhythms and resuscitation characteristics**

Between January 1st 2006 and December 31st 2012, 7925 resuscitation attempts for OHCA were observed. Fig. 2 shows the in-and exclusion of these patients. Of the 2643 patients with a non-shockable rhythm, 2333 patients (88%) had a bradyasystolic first rhythm. Of the included patients, 1508 patients (65%) died on site and were not transported to the hospital. Of the 825 patients transported to the hospital, 498 patients (21%) died in the emergency department, and 327 patients (14%) were admitted to the hospital; 45 patients (1.9%, 95%-CI 1.4–2.5%) survived to discharge, of which 42 (93%) had a favorable neurologic outcome. Fig. 3 shows the ECG classification. Important differences existed between witnessed ($n=1490, 64%$) and unwitnessed OHCA ($n=809, 35%$). Bradycardiac rhythms were more prevalent in witnessed than in unwitnessed OHCA ($P<0.001$). The mean ventricular rate was $32 \text{min}^{-1}$ ($±14$) with a mean QRS duration of $142 \text{ms}$ ($±49$). In witnessed OHCA, patients with sinus bradycardia had the highest survival (6.8%, 95%-CI 1.7–10.1%), patients with asystole the lowest (0.4%, 95%-CI 0–0.9%). In unwitnessed OHCA, no patients with sinus bradycardia survived. Of the patients with a sinus bradycardia 93 patients (4.0%) had a first degree AV-block and 33 patients (1.4%) had a second degree AV-block.

A third degree AV-block was present in 18% of bystander witnessed cases, and 13% in unwitnessed cases ($P=0.001$). This...
difference was mainly caused by the occurrence of a third degree AV-block with escape rhythm (12% vs. 5.1% for witnessed vs. unwitnessed cases, \(P < 0.001\)). Survival of witnessed and unwitnessed patients with a third degree AV-block with or without escape rhythm was not significantly different (\(P = 0.73\) and \(P = 0.76\) respectively).

EMS witnessed collapse was included in Fig. 3 in the ‘witnessed’ group. Of the patients with EMS witnessed collapse, 83% had a bradycardia, compared to 54% of patients with a bystander witnessed collapse (\(P < 0.001\). The prevalence of any third degree AV-block was not significantly different for EMS witnessed (18%) and bystander witnessed collapse (18%, \(P = 0.98\).

Table 1 shows the demographic and resuscitation characteristics of patients with different bradysystolic rhythms. Significant differences exist between the groups for all variables, except call-to-ECG delay. In general, patients with bradyarrhythms were older, more often female, and had more often a bystander witnessed or EMS witnessed collapse (\(P < 0.001\).

Table 2 shows that bystander witnessed collapse (\(P = 0.004\), EMS witnessed collapse (\(P < 0.001\) and public location of collapse (\(P = 0.050\)) were significantly associated with higher survival rates. There were 64 patients with one or more missing variables; patients with missing data were more often male (77% vs. 64%, \(P = 0.04\)) and less often had an AED attached (5% vs. 29%, \(P < 0.001\). All other demographic and resuscitation characteristics were not significantly different between patients with or without missing data.

Transcutaneous pacing

Table 3 shows the characteristics of the 110 paced patients (4.7%). In 62 patients (56%) there was electrical capture; the proportion of mechanical capture was not registered. Of the 371 patients with an initial third degree AV-block, only 24 patients (6.5%) were paced. Eight patients (13% of paced patients) were admitted to the hospital and only two patients survived to hospital discharge. None of the paced patients with a third degree AV-block survived.

Univariate and multivariate survival analysis

Table 4 shows that the presence of QRS complexes (\(P < 0.01\) and higher heart rate (added as continuous variable; \(P < 0.001\) were associated with higher survival rates. QRS duration (\(P = 0.12\), third degree AV-block (\(P = 0.86\) and pacing (\(P = 0.88\) were not significantly associated with higher survival rates.

Discussion

This study shows that in non-shockable OHCA, 88% of all patients had a bradysystolic initial rhythm. The survival to discharge was only 1.9%. Bystander- and EMS witnessed collapse, public location of collapse, the presence of a bradycardia and faster heart rate were associated with higher survival rates. A third degree AV-block was found in 16% of all bradysystolic patients. PACing was only initiated after a very long delay, irrespective of the initial bradysystolic rhythm, and not associated with survival.

