



# Prevalence of bradyarrhythmias needing pacing in COVID-19

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## Abstract

**Background:** The Sars-Cov-2 infection is a multisystem illness that can affect the cardiovascular system. Tachyarrhythmias have been reported but the prevalence of bradyarrhythmia is unclear. Cases have been described of transient high-degree atrioventricular (AV) block in COVID-19 that were managed conservatively.

**Method:** A database of all patients requiring temporary or permanent pacing in two linked cardiac centers was used to compare the number of procedures required during the first year of the pandemic compared to the corresponding period a year earlier. The database was cross-referenced with a database of all patients testing positive for Sars-Cov-2 infection in both institutions to identify patients who required temporary or permanent pacing during COVID-19.

**Results:** The number of novel pacemaker implants was lower during the COVID-19 pandemic than the same period the previous year (540 vs. 629, respectively), with a similar proportion of high-degree AV block (38.3% vs. 33.2%, respectively,  $p = .069$ ). Four patients with the Sars-Cov-2 infection had a pacemaker implanted for high-degree AV block, two for sinus node dysfunction. Of this cohort of six patients, two succumbed to the COVID-19 illness and one from non-COVID sepsis. Device interrogation demonstrated a sustained pacing requirement in all cases.

**Conclusion:** High-degree AV block remained unaltered in prevalence during the COVID-19 pandemic. There was no evidence of transient high-degree AV block in patients with the Sars-Cov-2 infection. Our experience suggests that all clinically significant bradyarrhythmia should be treated by pacing according to usual protocols regardless of the COVID status.

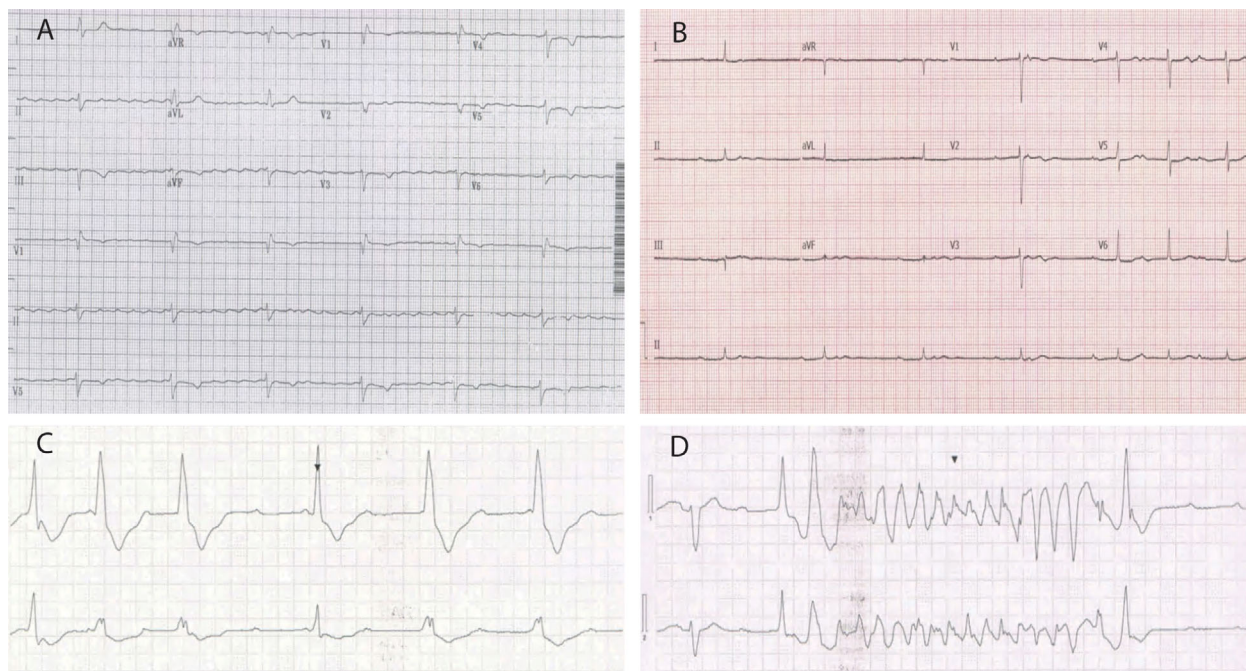
## KEYWORDS

bradycardia, COVID-19, high-degree AV block, pacing

## 1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) infection is a multi-system illness. Viral pneumonitis causing acute respiratory distress is the primary characteristic but cardiac injury and arrhythmia are well-recognized features.<sup>1-3</sup> Evidence of arrhythmia has been recorded in 16.7% of affected patients<sup>1,4</sup> and is associated with poor outcomes.<sup>5</sup>

