Statistical Analysis of Pacemaker Follow-up Data

Rate Stability and Reliability

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SUMMARY In a rate-stable pacemaker, pacemaker rate reflects battery voltage level and should remain constant or be slightly depleted with time in a linear fashion until failure occurs. Linear regression techniques are therefore particularly suited to the analysis of pacemaker rate data. Data on model 8114/8114A Starr-Edwards pacemakers followed at the University of Oregon Health Sciences Center were studied. For a given pacemaker both the slope of the regression line and the standard deviation about the regression line are proportional to the original rate. Natural indices of rate depletion and rate stability for each pacemaker can therefore be calculated by dividing the slope and the standard deviation, respectively, by the intercept of the corresponding regression line. This model pacemaker has a small average standard deviation so that significant variations from the line of regression, indicating impending pulse generator failure, can be detected in spite of random fluctuations. Emergency and prophylactic replacements can therefore be kept to a minimum so that pulse generator lifetime is maximized. Success in extending pulse generator longevity can be measured by actuarial techniques, which show this pacemaker to have a median battery depletion time of 38 months and a median replacement time of 35 months.

THE MAJORITY OF PATIENTS with implantable pacemakers face sudden death or severe disabling symptoms should failure of the system occur. Prophylactic replacement at a predetermined time interval is not satisfactory. Indeed, the recent report of the Inter-Society Commission for Heart Resources on Implantable Cardiac Pacemakers states that “replacement of the pulse generator solely on the basis of age can no longer be considered optimal care” and that “rate measurement is an essential feature of any check of pacemaker function.” Since 1970 a pacemaker has been available with negligible random fluctuation in rate. In this unit rate is exclusively geared to battery voltage. Since the voltage remains constant or is slightly depleted in a linear fashion until the time of failure, the graphs of rate versus time post-implant should cluster about a straight line which either remains flat or falls off slowly with time. As pulse generator failure begins there is a departure from this line.

This report describes methods based on linear regression analysis for quantitatively analyzing these rate data and proposes two indices of rate behavior that can be used to describe the performance characteristics of a given pacemaker. In addition it proposes actuarial methods for assessing the longevity of a group of pacemakers. These methods are illustrated using data from the model 8114/8114A Starr-Edwards pacemakers followed at the University of Oregon Health Sciences Center. The trans-telephone system employed in gathering these data has achieved a considerable reduction in time and effort in following large numbers of patients.

Materials and Methods

As of February 1, 1975, 375 Model 8114 and 76 Model 8114A Starr-Edwards pacemakers were implanted and followed at the University of Oregon Health Sciences Center. These models are identical except that the circuitry boards of the 8114 are soldered whereas those of the 8114A are welded. They have therefore been combined, resulting in 451 pacemakers with a total follow-up of 6845 pacemonths, for an average of 15.2 months per pacemaker (range 1 to 40 months). These units were implanted into 294 males and 157 females whose mean age was 66.6 years (range 2 to 95 years). Following implantation, each patient is given a transmitter by which his pacemaker rate is monitored via telephone every other month for the first year and monthly thereafter. If a questionable rate is encountered, the pacemaker is monitored more frequently until the rate returns to normal or the unit is replaced. This group has accounted for 4192 separate teletransmissions (average 9.3). The pacemaker is equipped with two rates, low (about 70 beats per minute) and high (about 90 beats per minute), both indicators of battery voltage.

Thirty-five of these pacemakers were more than 30 months post-implant and also had at least ten readings on both high rate and low rate. These were selected for in-depth rate analysis. They averaged 34.3 months post-implant (range 30.4-40.0), and had an average of 27 high rate readings and 24 low rate readings. Linear regressions were run on both high rate and low rate for each pacemaker. Since the purpose of the study is to describe the performance of functioning pacemakers the terminal readings on failed pacemakers were deleted. The number of readings necessary to obtain precise estimates is a function of several variables. Our policy is to attempt the first regression for each pacemaker at one year, when approximately six readings have been obtained at each rate.

Rate Analysis

The rates follow an underlying linear trend, with scatter about this trend presumably caused by random fluctuations from components of the system. Therefore linear regression analysis is appropriate for the resulting rate patterns: the regression line represents the underlying battery voltage, and the standard deviation about the regression line measures component variability. The scatter diagrams and regression lines for a typical pacemaker are shown in figure 1. Theoretically, parallel lines plus and minus two standard
deviations from the regression line contain about 95% of the readings before failure.

