Predictors of Complete Heart Block After Transcoronary Ablation of Septal Hypertrophy
Results of a Prospective Electrophysiological Investigation in 172 Patients With Hypertrophic Obstructive Cardiomyopathy

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Objectives
This study analyzed changes in intracardiac conduction during transcoronary ablation of septal hypertrophy (TASH) to identify predictors for pacemaker dependency after TASH.

Background
Transcoronary ablation of septal hypertrophy is an accepted therapeutic option in hypertrophic obstructive cardiomyopathy (HOCM). However, atrioventricular conduction disorders, requiring permanent pacemaker implantation, remain a major adverse effect.

Methods
This study measured changes in intracardiac conduction in 172 consecutive patients during TASH by simultaneously recording electrophysiological parameters and correlated these parameters with the occurrence of complete heart block during continuous electrocardiographic monitoring for 8 days.

Results
Intraprocedural complete heart block occurred in 36 patients (20.1%) and was associated with a pre-existing bundle branch block (p = 0.010) or advanced age (p = 0.023). All patients with delayed complete heart block during follow-up (n = 15, 8.7%), occurring 1 to 6 days after TASH, showed lack of retrograde atrioventricular nodal conduction after TASH (p = 0.018). None of the patients with intact retrograde conduction after TASH developed delayed complete heart block. Further risk factors for delayed block were advanced age, intraprocedural complete heart block, and prolonged QRS duration before or after TASH (p < 0.05 for all). Permanent pacemaker implantation was performed in 20 patients.

Conclusions
Measurement of intracardiac conduction during TASH improves the safety of the procedure by enabling identification of patients who are at risk of complete heart block after TASH. The duration of prophylactic temporary pacemaker backup should be prolonged up to day 6 after TASH in patients at increased risk (patients with retrograde atrioventricular block and at least 1 additional risk factor). (J Am Coll Cardiol 2007;49:2356–63)

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Methods

Patients. We enrolled 172 consecutive patients with HOCM in the study. All patients gave their written consent to the study. Patient characteristics are shown in Table 1. All patients suffered from severe symptoms caused by HOCM despite oral medication.

TASH procedure. We used titrated coronary flow and gradient-adapted ethanol injection aiming for at least 50% gradient reduction at rest and after provocation with programmed extrasystolic right ventricular stimulation (1,5–11). Continuous monitoring of the left ventricular outflow tract gradient was performed by a pigtail catheter placed in the apex of the left ventricle and a coronary catheter placed in the ascending aorta. Programmed stimulation with 1 extrasystole at 380 ms (every 7th beat) was used for gradient provocation. In addition, temporary pacemaker backup is recommended during and after the session. Therefore, 2 pacemaker catheters were inserted in the right ventricle (1 for pacemaker backup and 1 for gradient provocation). Before injecting ethanol, a selective angiography of the septal coronary branch was performed to visualize the target area in the septum, to exclude backflow in the left anterior descending artery, and to estimate the efficacy of the selected vessel regarding gradient reduction (ischemic effect of balloon occlusion and contrast medium). A target vessel was selected for ethanol injection, in case the selective contrast medium injection led to a significant reduction of obstruction (at least 25% gradient reduction). Intravenous sedation with 5.2 ± 2 mg diazepam (maximum 20 mg) and 25.3 ± 5 mg pethidine (maximum 50 mg) and body weight-adjusted intravenous injections of heparin (100 IU/kg) were administered at the beginning of the therapeutic session.

Intracardiac recordings. Intracardiac recordings were obtained by using the 2 electrophysiology (EP) catheters that are routinely recommended during TASH in our center (2). All parameters were measured at baseline and at the end of the session. Intravenous sedation was administered before the first measurement. A 5-F EP bipolar catheter was placed in the right ventricular apex via the femoral route. A second quadripolar catheter was then placed in the right atrium. Incremental atrial and ventricular pacing was performed by using either the atrial or the ventricular catheter beginning with a cycle length of 1,000 ms to determine the beat-to-beat interval with atrioventricular (AV) nodal Wenckebach block (antegrade and retrograde). Retrograde AV nodal block was defined as block of conduction to the atrium at a cycle length 10 ms shorter than the intrinsic rate. The atrial catheter was then used for His bundle recordings. The atrium-to-proximal-His (AH) and the distal-His-to-ventricle (HV) intervals were measured at baseline and at the end of the session. The AH interval was defined as the time interval between the atrial and the proximal His potential in the His bundle electrogram and the earliest onset of the R-wave in the surface electrogram. During the therapeutic session, the atrial catheter was moved to the ventricle for gradient provocation (see TASH procedure).

