Prevalence, Circumstances, Mechanisms, and Risk Stratification of Sudden Cardiac Death in Unipolar Single-Chamber Ventricular Pacing

Manfred Zehender, MD; Christoph Büchner, MD; Thomas Meinertz, MD; and Hanjörg Just, MD

Background. Permanent cardiac pacing is well established for the improvement of prognosis and quality of life in patients with severe bradycardia. However, sudden cardiac death still remains an unresolved problem, as it occurs in approximately 20–30% of paced patients. This 2-year follow-up study was directed at prospectively assessing prevalence, circumstances, and mechanisms of sudden death in 2,021 permanently paced patients.

Methods and Results. During the observation period, 220 patients (11%) died (mean pacing interval, 50.5 ± 7 months). Lethal cerebrovascular events in 66 of 220 patients (30%) and sudden death in 49 of 220 patients (23%) were the two most frequently reported modes of death. Nonsudden (first year, 20%; subsequent years, 6.9%; p < 0.01) and sudden death mortality rate (4% versus 1.8%, p < 0.05) were highest during the first year. Mortality was unrelated to the patient's activity status at the time of death. Sudden cardiac death occurred more often in male patients (increased risk, 1.7 versus female patients; p < 0.001) and patients younger than 60 years of age (5.2 versus patients older than 60 years, p < 0.001). Patients with severe bradycardia (sudden death rate, 28%), severe atroventricular block (25%), or atrial fibrillation with low ventricular rate (25%) before pacemaker implantation were more likely to suffer from sudden cardiac death than patients with previous syncopal attacks (sudden death rate, 15%) or sick sinus syndrome (17%). The highest incidence of sudden death was observed in patients with bifascicular and trifascicular bundle branch block. In this group, 35% of patients died suddenly during the follow-up period compared with 18% of patients without bundle branch block. In a subsequent study in 90 consecutive patients with various types of bundle branch block, undersensing of up to 13% of ectopic ventricular beats occurred in patients with bifascicular block. Pacing-induced tachyarrhythmias and ventricular fibrillation were documented in 10% of undersensed ectopic ventricular beats as well as in the setting of atrial fibrillation associated with ventricular arrhythmias.

Conclusions. Young age, male sex, and a severely diseased heart indicated by the presence of bifascicular and trifascicular bundle branch block are the strongest predictive clinical parameters for sudden cardiac death, especially in the first year after pacemaker implantation. (Circulation 1992;85:596–605)

Cardiac pacing is well established in the management of patients with severe disorders of impulse formation and transmission in the cardiac conduction system. Prognosis and quality of life are markedly improved in most patients. However, 12–31% of patients suffer sudden and unexpected death months and years after pacemaker implantation. Although meaningful data are missing, sudden death in these patients is frequently considered to be a result of progression of underlying heart disease. Several case reports, however, repeatedly stressed the importance of accidental inhibition of pacing and deleterious interaction of the pacing impulse and sinus rhythm or spontaneous ectopic ventricular beats in the genesis of sudden cardiac death. In the latter cases, torsade de pointes and/or ventricular fibrillation were the rhythms most
often documented during the fatal event.\textsuperscript{29–32,35} Because any pacemaker-related pacing deficits or fatal initiation or aggravation of ventricular tachyarrhythmias reflect potentially preventable mortality, data on the mode and mechanisms of death in pacemaker patients are most important.

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In this study, we prospectively followed 2,021 consecutive, permanently paced patients during a 2-year observation period to assess data on type and mode of death and to study clinical and ECG parameters in predicting the occurrence of sudden cardiac death. Based on this risk stratification, 90 matched patients with and without bundle branch block were subsequently studied by 24-hour Holter monitoring to assess data on potential electrophysiological mechanisms of sudden cardiac death.

**Methods**

**Patients**

Of 4,897 patients with a pacemaker implanted at the University of Freiburg, 2,021 surviving patients were examined annually after entering the study in 1984. All patients in this study were prospectively followed at 3-month intervals for a 2-year period. A total of 249 patients died, and data analysis could be performed in terms of mode of death, time of day, physical activities during the fatal event, prodromi, and whether death was witnessed or attended for 220 patients. In 29 patients, data on death circumstances were incomplete or unconfirmed.