Transient high-degree atrioventricular (AV) block has been described in COVID-19 but the prevalence is unclear<sup>6</sup>; only clusters of case reports are available in the literature suggesting it may be uncommon. The management of these cases has varied: in most of the cases described, AV conduction recovered spontaneously within 1-6 days,<sup>6,7</sup> but some patients underwent implantation of a permanent pacemaker.<sup>4,8</sup>



**FIGURE 1** Electrocardiograms confirming high-degree atrioventricular (AV) block in patients with active COVID-19 infection. (A) Patient with atrial fibrillation and complete heart block with a broad QRS (patient one). (B) Patient with intermittent high-degree AV block (patient two). (C) High-degree AV block with a broad QRS (patient four). (D) Patient with a short run of polymorphic VT in the context of bradycardia (patient four) [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

We examined the rate of presentation with AV block in the first year of the pandemic, compared to the same period a year earlier, to look for evidence of a surge in cases in response to the virus. We reviewed the COVID-19 status and clinical outcome of all patients presenting with AV block during this period, to determine the prevalence of COVID-associated AV block and to determine whether AV block was reversible in these cases.

## 2 | METHOD

Data on all patients requiring pacing therapy was obtained from catheter lab records across two linked institutions for 2 years to the end of March 2021. All referrals for temporary pacing and all new implantations of a permanent pacemaker (urgent and elective) were included and the cases of high-degree AV block were sieved.

Data were collected for all patients who were admitted to hospital with a Sars-Cov-2 infection between March 2020 and February 2021. All cases were confirmed with a reverse-transcriptase-PCR test on a nasopharyngeal specimen collected by a healthcare professional.

The databases of COVID-19 infection and pacing requirement were cross-referenced to identify patients requiring temporary or permanent pacing during COVID infection. Records were reviewed to determine whether AV block was present, and to determine the time course of it (Figure 1). Demographics, laboratory chemical and hematological profiles were recorded. For patients who underwent implantation of a permanent pacemaker, subsequent device interrogation data were interrogated for evidence of recovery of AV conduction.

Continuous variables are presented as a mean  $\pm$  standard deviation and categorical data as a number and percentage. Statistical analysis was performed using the Chi-squared and Mann-Whitney tests (Microsoft Excel 2019 v16.47, Microsoft Corp., WA, USA), a  $p < .05$  was regarded as statistically significant.