Surface ECG criteria. The PR interval and the QRS interval were measured at baseline and at the end of the session. A QRS interval prolongation of at least 120 ms was defined as bundle branch block.

Continuous ECG monitoring. After the procedure, all patients were supervised in the intensive care unit for 24 h with a temporary pacemaker lead in the right ventricle. Continuous telemetric monitoring was extended up to day 8 in all patients. Two patients with a primary preventive implantable defibrillator before TASH received telemetric monitoring for 24 h only. In these patients, detection of complete heart block was performed by interrogation of the device after 8 days.

Definition of complete heart block. Complete heart block was defined as third-degree AV block of at least 10 s duration. Intraprocedural third-degree AV block was defined as complete heart block occurring during the TASH procedure, and delayed third-degree AV block was defined as complete heart block observed after the intervention (up to day 8).

Statistics. Commercial software (SPSS version 10, SPSS Inc., Chicago, Illinois) was used for statistical analysis. The association between the occurrence of complete heart block and the presence of conduction delay was tested using the Student t test for continuous variables with normal distribution or the Mann–Whitney U test for continuous variables without normal distribution. The association between the occurrence of complete heart block and not continuous variables was tested using the chi-square test. Parameters that were significantly correlated with complete heart block were entered stepwise in one multivariate logistic regression model to analyze the predictive power of each parameter. Values are expressed by the mean ± SD. Values of p < 0.05 were considered statistically significant.

Results

TASH procedure. The TASH procedure was successfully performed in 169 of the 172 patients (success rate 98.2%; 0.90 ± 0.3 ml ethanol was injected in 1 or 2 side branches of the most proximal septal perforator of the left anterior descending coronary artery, leading to a significant reduction of the intraventricular gradients at rest and after provocation (p = 0.0001) (Table 1). No patient died during the hospital stay. Among the patients with ineffective treatment (gradient reduction <50% at rest or after provocation despite ethanol injection), 2 patients underwent...
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<th>Patient Characteristics and Electrophysiological Findings of the Whole Study Population and of Patients With or Without Complete Heart Block</th>
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<tr>
<td><strong>Table 1</strong> Patient Characteristics and Electrophysiological Findings of the Whole Study Population and of Patients With or Without Complete Heart Block</td>
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<tr>
<td><strong>Number of patients</strong></td>
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<td>------------------------</td>
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<tr>
<td>Age (yrs)</td>
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<tr>
<td>LV outflow gradient, mean mm Hg</td>
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<tr>
<td>After TASH at rest (mm Hg) (provocation†)</td>
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<tr>
<td>Maximum creatine kinase activity after TASH (U/l)</td>
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<td>Amount of ethanol, ml</td>
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<td>Median (interquartile 25th–75th)</td>
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<tr>
<td>Ineffective TASH, n (%)</td>
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<td>Pacemaker implantation after TASH, n (%)</td>
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<td>Bundle branch block before TASH, n (%)</td>
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<td>Bundle branch block after TASH, n (%)</td>
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<td>AV nodal Wenckebach point before TASH (after TASH), ms</td>
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<td>Retrograde block before TASH, n (%)</td>
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<td>Retrograde block after TASH, n (%)</td>
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<td>Heart rate at baseline (after TASH), beats/min</td>
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<td>Intraprocedural complete heart block, n (%)</td>
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<td>PR interval before TASH (after TASH), ms</td>
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<td>QRS interval before TASH (after TASH), ms</td>
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<td>AH interval before TASH (after TASH), ms</td>
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<td>Median (interquartile 25th–75th)</td>
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Values are mean ± SD or n (%). *p < 0.05. †Provocation = postextrasystolic gradient. ‡p < 0.07.

AH = atrium-to-proximal-His; AV = atrioventricular; HV = distal-His-to-ventricle; LV = left ventricular; TASH = transcoronary ablation of septal hypertrophy.
surgical myectomy and 1 underwent dual-chamber pacing. In 11 patients (6.3%), the TASH procedure was a repeat intervention because of ineffective or only partially effective treatment results at 6-month follow-up.