Of the 220 patients for whom death data were complete, 130 patients (59\%) were men and 90 patients (41\%) were women. The mean age was 73.3±7 years. Clinical and ECG parameters had been documented in all patients before pacemaker implantation. Standard ECG criteria were used for the diagnosis of bundle branch and fascicular block, as well as for arrhythmias.\textsuperscript{36,37}

In the case of the patient’s death, relatives and the personal physician had been instructed to contact our pacemaker clinic to provide data on the mode and circumstances of death. In all other patients failing to present at follow-up examinations, the patient or, in the case of death, the house physician as well as the patient’s relatives were personally contacted to collect all relevant data.

In patients with syncope attacks, pacemaker implantation was performed when the patient presented with high-degree atrioventricular (AV) nodal block (type II Mobitz), severe bifascicular and trifascicular bundle branch block, when severe bradyarrhythmia was documented at the time of syncope, or when the patient suffered from symptomatic bradyarrhythmia during Holter monitoring. In all other patients with syncope, we carefully tried to exclude other causes of syncope by means of a neurological checkup of all patients and more extensive techniques such as programmed electrical stimulation or tilt table measurements when required. For implantation, multiprogrammable ventricular-inhibited pacemakers (VVI,M) were used in the vast majority of patients (94\%); dual-chamber pacing (DDD pacing) was used in only 6\% of patients. Overall, in 1,983 patients (98\%), a unipolar stimulation mode was used. Pacemaker implantation was performed by three cardiologists, using the method described previously.\textsuperscript{38} Whenever possible, the cephalic vein was used. If insertion of the catheter proved impossible, however, the external or sometimes the internal jugular vein was used. For atrial insertion, catheter electrodes with a traumatic tip were used, and for ventricular insertion, catheter electrodes with an atraumatic tip were used.

**Definition of Sudden Cardiac Death**

Sudden cardiac death was defined as unexpected death resulting from natural causes occurring within 1 hour of the onset of acute symptoms or within 1 hour of being seen alive without symptoms.\textsuperscript{39,40} Sudden cardiac death was further subcategorized regarding the presence of prodromal symptoms before death and regarding whether death had occurred witnessed or unwitnessed.\textsuperscript{41} The specific circumstances of sudden cardiac death were also investigated as far as possible. To best differentiate between sudden cardiac death and sudden death from other causes (especially cerebrovascular events), all data available were reviewed by two independent investigators. In cases in which there was no consensus or when strong evidence of cardiac origin of sudden death was lacking, patients were not analyzed in this category.

**Holter Monitoring During Permanent Pacing**

The second part of the study was initiated to assess data on potential electrophysiological mechanisms of sudden cardiac death during permanent pacing and was directed at patients with various types of bundle branch block. In this study, 15 consecutive patients presenting for annual follow-up examination and suffering from one of the following types of bundle branch block ECG were studied by 24-hour Holter monitoring: left anterior hemiblock, left bundle branch block, right bundle branch block, right bundle branch block combined with left anterior hemiblock, and right bundle branch block combined with left posterior hemiblock. Fifteen matched patients without bundle branch block were additionally considered. Altogether, 10 patients suffered from atrial fibrillation. None of the 90 patients selected for Holter monitoring suffered from known or clinically suspected pacemaker malfunction at the time of inclusion in the study.

Holter recordings and analyses were performed using an amplitude-modulated Cardiodata MK 4 system. Holter recordings shorter than 18 hours were repeated. All episodes suggestive of pacemaker failure and all episodes of repetitive ventricular arrhythmias were documented with the use of interactive, semiautomatic analysis. Pacemaker problems during Holter monitoring were identified as 1) inadequate sensing: lack of
recognition of intrinsic cardiac electrical activity (as indicated by pacing at an inappropriate time interval); in the case of premature ventricular beats, occurrence of the impulse spike within 19 msec after QRS onset to 100 msec after the end of the TU wave was analyzed separately, 2) noncapture: lack of cardiac depolarization after an appropriately timed pacing spike, and 3) myoinhibition: inappropriate inhibition of the pulse generator by skeletal muscle (indicated by a parallel increase in heart rate and documentation of myopotential spikes by Holter recording).

**Analysis of Data**

A standard $t$ test was used for testing significance of difference between means, and a $\chi^2$ test with Yates' correction was used in frequency data analysis.

