Reporting of Mortality in a Psoriatic Arthritis Clinic Is Primarily a Function of the Number of Clinic Contacts and Not Disease Severity

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ABSTRACT. ***Objective.*** To identify processes that influence data collection, particularly in the reporting of deaths in mortality studies, using patient registry data.

Methods. The University of Toronto Psoriatic Arthritis Clinic has mechanisms for patient followup and identification of deaths. Logistic regression was used to identify patient characteristics that discriminate between 2 populations of deaths, those reported under regular followup and those reported in the context of special studies. Factors examined were based on information available at the patients' last clinic visit and the pattern of patients' clinic visits.

Results. A clear relationship was found between the number of contacts with the clinic and rapid death reporting. However, no particular link between severity of disease and the reporting of death was apparent in this study.

Conclusion. It is recommended that research databases routinely record the time between death and reporting of death and the method of ascertaining and reporting death. More detailed information on the scheduling of clinic visits may also be helpful. (J Rheumatol 2005;32:2364–7)

Key Indexing Terms:
MORTALITY PSORIATIC ARTHRITIS REPORTING DISEASE SEVERITY PROGNOSIS

Patient registries are increasingly being advocated as an important means to understand rheumatic disease. The effort and cost needed to provide high quality longitudinal data mean that methods to extract the most valuable information from registry data need to be well understood. An example of this is the recognition that losses to followup need to be minimal and consequently that studies of the pattern of losses to followup are needed[1,2]. In addition, identification of factors related to losses to followup may be useful to ensure the validity of conclusions, to implement procedures to minimize losses to followup and, in some situations, to adjust for losses to followup.

In mortality studies, a standard procedure is to define censoring times, the time beyond which death is known to occur for patients not observed to die, as the date that patients were last seen alive. Essentially, this assumes that losses to followup are independent of the risk of death. In so far as this is not true, studies of mortality may be biased. Moreover, death reports reach clinical databases in various ways, with each having characteristic delay patterns. A recent investigation[3] highlighted the particular value, for such studies, of knowledge concerning death reporting in studies of mortality based on registry data. Joint consideration of both the mortality process and the process of mortality reporting established that unbiased estimation of death rates depends on knowledge of the expected value of the gap to the last clinic visit given that an individual's death has not been reported at the time of analysis. The most natural way to provide some information on this quantity is to model the pattern of death reporting.

We report on an investigation of mortality reports based on the cohort of patients registered in the Psoriatic Arthritis (PsA) Clinic at the University of Toronto.

MATERIALS AND METHODS

The University of Toronto Psoriatic Arthritis Clinic began accruing patients in 1978 and has established what is now the largest registry of patients with PsA with detailed prospective followup.

In 1989, a specific study of followup was undertaken[4]. In that study, special efforts were made to contact patients who had not been seen in the clinic for more than 2 years. In 1994 studies of mortality[5,6] were undertaken and again special efforts, including linkage to the provincial mortality database, were made to contact patients to ensure up to date mortality infor-

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mation. Both these studies identified patients who had died but whose death was not yet recorded in the registry database. A total of 47 deaths were identified in this manner.

Regular followup procedures in the clinic are based on scheduling of clinic visits, monitoring of death notices in newspapers, and contacts with patients' relatives. Patients are scheduled for regular appointments at 6-month intervals, at which time a protocol is completed. Some patients are seen more often for changes of medications or specific flares, but these are not entered on protocol. When patients do not attend their scheduled clinic appointment, staff try to contact them to reschedule their appointments. Contacts with relatives may arise out of this activity or through relatives contacting the clinic directly to pass on information. Relatives also call the clinic as soon as the patient dies, at times within 3 days. By December 2003, these procedures had identified 22 additional patients who had died.

Logistic regression has been used to identify patient characteristics that discriminate between these 2 populations of deaths, those reported under regular followup and those reported in the context of special studies. Goodness of fit tests[7] and receiver operating characteristic (ROC) curves were used to assess models.

