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Electrocardiography

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Incidence and Prognostic Value of Electrocardiographic Abnormalities after Heart Transplantation

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Summary

Background: The improvement of surgical techniques and the use of immunosuppressive drugs within the past 15 years has made heart transplantation an increasingly performed procedure and an accepted treatment for end-stage cardiac failure.

Hypothesis: The aim of this study was to describe the changes of the 12-lead electrocardiogram (ECG) after heart transplantation and to determine their prognostic value on complications such as rejection or graft coronary artery disease during follow-up.

Methods: The ECGs of 62 consecutive patients were analyzed for 5 years at follow-up periods of 1, 2, 3, 6 months and yearly after transplantation.

Results: The most prevalent abnormality was the presence of complete or incomplete right bundle-branch block (RBBB). New RBBB appeared in 69% (43/62) of the patients, mainly during the first month (21/43). There was no left bundle-branch block. We detected nine episodes of supraventricular arrhythmias: one atrial fibrillation, six atrial flutter, one junctional tachycardia, one orthodromic tachycardia on a Wolff-Parkinson-White syndrome; all appearing during the first 3 months. Three of the six episodes of atrial flutter occurred during an episode of acute rejection. There was no relation between RBBB and the gender and age of recipients and donors, nor with the graft ischemic time and the pretransplantation hemodynamic values. Right bundle-branch block was not associated with acute rejection nor with graft coronary artery disease.

Conclusion: The ECG abnormalities after heart transplantation have no predictive value on the long-term evolution. Right bundle-branch block is very frequent and is not associated with adverse prognosis.

Key words: heart transplantation, electrocardiography, conduction delay, bundle-branch block, arrhythmia

Introduction

The improvement of surgical techniques and the use of immunosuppressive drugs within the past 15 years has made heart transplantation an increasingly performed procedure and an accepted treatment for end-stage cardiac failure.[1–3] The development of this therapy is also due to better selection criteria of potential recipients and donors and a careful postoperative management.[4–6] Regular follow-up is necessary to assess the cardiac function and to detect complications such as rejection, infection, or graft coronary artery disease.

The surgical technique and the denervated state of cardiac allografts result in new electrophysiologic properties.[7, 8] Electrocardiographic (ECG) abnormalities, mainly rhythm disturbances and conduction abnormalities, are often noted after orthotopic heart transplantation. Most of the publications so far focus on the immediate postoperative period and the early months, and there are only a few studies describing the late evolution of the 12-lead ECG. We reviewed our population of heart transplant recipients and identified the transient or permanent changes of the ECG at the early period and during a 5-year follow-up. We then examined the association of ECG changes with post-transplant complications.

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Methods

Between January 1986 and April 1994, 62 consecutive patients (54 men and 8 women) underwent orthotopic heart transplantation and were regularly followed in our hospital. We excluded one patient because of early death (48 h after surgery).

Electrocardiographic Criteria

Twelve-lead ECGs were obtained in all patients. All ECGs were analyzed for PR, QRS, QT intervals (ms), QRS axis (degrees), rate (beats/min), rhythm, conduction delays, and repolarization abnormalities, if present. The recipient atrial activity ("recipient P wave") was systematically looked for. Standard definitions for ECG evaluation were used,[9] and the following criteria were established at the beginning of our study. Complete right bundle-branch block (cRBBB) was defined as a QRS width of ≥ 120 ms, an rSR' pattern in lead V_1 (or a wide R pattern in V_1) and a wide S wave in leads I and V_6. Incomplete RBBB (iRBBB) was defined with the same patterns as cRBBB but with a QRS interval > 80 and < 120 ms. Left bundle-branch block (LBBB) was defined as a QRS duration ≥ 120 ms, a pure wide R wave in leads I and V_6, and a broad S wave in V_1. Nonspecific ventricular conduction delay was diagnosed with a QRS ≥ 120 ms without the specific RSR' patterns of right or left bundle-branch block. Axis deviation required a QRS axis < −30° (left axis deviation) or >+90° (right axis deviation). Normal sinus rhythm was diagnosed in the presence of P waves, with the P axis being positive in leads I, II, and aVF, and a heart rate ≥ 60 and ≤ 100 beats/min. Repolarization changes were classified as "specific" and "nonspecific." Specific modifications were characterized by ST segment alterations ≥ 1 mm and/or the presence of Q waves. Nonspecific modifications included T-wave flattening or inversion and ST changes secondary to bundle-branch block.