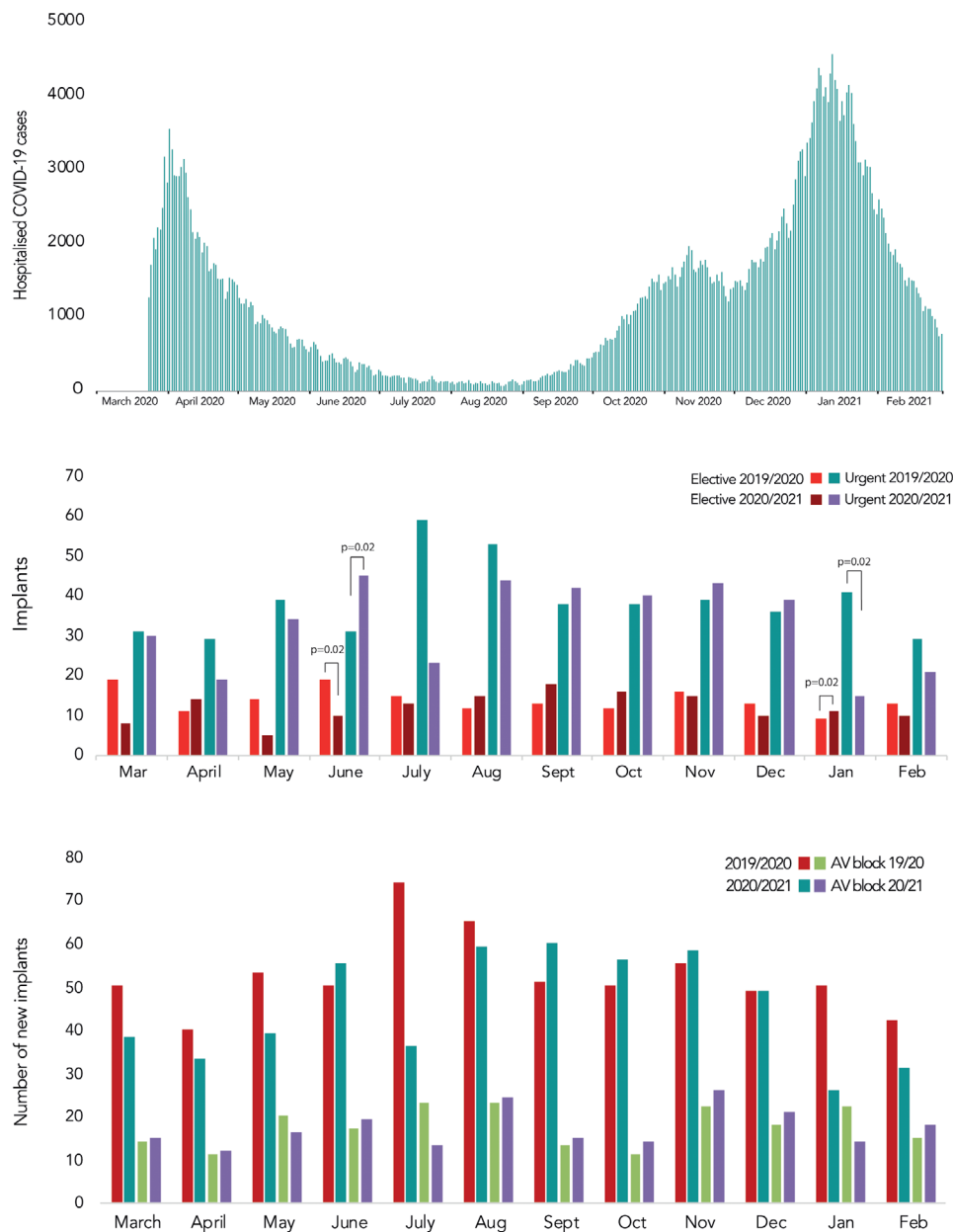
## 3 | RESULTS

Over the study period, a total of 3846 patients were hospitalized with the COVID-19 infection across the two institutions. A combined 540 new pacemaker implants took place of which 38.3% were required for high-degree AV block. This represented a slight reduction in novel implants from the same period a year earlier when a total of 629 new implants were recorded at the two sites of which 33.2% were for high-degree AV block (Figure 2). There was no significant difference in the number of pacemaker implants for high-degree AV block over the two periods ( $p = .069$ ). A significantly higher number of urgent pacemaker implants were performed in June 2020, than a year earlier (45 vs. 31, respectively,  $p = .02$ ), while in January 2021 there was a notable decline in this number comparatively to January 2020 (15 vs. 41, respectively,  $p = .02$ ); all the other months had a statistically similar number of urgent pacemaker implants over the two periods (Figure 2).