**Results**

In the 220 patients who died, death occurred after a mean interval of permanent pacing of 50.5±7 months (range, <1–256 months). Lethal cerebrovascular events in 66 of 220 patients (30%) and sudden cardiac death in 49 of 220 patients (22%) were the most frequently reported causes of death in our patients (Table 1).

**Nonsudden and Sudden Death After Pacemaker Implantation**

The time after pacemaker implantation and the mode of death (sudden or nonsudden) are given in Figure 1 for the 220 patients who died. Annual sudden (4%) and nonsudden death mortality rate (20%) was highest during the first year (mean sudden death rate during subsequent years, 1.8%, $p<0.05$; nonsudden death rate, 6.9%, $p<0.01$; Figure 1). Overall, sudden cardiac death occurred after a longer mean pacing period (62±9 months) compared with nonsudden death (48±7 months, $p<0.05$). However, mean impulse generator lifetime was similar in both groups (38.2±9 versus 32.6±8 months; implanted impulse generators, 1.69 versus 1.40 units). Seventy-six percent of nonsudden death patients and 73% of sudden death patients died after implantation of the first impulse generator.

The causes of death are summarized in Table 1. Lethal cerebrovascular events (30%) and sudden cardiac death (22%) were by far the most common modalities of death during permanent pacing. When sudden cardiac death occurred, 47% of patients died during sedentary activities, including 22% of patients who died during sleep (Table 1). Five patients (10%) died without prodromi while on the toilet. Prodromal symptoms were recognized before the fatal event in only three patients with sudden cardiac death (6%).

**TABLE 1. Causes of Death and Mode of Sudden Death in 220 Patients With Artificial Pacing**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Deaths</th>
<th>Sudden deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>66 (30%)</td>
<td>Sedentary activities 23 (47%)</td>
</tr>
<tr>
<td>Sudden death</td>
<td>49 (22%)</td>
<td>Resting (n=10)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>27 (12%)</td>
<td>Sleeping (n=11)</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>24 (11%)</td>
<td>Eating (n=2)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>9 (4%)</td>
<td>During physical activities 12 (25%)</td>
</tr>
<tr>
<td>In-hospital</td>
<td>7 (3%)</td>
<td>After standing up (n=3)</td>
</tr>
<tr>
<td>Accident</td>
<td>6 (3%)</td>
<td>Walking (n=7)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>4 (2%)</td>
<td>Working (n=2)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>4 (2%)</td>
<td>Specific activities 6 (12%)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>3 (2%)</td>
<td>Coughing (n=1)</td>
</tr>
<tr>
<td>Other diagnosis</td>
<td>9 (4%)</td>
<td>On the toilet (n=5)</td>
</tr>
<tr>
<td>Uncertain diagnosis</td>
<td>12 (5%)</td>
<td>&lt;48 Hours after implantation 3 (6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unknown 5 (10%)</td>
</tr>
</tbody>
</table>

**FIGURE 1. Graph shows time of death after pacemaker implantation for the 220 permanently paced patients who died suddenly (lower curve) or nonsuddenly (upper curve). Numbers along curves give annual mortality rate (percentage) for sudden and nonsudden death.**
Table 2. Clinical Characteristics of Patients With Permanent Cardiac Pacing During a Three-Year Follow-up