Transient rhythm or conduction disturbances occurring during or just after a cardiac invasive procedure (catheterization or endomyocardial biopsy) were excluded; they lasted only a few hours or days at most.

We analyzed and compared the standard 12-lead ECGs for 5 years at follow-up periods of 1, 2, 3, 6 months and yearly after transplantation.

Statistical Analysis

All data are expressed as mean with standard deviation (SD). Comparisons between groups were made using paired or unpaired data and Student's *t*-test. A p value of < 0.05 was considered significant.

Results

General Characteristics of the Recipients and Donors

There were 54 men (87%) and 8 women (13%), with a mean age at transplantation of 48 ± 12 for the recipients and 33 ± 13 for the donors. Idiopathic dilated cardiomyopathy was the main preoperative diagnosis (50%) followed by ischemic heart disease (31%). The mean ischemic time was 100.6 ± 39.3 min. Eight of the 62 patients (13%) died in a mean time of 14 months after transplantation (range 2–26 months). The cause of death was infection (three patients), acute rejection (two patients), coronary artery disease (one patient with acute infarct, one patient with sudden death and known significant coronary lesions), neoplasia (one patient), and trauma (one patient).

All patients were on triple immunosuppressive regimen (cyclosporine A 4 mg/kg/day, azathioprine 2 mg/kg/day, steroids) immediately after transplantation. Steroids were discontinued in almost all patients during the first year, and azathioprine during the second year.

Serial Electrocardiographic Analysis

The ECG characteristics and the prevalence of abnormal findings at selected follow-up periods after transplantation are summarized in Tables I and II.

Electrocardiographic intervals: The PR and rate-corrected QT intervals were normal and there was no significant change over time. The average QRS interval was prolonged throughout follow-up and increased from 87 ± 13 ms at 1 month to 102 ± 21 ms at 5 years. Mean heart rate increased over time (85 ± 15 beats/min at 1 month vs. 95 ± 12 at 2 years). P waves of different morphology and dissociated from the QRS complexes, representing the activity of the remaining part of the recipient

TABLE I Electrocardiographic characteristics after transplantation

	1 Month (n = 62)	2 Months (n = 62)	3 Months (n = 56)	6 Months (n = 55)	1 Year (n = 44)	2 Years (n = 31)	3 Years (n = 22)	4 Years (n = 17)	5 Years (n = 13)
PR interval (ms)	140 (20)	139 (22)	138 (18)	142 (22)	144 (20)	141 (22)	141 (23)	143 (24)	145 (23)
QRS interval (ms)	87 (13)	91 (18)	89 (15)	93 (18)	95 (21)	95 (20)	98 (19)	99 (19)	102 (21)
QT interval (ms)	357 (34)	354 (27)	349 (26)	348 (25)	354 (28)	346 (26)	346 (24)	349 (21)	346 (22)
QRS axis (degrees)	41 (43)	40 (43)	34 (43)	42 (44)	38 (48)	42 (47)	52 (44)	58 (38)	51 (43)
RR interval (ms)	727 (127)	682 (98)	661 (72)	644 (67)	660 (84)	643 (87)	642 (65)	640 (68)	646 (67)
Heart rate (beats/min)	85 (15)	90 (13)	92 (10)	94 (10)	92 (12)	95 (12)	94 (9)	95 (11)	94 (10)

All values are mean (standard deviation).

