Analysis of Turnaround Times in Pathology
An Approach Using Failure Time Analysis

Robin T. Vollmer, MD

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Abstract

This article introduces the use of failure time analysis methods for studying turnaround times in pathology. The key to understanding the approach is to view a laboratory specimen like a living patient. When the specimen enters the laboratory, the time is analogous to the time of diagnosis for a patient. When the specimen’s analysis is completed, the event is analogous to a patient who has died. To illustrate the approach, I use data previously published and data generated at the Durham, NC, Veterans Affairs Medical Center. I demonstrate that the Kaplan-Meier plotting method, the log-rank test, and the Cox model can all be applied to turnaround times and provide useful results.

The decision to perform a biopsy on a patient most often is driven by a clinician’s uncertainty about the presence or extent of malignancy, and, as a result, clinicians and their patients expect not only accurate, but also rapid surgical pathology reports. Additional pressures for short turnaround time (TAT) in surgical pathology come from economic issues that involve striving to reduce the lengths of hospital stays and to finalize bills shortly after discharge. Thus, an important measure for the quality of a surgical pathology laboratory is its TAT.1-5 TATs also are important in clinical pathology.6-15 For example, rapid TATs for tests such as troponin and creatinine kinase-MB significantly assist the early diagnosis and treatment of patients with acute myocardial infarction,11 and, in general, rapid TATs for laboratory tests reduce the length of stay for patients in emergency departments.14

As important as TAT’s are, however, there have not been consistent ways to report or analyze TAT’s.1,6 The usual statistics for TAT’s included means, medians, 90th percentiles, and fractions of tests beyond selected thresholds, but Valenstein1 and Valenstein and Emancipator6 have opined that each of these is limited. Furthermore, to improve TAT’s, one needs to identify variables that affect them. For example, in surgical pathology Zarbo et al2 identified 8 variables that significantly affected means or medians of TAT. Novis et al3 identified 3 variables that significantly affected TAT. In clinical pathology, Pellar et al9 identified 16 explanatory variables that affected TAT; and others have identified from 5 to 32 explanatory variables related to TAT.10,12-13 To demonstrate associations between TAT and explanatory variables, some have used univariate t tests for their analysis, and others have used analysis of variance, F tests, or linear regression. Nevertheless, such statistical tests are designed for normally distributed dependent variables, and...
TATs are not normally distributed.\textsuperscript{1,6,8} Furthermore, when there are multiple interrelated explanatory variables, a multivariate analysis is necessary to understand what influences TAT.

In this article, I introduce several straightforward ways to analyze TAT using statistical methods commonly used for failure times. In medicine, these methods also are called survival time analyses. To illustrate the approach, I use data available in the literature and data from the Durham, NC, Veterans Affairs Medical Center (VAMC).

Materials and Methods

Data Used

To illustrate the use of Kaplan-Meier plots and log-rank tests of TAT in surgical pathology, I used the data published by Zarbo et al\textsuperscript{2} and Novis et al.\textsuperscript{3} I converted their counts or frequencies of cases completed on each day into individual case times, and I preserved their designation of the cases into 2 categories: routine (\textit{Current Procedural Terminology} [CPT] codes \textless 88305) or complex (CPT codes 88307 and 88309).

To illustrate the use of Kaplan-Meier plots and log-rank tests of TAT in cytopathology, I used the data from 462 consecutive cases evaluated at the VAMC. These occurred during an approximately 2-month period, and 261 of the cases were evaluated and completed by me. Most of the remaining cases were received when I was on vacation, and they were sent to a referral laboratory for evaluation. TAT was defined as the time lapse from when the case was accessioned into the computer to when it was released electronically by the pathologist.

To illustrate multivariate analysis of TAT, I used 856 consecutive surgical pathology cases signed out at the VAMC. These occurred during an approximately 2-month period in the past year, and all but 4 of the cases were evaluated and completed by me. TAT was defined as the time lapse from when the case was accessioned into the computer to when it was released electronically by the pathologist. Because at the VAMC clinicians routinely obtain pathology results from the computerized patient record, the TATs for surgical pathology and cytopathology correspond to the combination of analytic and postanalytic times, but there were no data available to address preanalytic time lapses.

In addition to TAT, I recorded several explanatory variables for surgical pathology. These included whether the case was an outside case, the number of blocks, whether special stains were used, whether immunohistochemical stains were used, whether a consultation was obtained on the case before it was released, and the main CPT codes, which were categorized as 88305 or less, 88307, or 88309. The special stains category was for the use of stains other than immunohistochemical, which were obtained by contract from the Duke University Department of Pathology laboratory (Durham, NC). All consultations also were obtained from Duke University Department of Pathology faculty, whose offices are approximately one third of a mile from the VAMC.

