Advanced Detection of Time Trends in Long-term Cancer Patient Survival: Experience from 50 Years of Cancer Registration in Finland

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Timely monitoring of trends in long-term patient survival is an important task of cancer registries. Recently, a new method, denoted period analysis, has been proposed to enhance up-to-date monitoring of survival. The authors assessed the use of period analysis for advanced detection of time trends in long-term cancer patient survival based on data from the nationwide Finnish Cancer Registry by comparing estimates of 10-, 15-, and 20-year relative survival rates obtained by period analysis and by traditional (cohort) analysis of survival at various points of time between 1953 and 1997. Time trends are graphically displayed for the 15 most common forms of cancer. Long-term survival rates strongly improved over time for most forms of cancer. The slope and shape of trend curves obtained by period analysis are very similar to those obtained by traditional survival analysis. However, detection of progress in 10-, 15-, and 20-year survival rates of newly diagnosed patients could have been advanced by 5–10 years, 10–15 years, and 15–20 years, respectively, with the use of period analysis rather than traditional cohort survival analysis. The authors conclude that period analysis should be routinely used to advance detection of progress in long-term cancer patient survival.

neoplasms; prognosis; registries; survival

MATERIALS AND METHODS

Database

This analysis is based on data from the nationwide Finnish Cancer Registry that is among the highest quality population-based cancer registries in the world (7). The Finnish Cancer Registry covers the whole of Finland (population, 5.1 million). The law requires that new cancer cases be reported to the registry, and the registry obtains information from many different sources, including hospitals, physicians working outside hospitals, dentists, and pathology and cytology laboratories. The Finnish Cancer Registry also receives copies of all death certificates on which cancer is mentioned. Virtually complete cancer registration has been accomplished since 1953.

Very efficient and reliable follow-up of cancer patients with respect to vital status is achieved by matching registry records with annual lists of death using the personal identification number as the key (8). In addition, the cancer registry data file is actively matched with the central population register as an additional check on the vital status of patients.

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By the time of this analysis, the registration of new cancer patients and mortality follow-up had been completed through the end of 1997.

Method of analysis

We derived 10-, 15-, and 20-year survival rates that might have been obtained by traditional (cohort) survival analysis and by period analysis of survival in various time intervals between 1963 and 1997. The difference between the two approaches is illustrated for 10-year survival rates in figure 1.

In contrast to traditional cohort survival estimates, period estimates of survival exclusively reflect the survival experience during some recent time period. This is achieved by left truncation of observations at the beginning of that period in addition to right censoring at its end, as described in detail elsewhere (5, 6).

For example, with the database available by the end of 1987, we might have obtained a recent period estimate of 10-year survival for the 1983–1987 period (left dotted frame in figure 1). This estimate is based on the survival experience of patients diagnosed between 1973 and 1987. However, their survival experience is left truncated at the beginning of 1983, and different parts of the survival function are contributed by different cohorts of patients. The survival experience during the first year after diagnosis is contributed by patients diagnosed between 1982 and 1987, the survival experience during the second year after diagnosis is contributed by patients diagnosed between 1981 and 1986, and so on, until the survival experience during the 10th year after diagnosis, which is contributed by patients diagnosed between 1973 and 1978. The 1983–1987 cumulative period estimate of 10-year survival is then obtained as the product of these period-specific conditional survival rates.

Period analysis thus provides a first estimate of 10-year survival for patients diagnosed in 1983–1987 (which can be obtained only 10 years later by traditional cohort analysis),
assuming that the conditional survival probabilities observed in 1983–1987 remain constant over time. This suggests that period analysis should considerably advance the detection of time trends in long-term survival rates.

Period estimates of 10-year survival for the periods 1988–1992 and 1993–1997, which could have been obtained with the databases available by the end of 1992 and 1997, were calculated from the survival experience of patients diagnosed in 1978–1992 and 1983–1997, respectively, in an analogous way (middle and right dotted frames in figure 1).