TABLE II Prevalence of electrocardiographic abnormalities after heart transplantation

	1 Month (n = 62)	2 Months (n = 62)	3 Months (n = 56)	6 Months (n = 55)	1 Year (n = 44)	2 Years (n = 31)	3 Years (n = 22)	4 Years (n = 17)	5 Years (n = 13)
Sinus rhythm (%)	59 (95)	61 (98)	54 (96)	55 (100)	44 (100)	30 (97)	22 (100)	17 (100)	13 (100)
Recipient P wave (%)	42 (68)	41 (66)	32 (57)	26 (47)	17 (39)	13 (42)	7 (32)	6 (35)	3 (23)
QRS axis deviation (%)	10 (16)	8 (13)	4 (7)	9 (16)	7 (16)	5 (16)	4 (18)	3 (18)	2 (15)
Atrioventricular block (%)	0	0	0	1 (2)[a]	0	0	0	0	0
Ventricular conduction delay									
Nonspecific (%)	1 (2)	1 (2)	1 (2)	1 (2)	0	0	0	0	0
iRBBB (%)	18 (29)	14 (23)	16 (29)	17 (31)	12 (27)	10 (32)	10 (45)	9 (53)	4 (31)
cRBBB (%)	3 (5)	5 (8)	5 (9)	5 (9)	7 (16)	5 (16)	3 (14)	2 (12)	4 (31)
New iRBBB	18	2	5	3	1	3	1	1	0
New cRBBB	3	1	2	1	2	0	0	0	0
Rhythm disturbances									
Atrial fibrillation (%)	1 (2)	0	0	0	0	0	0	0	0
Atrial flutter (%)	2 (3)	1 (2)	1 (2)	0	1 (2)	1 (3)	0	0	0
Ventricular (%)	0	0	0	0	0	0	0	0	0
Others (%)	0	0	1 (2)[b]	0	0	0	0	0	0
Repolarization changes									
Nonspecific (%)	44 (71)	46 (74)	32 (57)	32 (58)	27 (61)	19 (61)	13 (59)	9 (53)	7 (54)
Specific (%)	9 (14)	4 (6)	3 (5)	1 (2)	1 (2)	0	0	0	0

[a] First degree AV block.

[b] Junctional rhythm.

Abbreviations: cRBBB = complete right bundle-branch block, iRBBB = incomplete right bundle-branch block, AV = atrioventricular.

auricle after surgery, can be seen in most of the ECGs. Their rate is slower than that of the donor. The recipient P wave was evident in 41 patients (68%) at 1 month, and in 23% of our patients it was still found at 5 years.

Rhythm: At the first month of follow-up, 95% of the patients were in normal sinus rhythm. Except for the immediate postoperative period, there was only one episode of transitory atrioventricular block (first-degree AV block) occurring at 6 months, and one patient needed a permanent pacemaker for recurrent episodes of symptomatic bradycardia and sinus pauses. The arrhythmias observed were atrial fibrillation (one patient), atrial flutter (six patients), and junctional rhythm (one patient). They mainly occurred during the first 3 months after transplantation. However, we noted two episodes of atrial flutter after 1 year follow-up: the first was diagnosed during an acute rejection and the second was not associated with rejection. These supraventricular tachyarrhythmias were treated either with drugs or by overdrive pacing, and there was no recurrence in the same patient. One of our patients presented with paroxysmal episodes of symptomatic supraventricular tachycardia 1 month after surgery.

The 12-lead ECG at that time showed the typical pattern of a Wolff-Parkinson-White syndrome, and we successfully treated the patient with flecainide. This case was detailed in a previous report.[10]

We found no significant ventricular arrhythmia.

Intraventricular conduction: Ventricular conduction delays, mainly complete or incomplete RBBB associated or not with hemiblocks, were a frequent finding throughout the follow-up period. There was no LBBB. The conduction delays were mostly permanent, but we noted transient episodes of RBBB lasting from less than a month to a maximum of 3 months. Twenty-one cases of RBBB were observed at 1 month follow-up (18 iRBBB and 3 cRBBB). Their incidence decreased over time: RBBB (complete or incomplete) newly appeared in seven patients at 3 months, in three patients at 1 year, and in only one patient at 3 years follow-up. Among all the RBBB occurring during the first 3 months, 39% (12/31) were transitory. However, in 50% (6/12) of the patients of this latter group, RBBB reappeared months or even years later and persisted.

Repolarization: The prevalence of repolarization modifications was high initially (at 1 month, 71% of nonspecific changes with T-wave flattening or inversion and 15% of specific changes with ST depression) and decreased progressively. However, mild, nonspecific repolarization changes were found throughout follow-up in over 50% of our population. One patient presented with a silent anterior myocardial infarct with typical ECG criteria (Q wave and ST elevation) 7 months after transplantation.