Statistical Analysis of TAT

Ordinarily, we apply survival analysis to patients and their outcomes. Specifically, we analyze the time lapse from some beginning event, such as the time of diagnosis or treatment, to a failure event such as death, and in statistics, such times also are called failure times. Patients who are followed up to death are uncensored, and patients who are alive at the time of last follow-up are censored. Other failure events such as time of tumor recurrence can be used and are treated the same way. The data then, for an analysis of overall survival time, consist of 2 entries for each patient: a time lapse and a binary variable to indicate whether the patient is alive or dead at the time. Survival times are always 0 or more, and the status of the patient at the time is usually coded 0 for alive and 1 for dead. The Kaplan-Meier plot commonly is used to illustrate the distribution of survival times, and it is a plot of the probability of survival on the vertical axis vs time on the horizontal axis. As time increases, the probability of survival decreases, so that Kaplan-Meier plots decrease with time. Commonly, we then test whether key variables such as tumor grade and stage affect survival. To test the importance of a single variable, the log-rank test commonly is used. To test the importance of multiple variables, the Cox proportional hazards model commonly is used.\textsuperscript{16,17}

The key to understanding the survival approach to TAT is to consider active cases or specimens like living patients, and a comparison is outlined in Table 1. When a case is accessioned in the laboratory, its TAT clock is set at 0. When the case is completed, its status is analogous to a patient who has died.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of Survival Analysis With TAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit of data</td>
<td>Patient</td>
</tr>
<tr>
<td>Beginning time</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>End time</td>
<td>Last follow-up</td>
</tr>
<tr>
<td>Dependent variable</td>
<td>Time lapse</td>
</tr>
<tr>
<td>Range of time lapse</td>
<td>≥0</td>
</tr>
<tr>
<td>Last status</td>
<td>Alive (0) or dead (1)</td>
</tr>
</tbody>
</table>

TAT, turnaround time.
and the time lapse from accessioning, or TAT, is its “survival” time. Thus for completed cases or specimens, there are no censored events, and the binary “death” variable is always 1.

Results

Use of Kaplan-Meier Plots for TAT

Figure 1 shows a Kaplan-Meier plot applied to TAT in surgical pathology. The vertical axis gives the fraction of incomplete cases, and the horizontal axis gives the days from receipt in the laboratory. On the plot are a total of 35,330 cases reported collectively by Zarbo et al2 and Novis et al.3 The mean TAT for all cases was 1.55 days, and the median TAT was 1 day. The Kaplan-Meier algorithm automatically provides estimates of the fraction of cases completed by days in the laboratory. For example, for the aforementioned combined data, 67% of cases were completed by day 1, 88% by day 2, and 98% by day 5. Figure 2 shows a Kaplan-Meier plot of TAT, this time broken into routine cases (ie, CPT codes ≤ 88305) vs complex cases (ie, CPT codes 88307 and 88309). The slightly higher curve is for the complex cases. The mean TAT for routine cases was 1.39 days, whereas that for complex cases was 1.8 days. The log-rank test provides a way of testing whether TAT depends on this categorization, and it does it by using all the data rather than relying on just differences between means or medians. Although the Kaplan-Meier plot showed that the TATs for routine and complex cases appeared close to one another, the log-rank test demonstrated that this small difference was significant ($\chi^2$ value, >1,200; $P \sim 0$).

Figure 3 shows a Kaplan-Meier plot of TAT applied to cytopathology cases at the VAMC. The vertical axis gives the fraction of incomplete cases, and the horizontal axis gives the days from receipt in the laboratory. The dotted line is for cases sent to a referral laboratory, and the solid line is for cases routinely evaluated at the VAMC.

Figure 4 shows a Kaplan-Meier plot applied to preanalytic TAT in clinical pathology using the data published by Persoon et al.15 The vertical axis gives the fraction of incomplete cases, and the horizontal axis gives the days from receipt in the laboratory. On the plot are a total of 35,330 cases reported collectively by Zarbo et al2 and Novis et al.3
incomplete specimens, and the horizontal axis gives the minutes from receipt in the laboratory. On the plot are a total of 471 specimens. The upper curve is for the specimens processed before the lean procedure was introduced, and the mean TAT for this group was 31.9 minutes (median, 31 minutes). The lower curve is for the specimens processed after the lean procedure was introduced, and the mean TAT for this group was 21.2 minutes (median, 19 minutes). Using all the data, the log-rank test demonstrated that the lean procedure significantly reduced TAT (χ² value, 125; P ~ 0).

Use of Cox Proportional Hazards Model for Multivariate Analysis of TAT

To illustrate a multivariate analysis of TAT in surgical pathology, I used 856 consecutive surgical pathology cases completed during approximately 2 months’ time at the VAMC. The mean TAT for these VAMC cases was 1.5 days, with a median of 1 day, and 92% were completed by day 2. I explored the influence of several variables on TAT, including the status of case as an outside slide case, number of blocks, the use of special stains, the use of immunohistochemical stains, a CPT code of 88307, a CPT code of 88309, and the use of Duke consultants. The number of blocks was categorized as 1 to 20 or more than 20.

