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Paroxysmal bradyarrhythmias are frequent among heart transplant recipients with unexplained syncope: a study based on implantable loop recorders

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Little is known about the underlying mechanisms of syncope in heart transplant (HT) recipients. Although the graft is typically denervated, neurally mediated reactions have been described in these individuals.[1] Both bradyarrhythmias and tachyarrhythmias may also occur after HT, often as a consequence of acute or chronic rejection.[2] Sudden cardiac death is, indeed, one of the leading modes of death in this population.[3]

We conducted a retrospective study aimed at addressing the diagnostic yield of implantable loop recorders (ILRs) in HT patients who present with syncope of an unknown origin. To the best of our knowledge, this clinical issue has never been investigated before, despite the consistent evidence that supports the use of ILRs in patients with syncope and a native heart.[4]

From January 2006 to December 2016, 22 HT recipients of our programme received an ILR after having experienced one or more episodes of syncope (or repetitive presyncope) of which the origin remained unexplained after routine diagnostic work-up. All patients had a left ventricular ejection fraction ≥40% and no other clinical indication for prophylactic pacemaker or defibrillator implantation.

The mean number of episodes of syncope per patient before ILR implantation was 1.8 ± 1. One patient had presented four episodes, seven patients had presented three episodes, and two patients had presented two episodes.

Devices implanted were Medtronic Reveal Plus® ($n = 8$), Medtronic DX® ($n = 6$), Medtronic XT® ($n = 1$) and Medtronic Linq® ($n = 7$). Baseline clinical characteristics of study subjects before ILR insertion are shown in *Table* 1.

Table 1. Clinical characteristics of patients at the time of implantable loop recorder insertion

Women, *n* (%)	5 (23%)
Age (years)	62 ± 10
Clinical presentation	
Syncope on exertion	9 (41%)
Prodromal symptoms	9 (41%)
Two or more episodes of syncope	10 (45%)
Time elapsed since transplantation (years)	7.6 ± 4.4
Age of the donor (at transplantation) (years)	38 ± 13
Coronary allograft vasculopathy	6 (26%)
Any previous episode of treated graft rejection	7 (32%)
Left ventricular ejection fraction	
≥50%	20 (91%)
40–49%	2 (9%)
Baseline 12-lead electrocardiogram	
Sinus rhythm	22 (100%)
PR interval ≥ 200 ms	2 (9%)
QTc interval ≥ 440 ms	9 (41%)
QRS interval ≥ 120 ms	3 (14%)
Intraventricular conduction abnormalities	6 (27%)
Left anterior fascicular block	3 (14%)
Right bundle branch block	2 (9%)
Right bundle branch block + left anterior fascicular block	1 (5%)

Values are numbers and percentage of total ($n = 22$), or mean ± standard deviation.

Laboratory tests, 12-lead electrocardiogram, transthoracic echocardiogram, and 24 h (or longer) external electrocardiographic monitoring were performed in all patients before ILR insertion. All individuals showed normal sinus rhythm at baseline; only a few minor rhythm abnormalities such as frequent premature ventricular beats (in three patients) and paroxysmal, night-time, type I second-degree atrioventricular block (in one patient) were detected by means of this routine diagnostic work-up.

Coronary angiography was performed in 20 (91%) patients, showing significant (≥50%) epicardial coronary disease in six cases. Endomyocardial biopsy was performed in 15 (68%) patients, with no evidence of significant acute cellular rejection (grade ≥ 2R) or antibody-mediated rejection (grade AMR ≥1). Only one (5%) patient underwent an electrophysiological study, which revealed no significant abnormalities.

Median duration of ILR monitoring was 156 days (range 4–1465 days). Over this period, 11 (50%) patients experienced at least one episode of relapsing syncope and two (9%) patients died suddenly.

The revision of ILR layouts showed clinically relevant bradyarrhythmias in nine patients who had relapsing syncope after ILR implantation—paroxysmal third-degree atrioventricular block in four cases, prolonged sinus arrest in four cases, and slow junctional escape rhythm in one case. Routine trace review also revealed paroxysmal third-degree atrioventricular block in one patient who remained asymptomatic during follow-up. All these 10 (45%) patients underwent permanent pacemaker implantation, with no further recurrences of syncope after this intervention.

No clinically relevant arrhythmia was detected in the remaining two (9%) patients who presented relapsing syncope during ILR monitoring; final presumed diagnosis in both cases was neurally mediated syncope. Overall, the cause of syncope was diagnosed on the basis of ILR monitoring in 12 (55%) patients, with a median time to diagnosis of 92 days (range 4–1078 days).

Two (9%) patients died suddenly during ILR monitoring, but, unfortunately, ILR layouts could not be reviewed in these individuals. Before ILR insertion, both patients had normal sinus rhythm, narrow QRS complex, normal PR and QTc intervals, and preserved left ventricular ejection fraction; only one of them had a previous diagnosis of coronary allograft vasculopathy.

In conclusion, this small, retrospective study supports the clinical usefulness of ILR monitoring for the evaluation of unexplained syncope in HT recipients. Interestingly, clinically significant bradyarrhythmias leading to permanent pacemaker implantation were detected by means of ILR monitoring in 45% of patients in our cohort; the overall yield of this strategy to diagnose the cause of syncope was 55%, with a median time to diagnosis of 92 days. Unfortunately, 2 out of 22 (9%) patients who received the device experienced unexplained sudden death during ILR monitoring.

Larger prospective studies are required to confirm our findings. In the absence of specific recommendations, the clinical management of syncope and the prevention of sudden cardiac death in HT recipients require an individualized approach.

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