Trends in 10-year survival rates that might have been obtained for various time periods between 1963–1967 and 1993–1997 are graphically displayed and compared with trends in 10-year survival rates that might have been obtained by traditional cohort analysis of survival during those time periods. The results of these analyses are shown for each of the 15 most common forms of cancer in Finland in 1963–1997. In addition, the results of analogous analyses of 15- and 20-year survival rates are shown for patients diagnosed below age 75 years with one of four selected common forms of cancer, the prognosis of which changed greatly over time.

Throughout this paper we present relative survival rates rather than absolute survival rates (4). Because most forms of cancer occur at advanced ages, a substantial proportion of cancer patients die from causes unrelated to their cancer. Therefore, trends in absolute survival rates also reflect reduction in noncancer mortality over time, whereas trends in relative survival rates exclusively reflect changes in “net survival” related to the cancer of interest. Relative survival rates, which are commonly reported by cancer registries, are derived as the ratio of absolute survival rates divided by the expected survival rates of subjects of the corresponding age and sex in the general population, as estimated from population life tables (4). In our analysis, the relative survival rates were estimated according to the method of Hakulinen (9) (with appropriate adaptations for the period analysis approach) by an extended version of a recently developed computer program (10).

Survival rates over the 15 or 20 years following diagnosis are less meaningful for older patients who have quite limited life expectancy even in the absence of cancer. Therefore, analyses of 15- and 20-year survival rates were restricted to age groups below age 75 years.

RESULTS

As figures 2, 3, 4, and 5 show, 10-year relative survival rates have greatly improved over time for most of the common forms of cancer. This trend would have been apparent with both period analysis (dotted trend curves) and traditional (cohort) analysis (solid trend curves). Apart from some sampling variation, the patterns of time trends of 10-year relative survival rates obtained by period analysis are very similar to those obtained by traditional survival analysis in terms of the shape of the trend curves. However, for those cancers whose prognosis improved over time, the period estimates available in a given calendar period are much higher than corresponding estimates from traditional survival analysis; this implies that improvements in survival are apparent much earlier by period analysis than by traditional survival analysis.

To illustrate this point further, figures 2–5 also include trend curves that were obtained if traditional survival estimates were available 5 or 10 years earlier, respectively. These trend curves, which are presented as dashed lines, simply equal the traditional trend curves shifted to the left by 5 and 10 years, respectively. For most forms of cancer, the period trend curves fall between the trend curves that were obtained if traditional estimates were available 5 or 10 years earlier. In other words, application of period analysis rather than traditional cohort survival analysis would have advanced the detection of time trends in 10-year relative survival rates by 5–10 years.

Among the most common gastrointestinal cancers (figure 2), improvement has been most pronounced for cancers of the colon and rectum. For these cancers, the most recent period estimates suggest that 10-year relative survival rates have now come close to or even exceed 50 percent, but experience from previous monitoring of time trends suggests that it will take another 5–10 years until this extent of improvement is apparent by traditional survival analysis. By contrast, 10-year relative survival rates of patients with pancreatic cancer have remained exceedingly poor without any major improvement over time, and virtually identical trend curves were obtained by period analysis and by traditional survival analysis.

Among the most common gynecologic cancers (figure 3), improvement in 10-year relative survival rates has been most pronounced for breast cancer, but major improvements were also achieved for cancer of the ovaries and the corpus uteri. Again, detection of these improvements could have been advanced by 5–10 years by period analysis compared with traditional cohort analysis. A somewhat unusual pattern is seen for cervical cancer. Here, monitoring time trends by traditional analysis would have shown an increase of 10-year survival rates in the 1970s, followed by a decrease in the 1980s. The same pattern would have been evident by period analysis 5–10 years earlier. Period analysis also suggests a reversal of the downward trend into a strong reincrease in 10-year relative survival rates in the 1990s, a pattern that so far remains unrevealed by traditional analysis of survival.