<table>
<thead>
<tr>
<th></th>
<th>Surviving (n=1,772)</th>
<th>Total (n=220)</th>
<th>Nonsudden (n=171)</th>
<th>Sudden (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (men:women)</td>
<td>1.13:1</td>
<td>1.47:1</td>
<td>1.28:1</td>
<td>2.27:1</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (years)</td>
<td>71.7</td>
<td>73.9</td>
<td>75.7</td>
<td>68.3</td>
</tr>
<tr>
<td>&lt;60 Years</td>
<td>354 (20%)</td>
<td>18 (8%)</td>
<td>8 (5%)</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>&gt;60-70 Years</td>
<td>248 (14%)</td>
<td>34 (15%)</td>
<td>25 (15%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>&gt;70-80 Years</td>
<td>798 (45%)</td>
<td>92 (42%)</td>
<td>71 (42%)</td>
<td>21 (43%)</td>
</tr>
<tr>
<td>&gt;80 Years</td>
<td>372 (21%)</td>
<td>76 (34%)</td>
<td>67 (39%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>284 (16%)</td>
<td>40 (18%)</td>
<td>32 (19%)</td>
<td>8 (15%)</td>
</tr>
<tr>
<td>Indication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syncope attacks</td>
<td>815 (46%)</td>
<td>97 (44%)</td>
<td>80 (47%)</td>
<td>17 (35%)</td>
</tr>
<tr>
<td>Presyncope attacks</td>
<td>195 (11%)</td>
<td>30 (15%)</td>
<td>24 (14%)</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Severe bradycardia</td>
<td>762 (43%)</td>
<td>93 (42%)</td>
<td>67 (39%)</td>
<td>26 (53%)</td>
</tr>
<tr>
<td>Electrical disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>549 (31%)</td>
<td>59 (27%)</td>
<td>50 (29%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>514 (29%)</td>
<td>64 (29%)</td>
<td>48 (28%)</td>
<td>16 (33%)</td>
</tr>
<tr>
<td>Heart block</td>
<td>709 (40%)</td>
<td>97 (44%)</td>
<td>73 (43%)</td>
<td>24 (49%)</td>
</tr>
<tr>
<td>Impulse generator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VVI,M</td>
<td>1,666 (94%)</td>
<td>212 (96%)</td>
<td>165 (96%)</td>
<td>47 (96%)</td>
</tr>
<tr>
<td>DDD</td>
<td>106 (6%)</td>
<td>4 (2%)</td>
<td>3 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>AAI</td>
<td>4 (2%)</td>
<td>3 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Permanent pacing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range (months)</td>
<td>&lt;1-276</td>
<td>1-256</td>
<td>1-256</td>
<td>1-175</td>
</tr>
<tr>
<td>Mean (months)</td>
<td>49.8</td>
<td>50.5</td>
<td>48.2</td>
<td>61.9</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>52±9%</td>
<td>44±11%</td>
<td>45±14%</td>
<td>41±16%</td>
</tr>
<tr>
<td>Antiarrhythmic therapy</td>
<td>113 (6%)</td>
<td>17 (8%)</td>
<td>11 (6%)</td>
<td>6 (12%)</td>
</tr>
</tbody>
</table>

VVI,M, ventricular inhibited; DDD, dual chamber; AAI, atrial inhibition.
*p<0.05.

Predictive Parameters for Sudden Death During Permanent Pacing

The prognostic impact of clinical variables to predict nonsudden and sudden death is summarized in Table 2. Except for the predominance of male sex and a lower ejection fraction, the overall clinical characteristics between surviving and dead patients were not different.

Clinical variables that were significantly associated with a higher prevalence of sudden cardiac death were male sex (1.7 times higher than female patients) and younger age (5.2 times higher in patients younger than 60 years, Table 2). Regarding the clinical indication for pacemaker implantation, severe bradycardia (sudden death rate, 26 of 93 patients, 28%), atrial fibrillation with low ventricular rate (16 of 64 patients, 25%), or presence of AV block (24 of 97 patients, 25%) were associated with a higher prevalence of sudden cardiac death compared with previous syncope (sudden death rate, 17 of 97 patients, 15%) and sick sinus syndrome (nine of 59 patients, 17%, p<0.01; Table 2).

Presence of certain types of bundle branch block predominantly present in patients with AV block and previous myocardial infarction (Table 3) was a predictive parameter for the occurrence of sudden cardiac death (Figure 2). Twenty-eight percent of all patients with bundle branch block and 35% of patients with bifascicular and trifascicular bundle branch block died suddenly. In all other 138 patients without this finding, the prevalence of sudden death was only 18% (27 patients). In patients with bundle branch block, the inducibility of nonsustained or sustained ventricular tachycardia during programmed electrical stimulation before pacemaker implantation was not different between patients who died suddenly and patients who died nonsuddenly.

Presence of coronary artery disease, indicated by a history of myocardial infarction, an abnormal ejection fraction, and the use of antiarrhythmic therapy was not predictive of sudden cardiac death (Table 2). Because of the small group of patients with DDD pacing (6%), survival analysis was not expected to show any difference from VVI pacing (Table 2).