Discussion

This study documents the main intermittent and long-term persisting ECG changes after heart transplantation.

The serial ECG analysis showed predominately sinus rhythm without significant changes in the PR and rate-corrected QT interval. The accelerated resting heart rate, and consequently the shortened QT, reflects the denervated state of the

TABLE III New right bundle-branch block 1 month after transplantation

	Complete or incomplete RBBB (n = 21)	Without (n = 41)
Recipient's age (years)	49.6 (12.5)	47.7 (12.1)
Donor's age (years)	33.9 (14.4)	33.1 (12.0)
Graft ischemic time (min)	101.3 (43.4)	98.5 (35.5)
mean PAP (mmHg)[a]	28.8 (13.6)	30.3 (11.8)

All values are mean (standard deviation).

[a] Preoperative measurement.

Abbreviations: RBBB = right bundle-branch block, PAP = pulmonary artery pressure.

transplanted heart.[11, 12] The prolonged QRS interval throughout the follow-up, even more marked later, is due to the high prevalence of RBBB.

Bradyarrhythmia and AV blocks have been reported to be common in the early postoperative period.[13] They are mainly secondary to sinus node dysfunction, often transitory, sometimes needing pacing.[14] This trend declines later on, permanent pacing being rarely needed.[15] We found one patient with transitory first-degree AV block, and only one of our patients needed a permanent pacemaker for recurrent symptomatic sinusal pauses.

In accordance with previous publications, tachyarrhythmias occurred during the first months after transplantation.[16–19] They were all supraventricular, with atrial flutter being the most frequent. Some authors found no influence of rejection in the prevalence of arrhythmias.[16, 17] They related these rhythm disturbances to prolonged mean graft ischemic time, surgical trauma, preoperative antiarrhythmic drugs, heart denervation, and hypersensitivity to cathecolamines.[16, 17]

However, in a study by Scott *et al.*, 69% of the episodes of atrial flutter were associated with acute rejection.[19] Our results also suggest a relation between acute rejection and atrial arrhythmias. Among the six cases of flutter that we observed, three were related to severe acute rejection, confirmed by endomyocardial biopsy. One explanation may be that the inflammatory process in the myocardium during rejection causes conduction disturbances resulting in reentrant arrhythmogenic circuits.

There were no significant ventricular arrhythmias in our survey. Some authors reported them to occur mainly in the immediate postoperative period,[15–17] but others found them to be unrelated to the time since surgery.[20] Ventricular arrythmias are also associated with graft coronary artery disease.[18, 20] Nonetheless, we may have underestimated the frequency of transitory arrhythmias, analyzing single ECGs rather than continuous recordings.

As previously reported, we observed a high prevalence of RBBB.[21–25] This finding was manifest as early as 1 month after surgery and persisted during follow-up. We did not analyze the immediate postoperative period, but right ventricular conduction defects tend to be present already in the first days after transplantation according to different studies.[24, 25] Right bundle-branch block had been described after cardiac surgery (bypass or correction of congenital defects), where it seemed to be related to surgical and thermal injury.[26, 27] The cause of RBBB after cardiac transplantation is subject to controversy. Most investigators relate it to the position of a new heart (posterior rotation on its long axis) resulting from the surgical technique, as well as to some degree to initial right ventricular dysfunction.[21, 22, 28–32] As in our series, no relation with gender, age, and weight of recipients and donors, or with the pretransplantation hemodynamic measurements (Table III) has been established. Graft ischemic time has not been described to influence the incidence of RBBB; however, according to a recent study by Leonelli *et al.*, it would influence the persistence of these conduction delays after the immediate postoperative period and even the degree of their severity.[25] Right bundle-branch block was not associated with acute rejection nor with significant graft coronary artery disease in our study, and has not been correlated with any reports.

Conclusion

Right bundle-branch block is the most frequent ECG abnormality found in the early as well as in the late follow-up periods in orthotopic heart transplant recipients. Except for the immediate postoperative period, no adverse prognosis has been reported so far to be associated with this finding. On the whole, there are only few ECG abnormalities after heart transplantation, and most of these are of little clinical significance.

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