Only six patients were identified who had clinically-important bradycardia within 28 days after first testing positive for COVID-19 (Table 1). These patients were all male, with an average age of  $82.7 \pm 9$  years; all underwent permanent pacemaker implantation. Hypertension was present in all six patients, atrial fibrillation in three, type

TABLE 1 Patient summary

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	82	89	83	78	95	69
Gender	M	M	M	M	M	M
Body mass index (kg/m <sup>2</sup> )	38	21	34	26	17	26
Hypertension	Yes	Yes	Yes	Yes	Yes	Yes
Diabetes	Yes	No	Yes	No	No	No
History of ischemic heart disease	Yes	No	No	No	No	No
Pacing indication	AF with complete AV block	Mobitz II	Complete AV block	Complete AV block	Sinus node dysfunction	Sinus node dysfunction
Escape QRS	Broad	Narrow	Narrow	Broad	Narrow	Narrow
QRS duration (ms)	136	90	92	144	98	98
Temporary pacing	No	No	Yes	No	No	No
Ventricular pacing burden at follow-up	94%	95%	100%	70%	2%	13%
Atrial pacing burden	NA	36%	52%	24%	8%	99%
Left ventricular ejection fraction (%)	55-60	55-60	55-60	55-60	55-60	55-60
Hs-Troponin (ng/L)	29	93	10	28	-	27
Potassium	4.9	4.3	3.8	3.6	4.5	3.9
Ph	7.37	-	7.42	7.5	7.43	-
C-reactive protein	24	77	43	45	11	103
AV nodal blocking agent	Bisoprolol 1.25 mg (discontinued)	0	Atenolol 2.5 mg (discontinued)	0	0	0
COVID medication	0	Co-amoxiclav	0	0	0	Azithromycin
Ventilation	0	0	0	0	0	Invasive
Symptoms on admission	Pre-syncope, shortness of breath, cough	Syncope, lethargy	Shortness of breath, pyrexia, cough	Lethargy, dry cough	Syncope, shortness of breath	Difficulty in breathing, cough, pyrexia, unwell
Timing of decision to pace	Day 1	Day 1	Day 2	Day 1	Day 2	Day 58
Pacing mode	VVI(R)	DDD(R)	DDD(R)	DDD(R)	DDD(R)	AAI with mode switch to DDD(R)
Follow-up outcome	Deceased 17-days post-implant	Alive and fully recovered	Deceased 107-days post-implant	Alive and fully recovered	Deceased 21-days post implant	Alive with lung fibrosis following COVID pneumonitis



**FIGURE 2** Bar graph demonstrating the number of new pacemaker implants across the study period (March 2020–February 2021) in comparison to the same period from a year earlier (March 2019–February 2020). There is no apparent excess of acute high-degree atrioventricular (AV) block during the periods of high incidence of COVID-19 despite the two separate peaks of COVID cases. On a month-to-month comparison, there was no statistically significant difference in the prevalence of high-degree AV block during the pandemic and in the same months a year earlier. (*statistically non-significant unless stated*) [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

2 diabetes in two patients and ischemic heart disease in one; two were clinically obese (BMI >30 kg/m<sup>2</sup>) and none were known to have pre-existing cardiac conduction abnormalities.

Bradycardia was due to high-degree AV block in most cases (4/6; 66.7%), the remainder were sinus node dysfunction and one patient had a short episode of bradycardia-induced non-sustained polymorphic ventricular tachycardia (Table 1). Of the high-degree AV block cases, 50% were maintained with a broad QRS escape rhythm; only one patient required temporary pacing as he did not tolerate the brady

arrhythmia. The pacing indication was confirmed within 24–48 h of hospitalization on a 12-lead ECG for the majority of the patients (5/6; 83.3%); one patient who had required invasive ventilation was diagnosed with sinus node dysfunction on day 57. Cardiac function was preserved (left ventricle ejection fraction 55–60%) in all cases and only one patient exhibited an elevated high-sensitivity Troponin I (hs-Tri) level at the time of pacing decision. Only two patients were taking AV nodal blocking pharmacological agents ( $\beta$ -blocker) on admission, which was discontinued on arrival.

### 3.1 | Chronology of infection and bradycardia

Patients one and two (Table 1) were admitted with pre-syncope or syncope associated with the high-degree AV block and the COVID-19 status was subsequently established from the swab performed on admission. Patient three was suffering from difficulty in breathing with third degree AV block and the Sars-Cov-2 infection; due to the severity of his symptoms, he had a temporary pacing system implanted at first which was replaced with the permanent system after 16 days from admission. Patient four was urgently admitted on the behest of the cardiologist as his 24-h Holter monitor in the community demonstrated episodes of high-degree AV block with a polymorphic ventricular tachycardia event (Figure 1); a permanent pacemaker was implanted within 24 h at which point the Sars-Cov-2 status was also confirmed as positive. The decision to pace in all cases was issued within 24-48 h of hospitalization and all episodes of high-degree AV block were confirmed on a 12-lead ECG.