Holter Monitoring in Patients With Increased Risk of Sudden Death

Based on the above results, we prospectively analyzed selected patients with different types of bundle
branch block in a second study using 24-hour Holter recordings. These patients were considered to have an increased risk of sudden death. All data were compared with a matched control group of patients without bundle branch block.

Only one patient with unipolar sensing suffered an episode of transient pacing inhibition caused by myopotentials during 24-hour Holter monitoring. Spontaneous ventricular arrhythmias were common in patients with bundle branch block (Table 4). Undersensing of ventricular premature beats was observed in up to 13% of ectopic beats and occurred in almost all patients with bifascicular bundle branch block and ectopic ventricular beats (Figure 3). Undersensing was very uncommon in patients without bundle branch block (Table 4). Altogether, 220 undersensed ventricular premature beats were documented. In 21 of 220 (10%) undersensed premature beats, the pacing impulse was effective and/or followed by spontaneous single or repetitive ventricular arrhythmias, being polymorphic in almost all repetitive episodes and lasting for a maximum of 12 beats (Figure 4). In two additional patients with bundle branch block (left bundle branch block, right bundle branch block plus left anterior hemiblock) and atrial fibrillation, occurrence of pacing-induced repetitive ventricular arrhythmias (and even ventricular fibrillation) was seen and found to depend on the presence and severity of the preceding spontaneous ectopic ventricular beats (Figures 5 and 6).

**Discussion**

This prospective 2-year follow-up study provides new insights into the mode and mechanisms of death of permanently paced patients. Cerebral events (30%) and sudden cardiac death (23%) are the two most frequently reported causes of death. Prevalence of sudden death is highest during the first year after pacemaker implantation and is unrelated to the patient’s activities but occurs predominantly in male patients, younger patients, and patients with severely diseased hearts indicated by the presence of severe AV block and fascicular or bundle branch block. In the latter patients, a delayed ventricular activation sequence, especially during late ectopic ventricular beats, may interfere with the pacemaker stimuli and occasionally results in the development of malignant ventricular tachyarrhythmias.

The prognosis of patients with severe impulse formation and conduction disturbances of the heart has been markedly improved by artificial pacing. However, 10–31% of these patients die suddenly during the follow-up, and this proportion of mortality has remained stable over the last 20 years. In this study, which was designed to obtain previously lacking data on prevalence and modalities of sudden death in a larger group of patients, artificial pacing was associated with a 23% prevalence of sudden and unexpected cardiac death. The fatal event occurred with similar prevalence during all types of physical and sedentary activities. Interestingly, 10% of patients died suddenly on the toilet without prodromal symptoms. This amounts to twice the prevalence known in nonpaced sudden cardiac death patients. Autopsy findings disclosed unrecognized thrombosis of the superior vena cava as one possible mechanism in 10% of paced sudden death patients, and Bernstein et al. reported on lethal embolism in four of 18 patients who died during the first year after pacemaker implantation. Overall, the sudden cardiac death rate in permanently paced patients is three
times higher during the first year after pacemaker implantation than in subsequent years. This is in accordance with the total mortality rate in previous studies and is likely due to more severe heart disease and known poor prognosis.4,7,9,45

Regarding the mechanisms of sudden cardiac death, it has been emphasized that sensing failure or asynchronous pacing rather than pacing failure20,25–27 may contribute to sudden cardiac death mortality by initiating malignant ventricular arrhythmias.28–35 In this study, we used restrictive criteria for the definition of sudden cardiac death39,40 and observed further clinical evidence of a tachyarrhythmic rather than asystolic sudden death. First, no patient who died suddenly had required pacemaker battery replacement, nor was there any evidence of any type of pacing deficit during annual follow-up. Second, 47% of our patients died during sedentary activities, which implicates a low risk of myopotential inhibition of the pacemaker, known to be the most frequent cause for pacing failure.20,26 Third, >80–85% of our pacemaker patients had a spontaneous ventricular escape rhythm during annual pacemaker follow-up, and pacing failure would rarely be fatal in these patients.

Fourth, neither prodromal symptoms nor evidence of progressive pacing failure was present before sudden death. Given that ventricular fibrillation is a relevant cause of sudden cardiac death in pacemaker patients, one can argue that this reflects progression of underlying heart disease.23,24 However, experimental data as well as case reports have stressed the potential role of undersensing56,47 and pacing-induced fatal arrhythmias.28–35 The risk was greatest in the abnormal and severely diseased myocardium and in the presence of multiple ectopic ventricular beats.16,48,49 Prospective clinical studies addressing this problem to identify patients at higher risk of dying suddenly are lacking.