Longevity Analysis

The purpose of rate analysis is to maximize pacemaker longevity. A method of estimating this longevity from a large number of implants should: (1) give the percent of pacemakers replaced in a time-associated manner for each postop interval; (2) give a breakdown of those replacements by whether they were for electrical component malfunction, full-term battery depletion, or other non-failure reasons; and (3) incorporate a feature for handling pacemakers lost to follow-up and deaths not related to pacemaker function. A method of analysis which satisfies all three of these criteria is the cumulative actuarial technique. Details of this method have been published previously.7

Results

Slope

The slopes of the regressions of low rate versus months postop ranged from +.004 to −.067 beats per minute (BPM) per month while the high rate slopes ranged from +.011 to −.089 BPM per month. Of the 70 regressions, 5 had positive slopes (not significantly different from zero at the 5% level by a two-sided t-test) and 65 had negative slopes (10 not significantly different from zero and 55 significant at the 5% level). The mean low rate slope was −.022 BPM per month which is equivalent to a drop of .79 BPM in 36 months; the mean high rate slope was −.032 BPM per month, which is equivalent to a drop of 1.15 BPM in 36 months. A steeper drop for high rate would be expected if both are linear measures of battery voltage, since a given voltage drop would be accompanied by an equivalent percent drop in both high rate and low rate, which would imply a larger absolute drop for high rate than for low rate. Thus, dividing the slope by the original rate (the intercept of the regression line) and multiplying by minus 100 gives the percent drop per month, which in a given pacemaker should be the same for high rate and low rate. This normalized rate of decrease is independent of rate, and could be used to compare two pacemakers of different rates. To check this theory, the normalized slope as determined from the high rate regression was plotted against that determined from the low rate regression for each of the 35 pacemakers. The results, in figure 2, show excellent agreement, confirming the fact that high rate and low rate support each other in measuring the rate of battery depletion. Accordingly this normalized slope is called the rate depletion index (RDI). The mean RDI from high rate is .033% per month, and from low rate is .032% per month. Note that a wide range of RDIs appear to be compatible with pacemaker longevity, since all these pacemakers, with RDIs ranging from −.01% per month to +.09% per month, have successfully completed at least 30 months.

Scatter

The standard deviation (sd) about the regression line for high rate ranged from .06 to .33 BPM, and for low rate from .05 to .28 BPM. The mean low rate sd was .12 BPM, which would imply that 95% of the low rate beats lie within ±.24 BPM of the low rate regression line; the mean high rate sd was .16 BPM, which would imply that 95% of the high rate beats lie within ±.32 BPM of the high rate regression line. Since those deviations are so small, a drop in rate due to abnormal function is easily detected. These sds are also rate-proportional; for a given pacemaker, dividing each sd by the intercept of the corresponding regression line produces another constant of the pacemaker, called the rate stability index (RSI), which is appropriate for comparison of rate stability between different pacemakers. Figure 3 contains a scatter diagram of the RSI s as determined from high rate versus the RDIs from low rate for each of the 35 pacemakers.

FIGURE 1 Scatter diagrams of high rate and low rate versus months post-implant for a typical pacemaker, with linear regressions indicated. The high rates have a proportionally steeper regression line and larger sd than the low rates. This pacemaker failed at 31 months, as indicated by a drop in low rate of 1.1 BPM and in high rate of 1.3 BPM during a period of 17 days. BPM = beats per minute.

FIGURE 2 Rate depletion index (RDI) calculated from high rate versus RDI from low rate for 35 pacemakers more than 30 months post-implant.
Table 1. Most Recent Status by Postoperative Interval for 451 Starr-Edwards Pacemakers

<table>
<thead>
<tr>
<th>Interval (months)</th>
<th>Currently followed</th>
<th>Discontinued follow-up</th>
<th>Patient death</th>
<th>Non-failure removals</th>
<th>Premature failure</th>
<th>Battery depletion</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6</td>
<td>40</td>
<td>2</td>
<td>39</td>
<td>12</td>
<td>8</td>
<td>0</td>
<td>101</td>
</tr>
<tr>
<td>7-12</td>
<td>61</td>
<td>1</td>
<td>17</td>
<td>6</td>
<td>8</td>
<td>0</td>
<td>93</td>
</tr>
<tr>
<td>13-18</td>
<td>53</td>
<td>5</td>
<td>18</td>
<td>3</td>
<td>7</td>
<td>0</td>
<td>86</td>
</tr>
<tr>
<td>19-24</td>
<td>46</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>10</td>
<td>0</td>
<td>63</td>
</tr>
<tr>
<td>25-30</td>
<td>47</td>
<td>0</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>31-36</td>
<td>21</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>37-40</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>272</td>
<td>10</td>
<td>93</td>
<td>28</td>
<td>35</td>
<td>13</td>
<td>451</td>
</tr>
</tbody>
</table>

pacemakers. The good agreement supports the validity of this index. The range of RSI is from .07% to .40%, and the mean is .170% for low rate and .174% for high rate.