The transient decrease in the survival rates of patients with cervical cancer may appear to be surprising at first view. However, it may be explained by the effects of widespread screening for precursors of cervical cancer by Papanicolaou smear, which led to a strong decrease in the incidence of invasive cervical cancer over time (by detection and removal of precancerous lesions) and a shift in the age distribution of patients with invasive cervical cancer to women at older ages, who tend to have much poorer survival (11, 12). It is also more likely that the precancerous lesions detected by screening would have developed more slowly as invasive tumors than those not detected by screening, leading to an overrepresentation of unfavorable stages among the invasive tumors after the introduction of Papanicolaou screening (13).

Improvement in the survival rates over time has been especially strong for patients with cancers of the urinary tract, in particular cancer of the urinary bladder (figure 4). Again,
period analysis would have advanced detection of this improvement by 5–10 years in all cases.

Similar patterns are seen for the other common forms of cancer (melanoma, cancer of the nervous system, and leukemia) shown in figure 5. Unfortunately, the prognosis of lung cancer, which remains a very common form of cancer in Finland, has hardly improved over time and continues to be very poor. Furthermore, the similarity of recent estimates of 10-year survival rates obtained by period analysis and by traditional survival analysis also suggests the absence of any major recent improvement for this form of cancer.

Figure 6 shows analogous graph presentations of time trends in 15-year survival rates for patients below age 75 years with selected forms of cancer obtained by period analysis.
(dotted lines) and cohort (solid lines) analysis. In addition, trend curves that were obtained if cohort survival estimates were available 10 or 15 years earlier are presented (dashed lines). We chose cancers of the colon, breast and cervix uteri, and melanoma for presentation, as their prognosis greatly changed over time (in which case the time of analysis makes a difference). Although there is some variation among cancer sites, the observed patterns suggest that, on average, the detection of trends in 15-year survival rates is advanced by 10–15 years by use of period analysis rather than traditional cohort analysis.

Finally, analogous graphs presenting time trends of 20-year relative survival rates are given in figure 7 for patients aged less than 75 years with the same forms of cancer. The
dashed lines and the asterisks included in this figure illustrate the hypothetical advancement of availability of the cohort survival estimates by 15 and 20 years, respectively. These analyses suggest that advancement in detection of time trends by period analysis compared with traditional cohort analysis is further increased to 15–20 years in the case of 20-year survival rates.

In figures 2–7, we compared period analysis and cohort analysis (pertaining to cohorts of patients who have been under observation for the entire follow-up time of interest) in the monitoring of long-term-survival time trends. The latter type of analysis (i.e., cohort analysis) (6) is frequently used by many cancer registries. For example, in the recent analyses of the EUROCare project, the most up-to-date 5-year
survival rates were reported for patients diagnosed in 1985–1989 who were under observation for at least 5 years at the closing date of follow-up (end of 1994) (14). Other traditional analyses have also included more recently diagnosed patients, who have not completed the entire follow-up time of interest and whose survival times were thus censored at

FIGURE 5. Ten-year relative survival estimates for patients with other common forms of cancer obtained in various calendar periods by period analysis (dotted lines) and by traditional (cohort) analysis of survival (solid lines), Finland, 1963–1997. The dashed lines indicate trend curves that were obtained if the availability of traditional survival estimates could be advanced by 5 years or 10 years, respectively.
patients who have been under observation for at least some minimal follow-up time have been included in most practical applications (15–18). The latter could thus be considered a “mixed” type of analysis that is somewhere between pure cohort and pure complete analysis.

To assess how much the delay in detection of time trends could be reduced by application of complete analysis rather than cohort analysis, we additionally assessed time trends in 10-, 15-, and 20-year relative survival rates that would have been obtained by complete analysis compared with cohort analysis and period analysis. These analyses revealed that the delay in disclosure of time trends compared with period analysis can be reduced indeed, but about half of the delay would remain even with a pure form of complete analysis.