In the present study, a large, consecutive series of patients was followed to assess data on the prevalence and circumstances of sudden and nonsudden death during permanent pacing. The indication for pacemaker implantation was of moderate help in identifying patients with a high risk of sudden cardiac death. The sudden cardiac death rate was lowest in patients with sick sinus syndrome or previous syncopal attacks when programmed electrical stimulation had excluded inducible sustained tachyarrhythmias.

Table 4. Twenty-four-hour Holter Monitoring in 90 Selected Pacemaker Patients During Standard ECG Before Pacemaker Implantation

<table>
<thead>
<tr>
<th>Pacemaker Implantation</th>
<th>EF mean (%)</th>
<th>Patients with VPB (mean %)</th>
<th>Paced beats (%)</th>
<th>VPB</th>
<th>Undersensed VPB (%)</th>
<th>Inhib pacing failure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No bundle BB</td>
<td>59.2</td>
<td>57</td>
<td>11/15</td>
<td>27.2</td>
<td>13</td>
<td>0.0</td>
</tr>
<tr>
<td>Left anterior HB</td>
<td>60.2</td>
<td>49</td>
<td>12/15</td>
<td>24.2</td>
<td>21</td>
<td>0.5</td>
</tr>
<tr>
<td>Right bundle BB</td>
<td>53.1</td>
<td>52</td>
<td>13/15</td>
<td>26.2</td>
<td>62</td>
<td>1.3</td>
</tr>
<tr>
<td>Left bundle BB</td>
<td>48.2</td>
<td>44</td>
<td>14/15</td>
<td>26.7</td>
<td>34</td>
<td>5.9</td>
</tr>
<tr>
<td>Right bundle BB</td>
<td>51.2</td>
<td>41</td>
<td>12/15</td>
<td>32.3</td>
<td>98</td>
<td>2.1</td>
</tr>
<tr>
<td>Right bundle BB /left anterior HB</td>
<td>46.2</td>
<td>40</td>
<td>14/15</td>
<td>37.0</td>
<td>111</td>
<td>13.5</td>
</tr>
</tbody>
</table>

Each group consisted of 15 patients matched for age, sex, duration of artificial pacing, and underlying heart disease. EF, ejection fraction; VPB, ventricular premature beats; undersensed VPB are considered when the pacemaker spike occurred ≥20 msec after QRS onset to 100 msec after the end of the TU wave; Inhib, inhibition; BB, branch block; HB, hemiblock.

Figure 3. Tracings show undersensing of ventricular premature beats (VPB) during multiprogrammable, ventricular-inhibited (VVI,M) pacing (surface ECG is used to better document the different morphology of VBB). Postextrasystolic undersensing and capture failure after VPB 1 (left part). VPB 2–4 with identical morphology (different from VPB 1) is once sensed (VPB 3) and once undersensed (VPB 2,4). In case of undersensing, the pacing impulse is captured (arrow).
before pacemaker implantation. In about 15–17% of these patients, death was sudden and unexpected during follow-up. The sudden death rate increased to 25–28% in patients with severe bradycardia, atrial fibrillation with low ventricular rate, or high-grade AV block. Other clinical parameters, such as male sex and young age, were more predictive. Male patients had a 1.7-times-higher risk of sudden cardiac death than female patients, and patients younger than 60 years had a 5.2-times-higher risk of dying suddenly than older patients. Ginks et al\textsuperscript{50} and Fitzgerald et al\textsuperscript{9} reported similar findings for the total mortality rate. They stressed the higher prevalence of atherosclerotic heart disease in male patients and a more severely diseased heart in younger compared with older patients when artificial pacing was required. Coronary artery disease indicated by a history of myocardial infarction was not predictive of sudden cardiac death, which contradicts other studies.\textsuperscript{9,50}

However, the sudden cardiac death rate increased when coronary artery disease had resulted in high-grade AV block or bifascicular and trifascicular bundle branch block.