AV conduction disorders

The prevalence of AV conduction disorders in OHCA is not well established. In a case-series of 132 patients with sudden cardiac death during Holter monitoring, the authors reported AV-block in 9 patients (7%), but bradyasystole was subdivided only in asystole and AV-block, and it is not clear how these AV-blocks were defined. Bayes de Luna et al. reviewed 7 case series of sudden death during Holter monitoring. Of the 157 cases presented in this study, 26 patients (17%) died after bradyarrhythmia, and in 3 patients (12% of bradyasystolic patients) an AV-block was present. The prevalence of third degree AV-block of 16% we report is within the range of the aforementioned studies. However, the Holter monitoring studies showed the arrhythmia at the exact moment of collapse. In the present study, it is uncertain if the initial recorded rhythm represents the primary rhythm of the cardiac arrest, because of considerable delay to initial rhythm assessment.

Survival

This study confirms the very poor prognosis of patients with initial asystole. Only 7 out of the 1282 asystolic patients (0.5%) survived to hospital discharge. Earlier studies showed survival rates between 2.0 and 3.3% for asystolic patients. Survival of bradyarrhythmic patients in our study was 3.6%; other studies reporting on PEA showed survival rates ranging from 2.4% to even 15%.
Table 2
Demographic and resuscitation characteristics and associated survival to discharge.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Survival</th>
<th>Unadjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>OR (95%-CI)</td>
</tr>
<tr>
<td>Age (n = 2333)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65 y</td>
<td>16 (1.9%)</td>
<td>0.95 (0.52–1.73)</td>
</tr>
<tr>
<td>&gt;65 y</td>
<td>29 (2.0%)</td>
<td>ref</td>
</tr>
<tr>
<td>Sex (n = 2333)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (1.7%)</td>
<td>0.76 (0.42–1.38)</td>
</tr>
<tr>
<td>Female</td>
<td>19 (2.3%)</td>
<td>ref</td>
</tr>
<tr>
<td>Location of collapse (n = 2333)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>13 (7.7%)</td>
<td>5.18 (2.77–9.67)</td>
</tr>
<tr>
<td>Public</td>
<td>32 (1.5%)</td>
<td>ref</td>
</tr>
<tr>
<td>Onset of later VF/VT (n = 2333)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (2.0%)</td>
<td>4.13 (1.45–11.8)</td>
</tr>
<tr>
<td>No</td>
<td>3 (0.5%)</td>
<td>ref</td>
</tr>
<tr>
<td>Call-to-ECG delay (n = 2333)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10 min</td>
<td>11 (1.5%)</td>
<td>0.94 (0.42–2.08)</td>
</tr>
<tr>
<td>&gt;10 min</td>
<td>22 (1.1%)</td>
<td>0.73 (0.41–1.32)</td>
</tr>
</tbody>
</table>

Binary variables are denoted as cases (percentage). Odds ratio (OR) calculated using univariate logistic regression analysis.

AED denotes automated external defibrillator; CPR cardiopulmonary resuscitation; EMS emergency medical services; VF ventricular fibrillation; VT ventricular tachycardia

Table 3
Transcutaneous pacing in relation to initial rhythm and rhythm preceding pacing.

<table>
<thead>
<tr>
<th>Delay EMS- assessment to pacing</th>
<th>Electrical capture</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min (IQR)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>All patients (n = 110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asystole (n = 34)</td>
<td>18.5 (12.8–26.2)</td>
<td>62 (56%)</td>
</tr>
<tr>
<td>3rd degree AV-block without escape (n = 10)</td>
<td>16.7 (14.0–26.3)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>3rd degree AV-block with escape (n = 14)</td>
<td>18.8 (12.6–26.4)</td>
<td>7 (50%)</td>
</tr>
<tr>
<td>Idioventricular/junctional (n = 41)</td>
<td>16.5 (11.3–22.9)</td>
<td>29 (70%)</td>
</tr>
<tr>
<td>Sinus bradycardia (n = 11)</td>
<td>30.1 (22.3–33.8)</td>
<td>6 (55%)</td>
</tr>
</tbody>
</table>

Delay presented as median (IQR). Binary variables are denoted as cases (percentage).