FIGURE 6. Fifteen-year relative survival estimates for patients below age 75 years with selected forms of cancer obtained in various calendar periods by period analysis (dotted lines) and by traditional (cohort) analysis (solid lines), Finland, 1968–1997. The dashed lines indicate trend curves that were obtained if the availability of cohort estimates could be advanced by 10 years or 15 years, respectively.
(data not shown). Obviously, a more severe delay somewhere between the delays observed for cohort analysis and complete analysis would remain for commonly used mixed forms of traditional survival analysis.

A potential advantage of complete analysis over both period analysis and cohort analysis is the somewhat higher precision of estimates due to the larger database included in its derivation. However, differences were generally quite modest in our analysis. For example, the standard errors for the most recent 10-year period for cohort and complete survival estimates were 0.58, 0.64, and 0.46 for breast cancer, the most common cancer among women, and 2.60,
DISCUSSION

To our knowledge, this is the first systematic empirical evaluation of the use of period analysis for advanced detection of time trends in long-term cancer patient survival. Overall, the patterns of trends disclosed with period analysis of survival were found to be very similar to those obtained by traditional survival analysis in terms of the shape of the trend curves. However, our analyses reveal that the detection of time trends of 10-year survival rates can be advanced by 5–10 years by application of period analysis compared with traditional cohort analysis. Advancement by 10–15 years and 15–20 years can be achieved for the detection of trends in 15- and 20-year survival rates, respectively. This advancement may appear dramatic on first view, but it is in close agreement with previous suggestions based on theoretical considerations (5). The advancement is somewhat less but still substantial if the monitoring of long-term survival by period analysis is compared with the monitoring by complete analysis or by mixed cohort and complete analyses.

The reason why the detection of progress in long-term cancer patient survival is delayed so much with traditional survival analysis is that traditional long-term survival estimates refer to patients whose cancer was diagnosed many years ago. With period analysis, only “late survival experience,” that is, survival experience many years after diagnosis, is contributed by these patients, whereas survival experience during the first years after diagnosis (when most cancer deaths occur) is contributed exclusively by more recently diagnosed patients. This unique feature of period analysis enables the strong advancement in detection of time trends in long-term prognosis demonstrated empirically in this paper.

Given the strong advancement in detecting improvement in long-term cancer patient survival, it is not surprising that the period estimates for the most recent calendar periods obtained in our analysis are considerably higher than previously available estimates for those forms of cancer with ongoing improvement in prognosis over time, including such common cancers as colorectal cancer, breast cancer, and prostate cancer. For these cancers, the full extent of recent improvement in long-term survival has so far remained undisclosed by traditional cohort survival analysis (15, 16). Unfortunately, no such improvement is seen for cancers of the lung and the pancreas, for which estimates obtained by period analysis and by traditional survival analysis continue to be almost identical and quite stable over time at a very low level.

So far, there have been only a few applications of period analysis for monitoring long-term survival rates of patients with cancer (19–23). Apart from the fact that the method was introduced only a few years ago, this may have been due to the lack of empirical evaluation (of the kind presented in this paper). Additional obstacles to the use of period analysis may have been the lack of pertinent computer programs, as the method is included in neither standard commercial software packages nor special computer programs for survival analysis that are widely used by cancer registries (24, 25). To overcome this obstacle, we have recently developed a user-friendly and easy-to-use computer program for period analysis of both absolute and relative survival rates, which we are glad to share with colleagues in the field who are interested in its use (10).

Whereas the period approach has not traditionally been used in survival analysis, it is well established in related fields. For example, the period approach is probably the most commonly applied approach in the derivation of population life tables, which are used as a basis for estimating life expectancy. Life expectancy is a special type of long-term survival measure, that is, a long-term survival measure pertaining to cohorts of newborns (26). Nevertheless, monitoring of trends in life expectancy is usually not done for “real cohorts” of newborn populations, because estimates of life expectancy for cohorts of newborns could be obtained only a lifespan after their birth. Rather, various parts of pertinent life tables are typically estimated in a periodwise fashion from the survival experience of various birth cohorts in some recent period (e.g., a recent calendar year) for up-to-date monitoring of trends in life expectancy. The period life tables quantify the life expectancy of people born in a recent calendar period, assuming that the age-specific mortality (or survival) rates observed in that period remain constant over time. In an analogous manner, the period estimates of long-term survival quantify the long-term survival rates that patients diagnosed in some recent calendar period have to expect given the conditional survival rates observed in that period.