Presence of right bundle branch block combined with left anterior hemiblock rather than posterior hemiblock as well as trifascicular block were the best predictive parameters and were associated with a twofold increase in the risk of sudden cardiac death. Overall, 35% of patients with bifascicular and trifascicular bundle branch block died suddenly. A naturally increased risk of sudden and tachyarrhythmic death in this group of patients is known from previous studies.\textsuperscript{51–53} In the study by Denes et al,\textsuperscript{51} ventricular tachycardias were observed in 23% of patients who died suddenly during follow-up; ventricular fibrillation was documented in four patients. These data indicate that antibradycardiac pacing will not be efficient in preventing sudden death in patients with bundle branch block; however, cardiac pacing itself carries a potential risk. We were therefore interested in the electrophysiological mechanisms that may initiate or promote the occurrence of malignant tachyarrhythmias in patients with severe bundle branch block after pacemaker implantation.

Pacemaker inhibition by electromagnetic interference was a rare finding in patients with different types of bundle branch block and unipolar pacing. By contrast, undersensing of ectopic ventricular beats of up to 13% of ectopic beats was a common finding but was restricted to patients with severe bundle branch block. Vera et al\textsuperscript{46} reported that this phenomenon may occur without evidence of pacemaker malfunction as a result of the myocardial conduction delay of contralateral ventricular premature beats. As a result, fusion beats may occur in a diseased heart known to carry an already increased risk of electrical instability. In our study, nearly 10% of clearly under-

**Figure 4.** Tracings show in upper part of figure (1–3) undersensing of ventricular premature beats of various amounts. Lower part of figure shows initiation of two types of ventricular tachycardia when early (4, arrow) and late undersensing (5) of ventricular beats occur after a postextrasystolic pause.
sensed ectopic beats resulted in pacing-induced repetitive ventricular arrhythmias of some variety and even in ventricular fibrillation. Overall, the risk of fatal undersensing is probably highest in patients with a high prevalence of spontaneous, polymorphic, and especially of late-occurring ectopic arrhythmias, as well as in patients with severe conduction disturbances and a lowered fibrillation threshold resulting from severely diseased myocardium. Despite the problems known in the diagnostic evaluation of patients with syncope, these results also stress the importance of carefully evaluating patients with severe bundle branch block, especially in the presence of syncpe by Holter monitoring and more important, by electrophysiological testing to determine the presence of inducible malignant arrhythmias before pacemaker implantation.

In our consecutive series of patients, unipolar ventricular pacing was the dominant pacing mode. This is the result of the study design and the time

FIGURE 5. Tracings show initiation of ventricular tachyarrhythmias by multiprogrammable, ventricular-inhibited (VVIM) pacing. During atrial fibrillation, the pacing device works properly (upper part). After a spontaneous ventricular premature beat, regular pacing impulse is followed by three rapid spontaneous beats (middle part). When pacing spike occurred after a couplet, a small run of ventricular premature beats was initiated.
when long-term follow-up started in 1984. During recent years, pacing modes have been changed in most centers, and it has been suggested that atrial and especially dual chamber pacing, which is used today in up to 40% of patients, may be more beneficial in patients with severely diseased hearts. With both pacing modes, patients are well known to be less vulnerable to any variety of cardiac illness, including death, because cardiac function is far better preserved. However, it is unclear but at least likely for atrial pacing that undersensing of ventricular ectopic beats or fatal fusion beats may be a more rare finding with these two pacing modes. In the present study, the subgroups of patients with heart block and dual chamber pacing was too small to obtain a difference in the sudden death rate.

Clinical Implications

This study indicates that sudden death is a rather common event in permanently paced patients. Patients at highest risk of dying suddenly are characterized by male sex, younger age, and the presence of severe bundle branch block most frequently caused by coronary artery disease. In a significant number of these patients, sudden cardiac death seems to be due to the interference of the pacemaker rhythm and spontaneous ectopic ventricular beats, occasionally resulting in the initiation of malignant ventricular arrhythmias. Therefore, Holter monitoring and even electrophysiological testing should be considered in patients with bundle branch block, especially in the presence of syncope, before pacemaker implantation. Holter monitoring should be directed at patients with bundle branch block and with evidence of repetitive ventricular arrhythmias, palpitations, presyncope, or syncope, especially in the first year after pacemaker implantation.

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M Zehender, C Büchner, T Meinertz and H Just

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