AV block denotes atrioventricular block; IQR interquartile range; EMS emergency medical services.

clear definition of PEA is lacking, but commonly all rhythms other than shockable rhythms and asystole are referred to as PEA. This includes also patients with heart rates over 60. We excluded all patients with a ventricular rate above 60, and as higher heart rate is associated with survival in the current study, we might have excluded patients with a favorable outcome.

Both bystander and EMS witnessed arrest were associated with better survival. A third degree AV-block, predominantly with escape rhythm, was more prevalent in these witnessed cases. This suggests that AV conduction disorders are not only present in unwitnessed OHCA with long delay. In OHCA cases presenting with AV conduction disorders with reasonably short delay (bystander witnessed) or no delay (EMS witnessed) pacing might be feasible.

Bystander CPR has been associated with higher survival rates, in shockable as well as in non-shockable OHCA. This was not the case in our study, as was also demonstrated earlier for asystolic OHCA. Our study only included patients with bradyasystolic rhythms, patients with the worst outcome that may not benefit from early bystander CPR as other patients in OHCA do.

AV-conduction disorders and indications for pacing

A symptomatic third degree AV-block in a non-OHCA setting is a Class I indication for pacing, but the currently available evidence shows no benefit of pacing in OHCA. The American Heart Association (AHA) guidelines explicitly state that pacing is not recommended in asystole, as this might delay or interrupt chest compression, but AV-block as presenting rhythm is not specifically mentioned. In patients with asystole, the European Resuscitation Council (ERC) guidelines recommend to check for P-waves and
when present pacing may be considered.23 The Dutch protocol for EMS care is based on the ERC Guidelines.24 Treatment of bradycardic rhythms in the AHA and ERC guidelines is only discussed in the context of symptomatic bradycardia (i.e. with cardiac output), not for patients in cardiac arrest.

In the three large controlled pacing studies in OHCA all causes of asystole were included, and also in some cases symptomatic bradycardias without true cardiac arrest.25–27 The first two of these controlled studies showed no benefit of pacing in OHCA, but also reported a median delay to pacing of more than 20 min.25,26 We also show this very long delay; pacing is only initiated after other treatment options are exhausted. This may explain why pacing has no impact on survival rate.

In order to be successful, pacing should be initiated as soon as possible after cardiac arrest, before irreversible myocardial damage occurs.28,29 Cummins et al. studied pacing before advanced life support resulting in a short delay of only 9 min from collapse to pacing initiation.27 That study also showed no benefit of pacing in asystolic OHCA and pacing has therefore been discouraged in the guidelines ever since. However, none of these studies restricted their inclusion to patients who theoretically are more likely to respond to pacing, such as patients with a third degree AV-block. Asystolic cases comprised almost 50% of all patients in our study and a similar proportion probably also was present in these studies. None of these studies specifically selected patients that might actually benefit from pacing.

Limitations

This study is based on analyses of mostly single lead recordings. Only after ROSC or in EMS witnessed collapse, 12-lead ECGs were available. Assessing the initial rhythms using single lead ECGs is less reliable than using 12-lead ECGs, limiting the diagnostic reliability of rhythm assessment during CPR.

Due to the retrospective nature of our analysis, we could not identify the reasons to initiate or withhold pacing. We also did not collect detailed data on pre-hospital treatment by EMS other than CPR and defibrillation, or reasons to terminate the resuscitation attempt. Any association of patient- or resuscitation characteristics with survival could be influenced by treatment decisions of EMS personnel, which (other than defibrillation and pacing initiation) were not incorporated in our analysis. Also, the in-hospital treatment following ROSC, such as percutaneous coronary interventions, intra-aortic balloon pump, percutaneous ventricular assist devices or targeted therapeutic hypothermia might influence survival. Due to the low number of surviving patients, we did not assess the in-hospital treatment for these patients.

Conclusion

In bradysystolic OHCA 16% of patients present with a third degree AV-block. The survival to discharge remains as poor as in other patients with bradysystole. Pacing is rarely initiated, also in patients with third degree AV-block, and if so, very late. In its current form, no survival benefit can be expected from pacing. It remains to be elucidated if there is subset of patients among those with bradysystolic cardiac arrest, such as third degree AV-block, that could benefit from pacing if initiated without any delay.

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Conflict of interest statement

RWK receives an unconditional grant of Physio Control Inc., Redmond WA to support the ARREST study data collection. Physio Control Inc. was not involved in study design, data-collection, analysis, interpretation or in writing of the manuscript. Other authors report no conflicts of interest.

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