Patient five (table 1) was admitted with syncope and sinus pauses were confirmed on cardiac telemetry; a permanent pacemaker was implanted within 24-h and the Sars-Cov-2 PCR test was positive on the same day. He was discharged without any sequelae. Patient six was admitted severely unwell with COVID-19 requiring emergency mechanical ventilation immediately upon hospitalization. He developed sinus node dysfunction from day 57 of admission with the longest sinus pause of 12 s. The permanent pacemaker was implanted on day 63 and he was discharged after 65 days in hospital.

### 3.2 | Medium-term outcome

Patient one succumbed to the Sars-Cov-2 infection at 17-days of having the pacemaker implant for high-degree AV block and patient three perished following an admission for non-COVID sepsis 107 days after having had the device implant. The pacing interrogation of these two patients revealed that for the period from implant to their death, the pacing burden remained high (94%-100%). The other two patients with high-degree AV block remain well to date, 142 and 344 days after pacemaker implant with 70%-95% ventricular pacing requirement. Patient six, who had sinus node dysfunction, expressed a high atrial pacing burden (99%) on the 6-months pacing interrogation; at present he has significant interstitial lung fibrosis with ongoing shortness of breath secondary to the COVID pneumonitis. The other patient with sinus node dysfunction was not pacing dependent (8% atrial & 2% ventricular) until his death from COVID pneumonia 21 days after pacemaker implantation.

## 4 | DISCUSSIONS

We found no evidence of a surge in AV block attributable to COVID-19; rather, the overall number of new pacemaker implants at our institutes reduced during the first year of the pandemic compared to the

same period a year earlier. The number of pacemaker implants for high-degree AV block showed no significant change on a year-to-year basis ( $p = .069$ ). There were shorter term fluctuations, with a significantly higher number of urgent pacemaker implants occurring in June 2020 ( $p = .02$ ), while this number significantly dropped in January 2021 ( $p = .02$ ). Personal experience suggests that this was related to patient behavior: many patients avoided all healthcare settings when infection was most prevalent,<sup>9</sup> resulting in a catch-up surge in cases of other conditions when concern about COVID waned (Figure 2).

Prior reports have described a transient state of high-degree AV block with the Sars-Cov-2 infection.<sup>6,7</sup> In our series, we describe a small number of cases of high-degree AV block and sinus node dysfunction in patients with COVID-19, all of whom were treated with permanent pacing. Subsequent pacing interrogation confirmed an ongoing high pacing requirement in all patients.

Our strategy contrasts with that described in the series by Dagher et al., in which four cases of high-degree AV block in COVID-19 were managed conservatively, and all reverted to normal AV conduction.<sup>6</sup> There were similarities in the patient cohorts: one required temporary pacing, two patients managed with a broad escape rhythm and one patient had a mildly elevated hs-Tri. Our more interventionist approach to pacing in this group appears to have been vindicated by the high pacing burden confirmed on subsequent device interrogation. All patients have continued to require pacing, indicating that the initial abnormality has persisted. The lack of follow-up data in previously reported cases of COVID-19 associated AV block raises uncertainty regarding the completeness of reversibility.

There has been speculation regarding the mechanism of transient AV block in COVID-19. A systemic inflammatory burden causing injury to the myocytes disrupting intrinsic conduction has been proposed.<sup>6</sup> Viral myocarditis causing local injury to the conduction system has also been suggested,<sup>6</sup> and the presence of the Sars-Cov-2 virus in the myocardium on autopsy has led to the hypothesis of the virus invading myocardial cells directly.<sup>7</sup> Early histological reports from China suggested minimal myocardial infiltration by the Sars-Cov-2 virus<sup>10</sup> while individual case reports have described extensive myocardial inflammation.<sup>11</sup> These phenomena are not evident in our series; only a single patient suffered myocardial involvement as evidenced by a hs-Tri rise and all patients had normal cardiac function.