In a study of mortality itself, all patients must be followed in a common fashion over the same period of calendar time. Here, however, interest lies only in the period of time after death, and the special followup procedures are only used to identify deaths with potentially long reporting times for inclusion in the study. The assumption required is that the use of comparable special procedures at other calendar times would have produced death reports for patients with similar characteristics. This has similarities to the approach in case-control studies where cases and controls are identified separately and the fraction of cases is an artifact of the design and not linked to disease incidence rates.

Factors examined were based on information available at the patient's last clinic visit and the pattern of the patient's clinic visits. For each patient, an estimate was made of the predicted or expected time between any 2 of their clinic visits. This was used as a variable that reflected the pattern of a patient's clinic visits. For this purpose we used model-based estimates of inter-visit times that provide more robust estimates than simple observed averages for individual patients. This prediction was used as an explanatory variable termed *inter-visit time*. Another variable was defined as:

$$1/\text{inter-visit time} = \text{rate of visits}$$

as a possible alternative for use in the logistic regression models. Technically, these variables derive from a log-logistic model for the inter-visit times, with random patient effects included in the model.

RESULTS

Table 1 presents characteristics of the 69 patients included in this study including actively inflamed, swollen (effused), and clinically damaged joint counts, functional class at their last clinic visit before death, and distance between the clinic and their address at the time of the last clinic visit. Consistent with the study of risk factors for mortality[6], these patients who died have more serious disease than a general clinic population. The inter-quartile range for the distribution of the time between death and the reporting of the death for patients reported under regular followup was 1 to 10 days, with a range of 1 to 3654 days. For deaths reported as a result of special studies, the inter-quartile range was 901 to 1903 days with a range of 77 to 5224 days. The large degree of separation between distributions supports the use of a simple yes/no classification for delayed reporting.

Analysis of inter-visit times for all patients led to an estimated median inter-visit time over all patients of 1.04 years (95% confidence interval, CI: 0.96-1.13. The estimation indicates that, for individual patients, the population median of 1.04 years is multiplied by factors between 0.29 and 3.47, corresponding to individual patient medians between 0.3 and 3.6 years, in 95% of the patients.

Table 1. Characteristics of the 69 patients involved in the study.

Variable	
Male/female	36/33
Mean age, yrs (range)	62.9 (31.62–87.74)
Median number of clinic visits (range)	3 (1–32)
Mean interval between first and last clinic visit, yrs (range)	5.11 (0–20.58)
Median distance from clinic, km (range)	17.1 (1.6–201.3)
Median number of active joints (range)	3 (0–39)
Median number of effusions (range)	0 (0–8)
Median number of damaged joints (range)	3 (0–48)
Functional class	
1	11
2	40
3	17
4	1

Initial consideration of sex and age as explanatory variables indicated the possibility of an interaction between these variables ($p = 0.04$). This suggested that increasing age increases the chance of delayed death reporting for females but decreases the chance for males. These variables and their interaction were therefore included as adjustment variables in single predictor analyses of other possible predictors of delayed reporting.

Table 2 presents results of these single predictor analyses that relate a binary (yes/no) indicator of delayed death reporting to various patient characteristics. It can be seen that only number of clinic visits and time in the clinic are strongly related to the type of death reporting. The more clinic visits a patient has made and the longer they have been registered in the clinic, the lower the chance of delayed mortality reporting. A high rate of visits and a larger number of deformed joints demonstrate marginally significant relationships with a lower chance of delayed reporting. Note, in particular, that there is little evidence of a relationship between variables that reflect disease activity and delayed death reporting, nor any evidence of a relationship between death reporting and the patients' proximity to the clinic, and only marginal evidence of any relationship with damage.

When multi-predictor logistic regression models were considered, the strongest predictor of delayed reporting was the number of clinic visits ($p = 0.003$). When this variable was included, time in the clinic was no longer significant ($p = 0.25$). Visit rate was also not significant ($p = 0.62$) and the number of deformed joints was still only marginally significant ($p = 0.11$).

The multi-predictor model that includes number of clinic

Table 2. Single predictor analyses (adjusted for age and sex).