**Influence of TASH on intracardiac conduction.** Various patterns of conduction disorders during the TASH procedure were noticed. Overall significant prolongation of all measured parameters was observed (Fig. 1): QRS interval was the parameter with the most pronounced change (23% prolongation), followed by antegrade AV nodal Wenckebach point (22% prolongation), AH interval (15% prolongation), HV interval (15% prolongation), and PR interval (7% prolongation). The percentage of patients with bundle branch block was 54% after TASH (baseline 11%), 42% with right and 12% with left bundle branch block (Fig. 2). Lack of retrograde AV nodal conduction was present in 60 patients (34%) at baseline and in 96 patients (56%) after TASH (Fig. 1). No patient with pre-existing retrograde AV block showed recovery of VA conduction after ethanol ablation.

**Complete heart block.** Intraprocedural complete heart block occurred in 36 patients (21%). In 15 of 36 patients, we were able to perform continuous recording of the His bundle ECG during the onset of complete heart block showing intra-His or infra-His block in 14 of 15 patients (Fig. 3). In only 1 patient, we observed a supra-His block during the onset of third-degree AV block. The duration of intraprocedural complete heart block varied from 10 s to 3 h. Delayed complete heart block occurred in 15 patients (8.7%) at a mean time of 74.5 ± 38.4 h (range 1 to 6 days) after TASH (Fig. 4). The duration of delayed complete heart block varied from 10 s to 4 h (mean 5.6 ± 3 min). Of the 15 patients with delayed complete heart block, 13 had recurrent episodes (mean 3.2 ± 1). All patients with delayed complete heart block received permanent dual-chamber pacemaker implantation. In 5 patients, pacemaker implantation was performed after persistent intraprocedural complete heart block for more than 2 h after TASH.

**Association between complete heart block and conduction disturbances. INTRAPROCEDURAL COMPLETE HEART BLOCK.** In patients with intraprocedural complete heart block, we measured higher levels in most of the parameters compared with patients with unimpaired AV nodal conduction, however, not in the maximal creatine kinase activity values after TASH and not in the average amount of ethanol (Table 1).

Patients with intraprocedural complete heart block were significantly older (62.5 years vs. 55.9 years, p = 0.025) and
had a prolonged QRS interval before TASH (117.7 ms vs. 104.9 ms, \( p = 0.017 \)). In addition, there was a trend toward a more prolonged HV interval (50.7 ms vs. 47.2 ms, \( p = 0.056 \)). At the end of the session, the patients with third-degree heart block during the procedure showed a significant prolongation of the PR interval (217.4 ms vs. 192.1 ms, \( p = 0.060 \)), QRS interval (141.9 ms vs. 128.2 ms, \( p = 0.026 \)), and HV interval (70.0 ms vs. 53.8 ms, \( p = 0.001 \)).

A pre-existing left bundle branch block was associated with the occurrence of intraprocedural complete heart block (\( p = 0.013 \)) as well as a pre-existing right bundle branch block (\( p = 0.044 \)). Positive and negative predictive values and the sensitivity and specificity of the parameters regarding the risk of intraprocedural third-degree AV block are shown in Table 2. Positive predictive values of the parameters, which were associated with intraprocedural complete heart block, were low, but negative predictive values were \( >80\% \).

### DELAYED COMPLETE HEART BLOCK.

Patients who experienced delayed complete heart block were significantly older compared with patients without complete heart block (66.3 years vs. 55.5 years, \( p = 0.013 \)). The QRS duration was significantly prolonged at baseline (119.6 ms vs. 106.3 ms, \( p = 0.014 \)) and after TASH (146.2 ms vs. 129.8 ms, \( p = 0.029 \)) in this patient group. Retrograde AV nodal block after TASH (assessed by incremental ventricular pacing) was noticeable in all patients with delayed complete heart block, but in only 56% of the subset without complete heart block during follow-up (\( p = 0.003 \)). Patients with intact retrograde conduction at baseline and retrograde block after TASH had no higher risk of pacemaker dependency compared with patients with a pre-existing retrograde AV block.

