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Correspondence: José Luis Díez-Martín, Clinical chief of bone marrow transplantation unit, Hospital General Universitario Gregorio Marañón, Oncology Department, St. Máiquez, 7. Madrid 28007, Spain. Fax international +34.1.5868018.

Median versus mean lifetime survival in the analysis of survival data

Sir,

In survival studies, the median has traditionally been used to quantify the survival pattern of a particular patient population through a single parameter. Medians, however, demonstrate a well-known limitation because they are not influenced by the shape of the survival curve after 50% of residual survival has been reached. In other terms, medians are unaffected by the size of the *right tail* of the survival curve and are insensitive to the presence (or absence) of a small proportion of long-term survivors. In recent reports,[1-7] a new methodology of *lifetime* survival analysis has been proposed wherein the survival curves are evaluated by quantifying the area under the survival curve from time zero to infinity (AUC). According to this lifetime methodology, the portion of the curve from zero time to the last time point of the follow-up is estimated by direct numerical integration, whereas the right tail of the curve (from the last timepoint of the follow-up to infinity) is determined by an extrapolation based on the Gompertz model (Figure 1). If the AUC is normalized to a single patient, its value provides an estimate of mean lifetime survival (MLS).

Regardless of its useful applications in the analysis of cost-effectiveness,[1-7] MLS can be advantageous because it is sensitive to the shape of the curve after achievement of 50% residual survival, and therefore takes account of the presence (or absence) of a small proportion of long-term survivors.

Initial experience has been gained in the use of MLS. The literature has already reported MLS values of: 16.7 yrs in patients with node-positive breast cancer given adjuvant CMF chemotherapy vs. 13.2 yrs in patients given no adjuvant chemotherapy,[2] 2.9 yrs in patients with advanced ovarian cancer given first-line treatment with paclitaxel+cisplatin vs. 2.5 yrs in patients given cyclophosphamide+cisplatin;[3] 15.4 yrs in patients with colorectal cancer treated with adjuvant intraportal chemotherapy vs. 13.2 yrs in patients given no adjuvant chemotherapy;[4] 18.4 yrs in patients with relapsed chemosensitive non-Hodgkin's lymphoma treated with autologous bone marrow transplantation vs. 4.4 yrs in patients treated with salvage chemotherapy;[5] 9.6 yrs in patients with high-risk resected cutaneous melanoma treated with adjuvant interferon vs. 6.6 yrs in patients given no adjuvant therapy.[6]

Because simple theoretical considerations underscore an advantage of MLS for its sensitivity to the shape of the final portion of the survival curve, MLS can presently be regarded as a useful parameter for interpreting survival data. The Gompertz model for extrapolation of survival curves implicitly incorporates a prediction of the life expectancy of the patients. Other attempts have recently been made to include life expectancy data into survival curves.[8] The method of Vaidya and Mittra[8] seems to be more suitable for disease conditions characterized by a substantial chance of cure, whereas the Gompertz model is better suited for diseases with a low rate of cure. When the survival data derive from a particularly long follow-up, both models can be appropriate.

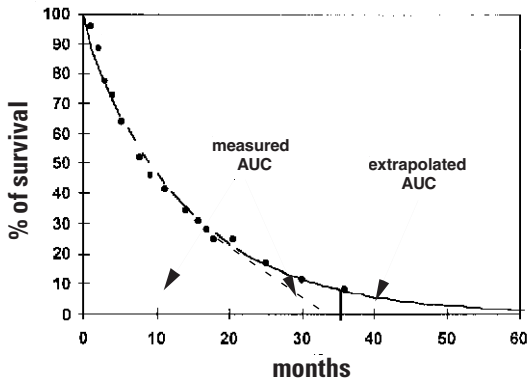

Figure 1. A least-squares fit of the trial's survival percentages (solid circles) to the Gompertz function allows to determine the whole survival curve as a mathematical function from time zero to infinity (solid line). The area under the survival curve can be split into a first component (measured AUC), which corresponds to the follow-up duration of the clinical trial, and a second component (extrapolated AUC), which corresponds to a survival prediction after the period over which the experimental data were available. If total AUC is normalized to 100 patients, MLS can be calculated as total AUC/100. The dotted line shows the time-course of another survival curve with no long-term survivors in which the median remains unchanged but both AUC and MLS are markedly reduced.

Andrea Messori
Paola Becagli
Sabrina Trippoli

Meta-analysis Study Group, Drug Information Center, Pharmaceutical Service, Azienda Ospedaliera Careggi, Florence, Italy

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Correspondence: Dr. Andrea Messori, Drug Information Center, Pharmaceutical Service, Azienda Ospedaliera Careggi, viale Morgagni 85,50134 Florence, Italy, Tel international: +39.55.4376878, Fax international: +39.55.4279738. E-mail: md3439@mclink.it