Longevity

Table 1 lists the most recent status of all 451 pacemakers in this series as a function of postoperative interval. The cause of each failure is determined by laboratory inspection of the recovered pulse generator. None of the deaths were pacemaker-related. Figure 4 contains actuarial curves for all pacemakers in this group. At 30 months 97% are free of battery depletion, 77% are free of any failure and 70% are free of removal for all causes, including infection, lead problems and prophylactic replacement. The median lifetime (when half the events may be expected to have occurred) is read from the graph as the time postop at which the curve intersects the horizontal 50% line. For this series, the median battery depletion time is 38 months and the median replacement time is 35 months.

Discussion

Analysis of pacemaker rate data can be an excellent means of assessing pacemaker function and predicting imminent failure.1, 2 It is simpler than wave form analysis and frequent readings can be taken via teletransmission quickly and easily. With more frequent readings, the regression of rates versus time is more precisely estimated; also the chance of a complete failure occurring between readings is reduced. Such a system can supplement and thereby reduce the number of office examinations necessary to assess pacemaker function. However it requires a rate stable pulse generator so that a significant drop in rate can be detected. Linear regression analysis of the individual pacemaker rates then provides measures of overall battery depletion (slope of the regression line) and random fluctuation (standard deviation). Both are rate-dependent: if expressed as percentages of the original rates (by dividing by the intercept of the regression line), they provide two constant parameters of the pacemaker, called the rate depletion index (RDI) and the rate stability index (RSI), respectively. These indices permit valid comparisons of rate behavior between pacemakers of different intrinsic rates, and may ultimately be useful as predictors of aberrant pulse generators.

A small RSI permits rate analysis as an excellent means of detecting impending failure, since small deviations from the established trend can be detected. This allows maximization of pacemaker longevity. The quantification of success in achieving this longevity in a given model of pacemaker is provided by the use of actuarial lifetime analysis, which provided estimates of the percent of pacemakers free from removal for all causes, or for certain causes only, at each postoperative interval. Actuarial techniques were applied to the analysis of prosthetic valve replacement by the Mayo Clinic,8 and have subsequently been used increasingly often.10-13 Their advantages have been dealt with in two re-

![Figure 3](image-url) **Figure 3** Rate stability index (RSI) calculated from high rate versus RSI from low rate for 35 pacemakers more than 30 months post-implant.

![Figure 4](image-url) **Figure 4** Battery depletion-free, pulse generator failure-free and removal-free curves for 451 model 8114/8114A Starr-Edwards pacemakers.
Table 2. Failure Rates per Pacer-month for Different Postoperative Intervals

<table>
<thead>
<tr>
<th>Interval (months)</th>
<th>Follow-up (pacer-months)</th>
<th>Premature failures</th>
<th>Failure rate per pacer-month (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6</td>
<td>2354</td>
<td>8</td>
<td>.34</td>
</tr>
<tr>
<td>7-12</td>
<td>1767</td>
<td>8</td>
<td>.45</td>
</tr>
<tr>
<td>13-18</td>
<td>1248</td>
<td>7</td>
<td>.56</td>
</tr>
<tr>
<td>19-30</td>
<td>1271</td>
<td>11</td>
<td>.87</td>
</tr>
</tbody>
</table>

...cent papers, both of which pointed out the misleading aspects of using a total or overall complication rate approach.

An alternative method of summarizing pacemaker experience is to express the premature electrical component failures, which are presumed to occur at random and be unrelated to time, as the percent of failures per pacer-month by dividing the number of such failures by the total months of follow-up and multiplying by 100. If these failures are truly random, in the sense that the risk during each month is the same, then this is a satisfactory method for expressing that risk. If not, however, it is misleading, since it does not distinguish between 300 months of follow-up attributed to 10 pacemakers at 30 months and 300 pacemakers at 1 month, yet extrapolation of results from the latter to the former would be erroneous.

To determine whether our data support the time-independence of these premature failures, we divided them into four postoperative intervals and calculated the percent failures per pacer-month for each group. The results, in table 2, show an increasing risk with time, implying there is an aging factor to the risk of premature failure. Until the validity of the assumption of time-independence can be assured, it is safer to use an actuarial representation, which does not assume a constant risk.

Consideration of the curves in figure 4 shows why elective replacement at a time when, say, 10% of the failures are expected to occur is unacceptable for this model pacemaker. The middle (failure-free) curve shows that 10% of all failures will have occurred by about 25 months. Of the 90% that are still functioning at that time, the median total life expectancy is about 37 months (the time at which the failure-free curve intersects the horizontal 45% line). Therefore, the median additional life expectancy which would be wasted by universal replacement at 25 months is about 12 months. This fact supports a policy of replacement on an individual basis, for reasons of aberrant pulse generator behavior, rather than at a predetermined time.

We urge a profession-wide adoption of standardized reporting methods so that valid comparisons between various models of pacemakers may be made.

References