Factor	Odds Ratio	95% CI	p
No. of clinic visits	0.79	(0.68, 0.92)	0.003
Time in clinic, yrs	0.79	(0.68, 0.91)	0.001
Rate of visits	0.36	(0.12, 1.14)	0.08
Inter-visit time	0.93	(0.41, 2.13)	0.87
Distance, km			
0–10	1.00		0.860
10–40	0.69	(0.18, 2.61)	
> 40	0.80	(0.21, 3.11)	
Functional class			
1	1.00		0.25
2	0.17	(0.02, 1.56)	
3	0.19	(0.02, 2.19)	
4	∞	(0, ∞)	
No. of active joints	0.99	(0.94, 1.06)	0.91
No. of effuse joints	0.95	(0.69, 1.30)	0.75
No. of deformed joints	0.95	(0.90, 1.01)	0.10

CI: confidence interval.

visits along with age and sex terms is given in Table 3. In this dataset therefore, the odds of delayed reporting were estimated to be reduced by 0.8 for each clinic visit attended. A formal test for the interaction between sex and age, based on an alternative but equivalent formulation of this model is only marginally significant (p = 0.08). A Hosmer-Lemeshow[7] goodness of fit test for this model gives a value of 8.98 on 5 degrees of freedom, p = 0.11. The area under the ROC curve based on this model is 0.78.

In a routine check of the model, it was noted that when the variable inter-visit time is added to the model in Table 3, then a significant (p = 0.04) effect was found. The p value associated with the goodness of fit test increased to 0.39, and the area under the ROC curve is 0.83. The model indicates that, for patients with the same number of assessments, a longer average time between visits decreases the chance of late reporting. While this might reflect some link to longer times in the clinic, there was one patient, whose death was reported with regular followup, with a very large value for inter-visit time, 4.22 years. If this patient is removed from the analysis then the p value associated with inter-visit time is increased to 0.14. Thus, while we report this finding for completeness, no firm conclusions can be drawn from this observation and the model in Table 3 represents the most robust summary of factors related to delayed death reporting.

Table 3. Multi-predictor model including clinic visits, age and sex terms.

Factor	Odds Ratio	95% CI	p
Clinic visits, n	0.79	(0.68, 0.92)	0.003
Male sex at mean age 62.9 yrs	0.76	(0.21, 2.80)	0.68
Age, women	1.07	(0.95, 1.20)	0.26
Age, men	0.95	(0.88, 1.01)	0.11

CI: confidence interval.

DISCUSSION

Sources of information on death reporting for patients whose records form part of a longitudinal clinical database appear to be scarce. Yet, such information could be of considerable value in reducing the potential bias in studies of mortality based on a database. At the very least, this information could be used to direct sensitivity analyses to illustrate the robustness of any clinical findings to modeling assumptions. Comparable studies of the reporting pattern for other outcomes might also be useful.

The University of Toronto PsA Clinic has provided an opportunity for a small preliminary investigation of factors related to the reporting of mortality. Limited data preclude comprehensive conclusions. A clear relationship between number of contacts with the clinic and rapid death reporting has been found. This is, perhaps, not surprising but provides motivation for further investigation of other aspects of clinic attendance, such as inter-visit times, if larger datasets can be identified. For this purpose, collection of more detailed information on the scheduling of clinic visits may also be helpful.

General conclusions from such investigations may be informative across different disease clinics and help in the development of methods of analysis that protect against biases caused by informative patterns of observation. Note, in addition, that, in our dataset, no relationship between disease severity and inter-visit times was found. The possible presence of age and sex effects on death reporting has been identified and should be considered in subsequent studies.

No particular link between severity of disease and death reporting was apparent in our study, suggesting that in studies of mortality when reporting is not guaranteed (i.e., through a link to a government database), bias adjustment or sensitivity analyses may only require consideration of the pattern of clinic visits. This is also a potentially important

finding for studies of other clinical outcomes when selective followup is a concern. Confirmation of this in other settings would be particularly valuable.

As a result of previous studies, including this one, attention has been directed towards improvement of mortality reporting in the PsA clinic. Thus, the current investigation cannot easily be extended to include later deaths. Nevertheless, we recommend, as previously[3], that information on death reporting be collected routinely as part of any clinical database. Therefore, along with a database record of the date of death, there should be a record for the date that the death was reported and, if possible, the means by which it was reported. This will allow statistical analyses to establish the validity of studies based on the database through characterization of the possible influence of unreported deaths.

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