A commonly used measure to monitor trends in cancer incidence over time is the cumulative risk to develop a certain cancer up to a certain age (e.g., age 75 years) in the absence of competing causes of death (27). The cumulative risk is complementary to a special long-term survival measure, that is, the cumulative probability of cancer-free survival up to a certain age in the absence of competing causes of death. Again, the monitoring of period trends in cancer incidence using cumulative risk is not done in a cohortwise fashion for real cohorts of newborns; such analyses could be performed only by cancer registries that have been in operation for a very long time, for example, at least 75 years. Rather, estimates of cumulative risk are commonly derived in a periodwise fashion from cancer incidence at various ages within a recent time period.

The analyses presented in this paper have several limitations. We presented only the trends in overall cumulative survival rates by type of cancer, without further stratification by age or stage at diagnosis (except for the exclusion of patients aged more than 75 years in analyses of 15- and 20-year survival rates). Therefore, our analyses do not allow (and were not designed for) the drawing of conclusions regarding the reasons for improvements of survival rates over time. Such reasons may be manifold and may include, among others, earlier diagnosis (or eventually even overdiagnosis) and progress in treatment. Like traditional analysis of time trends in long-term survival rates, period analysis of time trends could easily be used in more detailed fashion, however, for example, in age- and stage-specific analyses, where these are of interest. Such analyses would at the same time allow adjustment of time trends for...
possible changes in the age distribution of cancer patients over time.

Clearly, cohort analysis of survival trends is the method of choice if the prognosis of specific, well-defined cohorts of patients, such as patients diagnosed within some time interval in the past, is of primary interest. Cohort analysis of time trends is likewise useful for retrospective assessment of trends in survival rates over time for patients diagnosed in various epochs, in particular, if there have been clear-cut changes in modalities of primary treatment by date of diagnosis. Complete analysis may be the method of choice in specific situations in which there is little change in prognosis over time, as it may provide somewhat more precise estimates than the other methods do. Period analysis of survival trends should therefore supplement, not replace, traditional monitoring of long-term cancer patient survival.

One of the main goals of monitoring long-term survival trends by cancer registries is, however, to disclose changes in survival rates as soon as possible and to provide the most up-to-date possible estimates of long-term survival rates. Our analyses illustrate that period analysis can make a major contribution to this end. Advanced detection of long-term survival trends is not primarily of academic interest. Rather, it should help to provide a more up-to-date data basis for both clinical and public health planning and decisions, such as decisions regarding treatment options, planning of clinical trials, cost effectiveness studies, evaluation of intervention measures, planning and implementing of screening programs, and so on. Last but not least, early disclosure of improvements in long-term survival rates may also help to prevent clinicians and their patients from being unduly discouraged by outdated, overly pessimistic survival statistics. The latter issue is likely to become increasingly important in the future, given the rapidly increasing access of patients to published cancer survival figures, for example, via the Internet.

Period analysis is but one (albeit a quite powerful) way to advance the detection of trends in long-term survival rates over time. Additional efforts to be made include the timeliness of cancer registration, analysis, and publication and dissemination of results. The chances for timely dissemination of cancer statistics have greatly improved and should continue to improve in the era of the World Wide Web, but there still is often substantial delay of cancer registration in many registries, often because of inadequate resources. In such cases, the detection of improvements in long-term survival rates by traditional survival analysis is even more postponed than in the analyses presented in this paper, which did not take such delay into account. The use of period analysis to advance the detection of trends in long-term survival rates should therefore go along with efforts to enhance the timeliness of cancer registration and mortality follow-up.

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REFERENCES