It is possible that the severe-acute-respiratory-syndrome coronavirus-2 selectively affects the conduction system as seen in other infectious aetiologies of cardiac conduction defect. Lyme carditis is an established cause of reversible AV block, though a proportion of patients require permanent pacing.<sup>12</sup> The key difference between the management of Lyme carditis and COVID-19 associated AV block is the well-established nature of the former. Lyme disease is a familiar infection; the nature of the illness, the natural history and the response to treatment have been observed over decades and are well understood. AV block occurs at the level of the AV compact node and is associated with the host immune response to the spirochete.<sup>13</sup> Antibiotic treatment is proven and the reversibility of Lyme carditis is predictable.<sup>14</sup> In contrast, the

Sars-Cov-2 infection is novel and the full impact of this infection on the heart and its treatment is yet to be determined; the long-term effects are currently unpredictable. The previous severe acute respiratory syndrome (SARS) outbreak is the closest indicator of the long-term course of COVID-19 illness and during that pandemic, bradycardia was uncommon.<sup>15</sup>

It is plausible that the COVID-19 infection has revealed an underlying cardiac conduction tissue anomaly in our patients, rather than causing it. Our cohort was older than that of Dagher et al. and therefore more likely to have had pre-existing conduction tissue fibrosis.<sup>16</sup> The infection may have precipitated an increase in cardiac demand, accelerating the identification of a pre-existing conduction abnormality. It is also possible that our cases represent pure co-incidence: In the past year, COVID-19 has been very common in our region, and clinically significant bradycardia is always common; co-existence of the conditions is inevitable. We also cannot rule out the possibility that COVID-19 infection brought to our attention patients with pre-existing bradycardia who had previously gone undiagnosed. We do not believe that any of the patients described acquired COVID-19 in a healthcare setting due to the clinical bradycardia as the interval from hospital attendance to COVID-19 diagnosis was shorter than the known incubation period in all cases.

The Dagher et al. series included a young patient (42 years of age) with transient Mobitz II block associated with a narrow QRS which resolved quickly. At this young age, the site-of-AV-block may have been proximal to the His bundle and the mechanism vagal, therefore prognostically insignificant.<sup>17</sup> Half of the Dagher et al. cohort had a broad-QRS escape rhythm as in our patients with AV block; we believe that they should have been considered for pacemaker implantation. Experience from other clinical situations is that AV block that is initially thought to have a reversible cause often recurs despite the correction of that cause.<sup>18–20</sup> Transient AV block has been previously described in patients with fibrous conduction tissue and may go on to produce persistent block.<sup>16</sup> AV block is dangerous but easily treatable by pacemaker implantation; omission of this normal treatment of requires a high burden of evidence.

## 5 | LIMITATION

The full long-term effect of COVID-19 on the heart is currently undetermined; long-term follow-up data is required.

## 6 | CONCLUSIONS

Clinically important bradycardia has remained a common problem during the COVID-19 pandemic. COVID-19 has been prevalent in our region in the past year and occurred in association with clinically important bradycardia in a small number of patients. We did not identify any case of transient AV block associated with COVID-19, suggesting that it is an unusual phenomenon.

## ACKNOWLEDGMENTS

Zaki Akhtar has received research funding from Abbott Medical. Mark Gallagher has received research funding from Attune Medical and has acted as a consultant and a paid speaker for Boston Scientific and Cook Medical. Manav Sohail has received a research grant from Abbott Medical. Sumeet Sharma has received educational grants and has acted as a paid speaker for Boston Scientific, BAYER, Abbott medical, Pfizer and Bristol-Myers Squibb.

## DATA AVAILABILITY STATEMENT

Data is on file and available upon reasonable request.

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**How to cite this article:** Akhtar Z, Leung LWM, Kontogiannis C, et al. Prevalence of bradyarrhythmias needing pacing in COVID-19. *Pacing Clin Electrophysiol.* 2021;44:1340–1346  
<https://doi.org/10.1111/pace.14313>.