The results are given in Table 2, and they demonstrate that all of these variables except the number of blocks and a CPT code of 88307 were related significantly to TAT. The positive coefficient for outside case indicates the TAT was shorter for outside cases than for the rest. The negative signs for the coefficients for other variables imply that each of these slowed TAT. The magnitude of the coefficient is related directly to the magnitude of the effect on TAT. For example, the coefficient of –2.02 for immunohistochemical stains implies that this factor prolonged TAT more than any of the others. By contrast, the coefficient of –0.597 for cases coded as CPT 88309 implies that this factor affected TAT the least.

The last 2 variables in Table 2 are interaction variables for when cases included, respectively, special stains and immunohistochemical stains or immunohistochemical stains and consultation. Both of these interaction variables were significant, and their positive coefficients indicate that TAT was not slowed as much as would be expected if their individual effects were truly additive. Because the final Cox model showed evidence for not following the proportional hazards assumption, the coefficients of Table 2 are rough approximations, and the model cannot be used for predictive purposes. Nevertheless, the P values are so low and the number of uncensored cases is so large that the results provide a reasonable test for the effects of multiple key variables on TAT. For the study of TAT, this is the most important goal, and it was reasonably achieved by the Cox model analysis.

Discussion

Laboratory TATs clearly are important in anatomic pathology and in clinical pathology. Clinicians depend on fast TATs to achieve early diagnosis and treatment of their patients and to achieve early patient discharge from emergency departments or hospital in-patient services. For better or worse, TATs also influence the perception of the laboratory in the community of health care providers. With the
widespread use of laboratory computer systems, measuring and reporting TATs has become routine, and yet the methods for analyzing the details about TATs have not been optimized. If laboratory TATs are important, the analysis of TATs also should be important. If laboratory TATs are important, identifying variables that speed or slow TATs also should be important.

Nevertheless, TATs are not like many clinical or pathologic variables. TATs are times to an event like the completion of a case or specimen, and they are not normally distributed. To analyze TAT while avoiding the problem of nonnormally distributed data, one could use other nonparametric statistical methods. For example, the Kruskal-Wallis test could be used, but it is limited to the analysis of 1 explanatory variable. To analyze multiple explanatory variables, one could use logistic regression, but logistic regression discards information by collapsing the dependent, continuous variable of TAT into categories—usually 2 categories, such as 2 or fewer days vs more than 2 days. The cost of this collapsing is a decrease in statistical power for identifying significant explanatory variables. For example, a logistic regression analysis of the TAT data used in Table 2 found as significant just 5 of the 7 variables found significant by the Cox model, and many of the P values for the variables found to be significant by logistic regression were higher than those obtained by the Cox model.

Thus, as times to an event, TATs are ideally suited to the same analyses that are used routinely for survival times. Whereas survival times are times to a failure event, TATs are times to the release of the report from the laboratory.

Kaplan-Meier plots and log-rank tests are nonparametric methods commonly used for survival analysis, and the Cox model is a semiparametric method for identifying multiple variables that relate to survival. In clinical medicine and in diagnostic pathology, these 3 methods have identified many important variables and treatments that affect outcomes. Here, I have shown that Kaplan-Meier plots and log-rank tests identify variables that affect TAT.

Beyond the illustrations I have given, Kaplan-Meier plots and log-rank tests could be used in surgical pathology to test whether different pathologists achieve significantly different TATs. In the clinical laboratory, these 2 methods could readily be used to test how TATs depend on different assays. For most laboratory tests, however, it is likely that there are multiple, interrelated variables that affect TAT. Here, I have demonstrated that the semiparametric Cox model identifies which among several explanatory variables are important to TAT. Furthermore, the Cox model demonstrated that after controlling for obvious factors such as special and immunohistochemical stains, the CPT code of 88307 did not affect TAT. Cases with CPT codes of 88309 affected TAT but with less magnitude than special stains, immunohistochemical stains, or consultations. With such a multivariate approach, a laboratory should be able to identify variables affecting TAT and the relative magnitudes of their effects. Having identified the key variables, laboratory personnel can improve TAT by modifying the variables that can be manipulated, or they can at least know what they are confronting.

All of these approaches are done routinely in analysis of survival times for patients, and they can all be done routinely for TAT using the same software. Using such a robust scientific approach also could help pathologists convince administrators to change factors adversely affecting TAT. For all of these reasons, I encourage those studying TATs in their laboratories to use the survival analysis approach.

From the Veterans Affairs Medical Center and Duke University Medical Center, Durham, NC.

Address reprint requests to Dr Vollmer: Laboratory Medicine 113, VA Medical Center, 508 Fulton St, Durham, NC 27705.

References