The percentage of patients with intraprocedural complete

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**Table 2**

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<th>Parameter</th>
<th>Intraprocedural Complete Heart Block</th>
<th>Delayed Complete Heart Block</th>
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| Intraprocedural complete heart block | Sensitivity 47  
Specitivity 76  
Positive predictive value 19  
Negative predictive value 93 |
| Retrograde AV nodal block after TASH | Sensitivity 100 | Specitivity 31  
Positive predictive value 16  
Negative predictive value 100 |
| Age \( >58\) yrs                   | Sensitivity 65  
Specitivity 51  
Positive predictive value 29  
Negative predictive value 83 |
| QRS \( >120\) ms before TASH      | Sensitivity 36  
Specitivity 82  
Positive predictive value 39  
Negative predictive value 82 |
| QRS \( >120\) ms after TASH        | Sensitivity 53  
Specitivity 40  
Positive predictive value 23  
Negative predictive value 88 |

Abbreviations as in Table 1.
heart block was significantly higher in the group with delayed block (47%) compared with the patient group without delayed block (18%, \( p = 0.023 \)). In the subset of patients with delayed complete heart block, maximal creatine kinase release after TASH tended to be higher (804 vs. 630 U/l), although this was no statistically significant (Table 1). The amount of ethanol was no different in the subgroups with delayed third-degree AV block or no complete heart block (Table 1). There were no significant correlations between the cycle length of antegrade or retrograde Wenckebach block and delayed complete heart block. Prolongation of the cycle lengths of Wenckebach block (value after minus value before block) did not significantly correlate with complete heart block. Positive and negative predictive values and sensitivity and specificity of the parameters are shown in Table 2. All parameters that were associated with delayed complete heart block were characterized by a low positive and a high negative predictive value. The negative predictive value of retrograde AV nodal block after TASH was 100%. To study the predictive power of the parameters that were significantly associated with delayed total heart block, we performed a logistic regression analysis. After including all 4 parameters in 1 regression model, retrograde AV block after TASH and age had the strongest predictive power (\( p = 0.002 \), odds ratio = 1.059; \( p = 0.040 \), odds ratio = 1.005) regarding the occurrence of delayed complete heart block. The QRS interval after TASH and intraprocedural complete heart block, although significantly correlated with delayed complete heart block, did not improve the predictive power.

None of the patients without any risk factors developed delayed complete heart block during follow-up. Patients with a single risk factor had a 3.5% risk of delayed complete heart block (2 risk factors, 16%; 3 risk factors, 16%; 4 risk factors, 33%). Patients with retrograde AV block after TASH and at least 1 additional risk factor had a 26% risk of complete heart block.

6-month follow-up. MORTALITY. After 6 months, 3 patients had died, resulting in a mortality of 1.7%. One patient died of noncardiac reasons (pulmonary carcinoma), 2 patients experienced sudden cardiac death (i.e., cardiac death mortality 0.6%/year). A 75-year-old woman died suddenly 6 months after TASH. After a successful TASH procedure, retrograde AV block was present and QRS duration increased from 120 ms to 160 ms because of right bundle branch block. She developed delayed complete heart block 3 days after TASH, received a permanent pacemaker on day 4, and left the hospital on day 8. The remaining patient (74 years, female) died suddenly 5 months after an uneventful TASH procedure and hospital stay (QRS prolongation from 115 ms to 125 ms because of ethanol-induced right bundle branch block, no AV nodal conduction disturbances).

PACEMAKER DEPENDENCY IN FOLLOW-UP. We performed pacemaker interrogation in all patients at 6-month follow-up. In 3 patients, we found permanent third-degree AV block after pacemaker inhibition (2 patients received the device after sudden unexpected complete heart block and 1 after persisting intraprocedural complete heart block). According to this, the overall permanent pacemaker dependency after 6 months is 15%. The ventricular pacing rate in patients without permanent complete heart block was 3.1 ± 1.6% at 6-month follow-up; however, the reason for ventricular pacing (sinus bradycardia or third-degree AV block) could not be specified. We are not able to state precisely the rate of temporary pacemaker dependency during follow-up.

Discussion

Various patterns of conduction disturbance after the TASH procedure have been described (2,8–16). Disorders of AV conduction (intraprocedural or delayed complete heart block) are the most frequently observed serious complications after alcohol ablation and lead to permanent pacemaker implantation in 7% to 38% of patients (8–16). The intracardiac recordings obtained in our study during the onset of intraprocedural third-degree AV block provide strong evidence that the site of injury is located distal or inside the bundle of His in most cases. The significant prolongation of the HV and the QRS interval after TASH in the patient group with intraprocedural third-degree AV block supports this hypothesis. Presumably, VA block after TASH also reflected VH block. Although the frequency of intraprocedural complete heart block could be reduced by reducing the amount of ethanol, the risk of delayed complete heart block remains constant (5). A period of telemetric monitoring up to day 8 is recommended after TASH because of the sometimes late and unexpected occurrence of complete heart block (10), which increases procedure costs. Temporary pacemakers are routinely placed at the time of alcohol injection, but there are no widely accepted guidelines for their management after the procedure. The identification of patients who are at high risk for delayed complete heart block after TASH is still an unresolved issue. However, some groups identified QRS duration and/or the presence of left bundle branch block at baseline as a risk factor for the development of pacemaker dependency (8,12–16). Our study indicates that the occurrence of pacemaker dependency is not rare after TASH, even when low amounts of ethanol are used. The pacemaker implantation rate in our study population was 11.6%. For the vast majority (75%), delayed complete heart block was the reason for pacemaker implantation. The proportion of delayed complete heart block after TASH was 8.7% in this series. We previously published a rate of delayed complete heart block of 3.5% in a series of 198 patients (10). Delayed complete heart block was reported in only 2 of 297 patients (0.8%) who were included in the German TASH registry (9). A recent study reported complete heart block in 13 patients (25%) occurring 36 ± 22 h after alcohol ablation in a series of 48 patients (16). The variability of subacute complete heart block reported after TASH may be explained by different definitions of delayed
complete heart block. Asymptomatic complete heart block, especially if remaining for only a few seconds, might be underestimated in centers with a shorter period of telemetric monitoring, resulting in a lower rate of delayed complete heart block. However, the prognostic relevance of a transient complete heart block after TASH remains unclear. On the other hand, intraprocedural differences (ethanol doses, number of vessels ablated, or even the presence of an EP catheter in the His bundle position) among the centers performing the TASH procedure may have influenced the rate of complete heart block.

Permanent pacemaker dependency at 6 months was low in the group of 20 patients with a permanent pacemaker after TASH (3 of 20). Therefore, a watchful waiting strategy in patients with TASH-induced complete heart block seems to be reasonable. However, no data exist regarding temporary pacemaker dependency during follow-up. Those patients might be at high risk of at least syncope unless they are treated with a permanent device. Considering the lack of available data on patients with transient high-degree AV block after TASH and the potential risk for the patient, we believe that all patients with TASH-induced late complete heart block should receive a permanent pacemaker for safety reasons, even if complete heart block is transient.

In our study we identified several risk factors for the occurrence of complete heart block. Pre-existing conduction disorders were associated with a higher risk of intraprocedural complete heart block and conduction disorders after TASH with a higher risk of delayed block. Retrograde AV nodal block after the session and age turned out to be independent risk factors for delayed heart block. A QRS interval prolongation and intraprocedural complete heart block, although associated with a higher risk of delayed complete heart block, did not improve the predictive power. A QRS interval prolongation at baseline and older age were risk factors for the occurrence of an intraprocedural complete heart block. All of these parameters are characterized by high negative predictive values and low positive predictive values. None of the patients with unimpaired retrograde AV nodal conduction after TASH developed pacemaker dependency (negative predictive value 100%). Therefore, the patient group without retrograde AV nodal block after TASH (44%) can be considered to be at very low risk of complete heart block after TASH. Patients without any risk factor (59 patients, 34%) did not develop complete heart block during follow-up in our study collective. Patients with a single risk factor had only a 3.5% risk of delayed complete heart block. On the other hand, patients with retrograde block after TASH and at least 1 additional risk factor (53 patients, 30% of the study population) had a 26% risk of delayed total heart block. Considering the risk associated with complete heart block, prolonged temporary pacemaker backup up to day 6 is recommended in these 30% of the patients after TASH, which means treatment of 53 patients to protect 14 patients from developing delayed total heart block. Only 1 patient with delayed complete heart block would have been missed using this approach.

**Study limitations.** Risk factors for pacemaker dependency were identified from the data obtained in our study. It would be desirable to evaluate these criteria in a prospective multicenter study.

**Conclusions**

Postprocedural continuous telemetric ECG recording for 8 days after TASH disclosed delayed complete heart block in 8.7%. The EP investigation during TASH improves the safety of the procedure by enabling identification of patients who are at high risk of complete heart block. The duration of temporary pacemaker backup should be prolonged up to day 6 after TASH in patients who are at high risk of delayed complete heart block (patients with retrograde AV block and at least 1 additional risk factor). In the absence of risk factors, prolonged temporary pacemaker backup is not necessary.

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