Variables Influencing the Timing of Marrow Transplantation in Patients With Chronic Myelogenous Leukemia

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The prognosis for patients with chronic myelogenous leukemia (CML) has improved only for patients who can receive marrow transplantation from a histocompatible sibling. The timing of the marrow transplant is made difficult by the high peritransplant mortality of 20% to 35% and a group of patients with a prolonged chronic phase of CML, which can be identified on the basis of prognostic indexes (age, percent blood myeloblasts, spleen size, and platelet count). We have developed a mathematic model and computer program that consider age, prognostic index, and projected survival rate by transplantation to balance the risk of peritransplant mortality against the risk of delaying the transplantation of patients with Philadelphia chromosome-positive CML. The computation assesses the risk of delaying transplantation; it does not offer the option of avoiding transplantation, since long-term survival ultimately requires transplantation. Three prognostic groups were considered as described by Sokal and co-workers (Blood 63:789, 1984) (I, best; II, intermediate; III, worst prognosis). The computation used the projected survival rates of transplantation from the Seattle experience and from the International Bone Marrow Transplant Registry. As an example of the model's utility, we have determined the ratio of the calculated life expectancy to the normal life expectancy for hypothetical patients up to 50 years of age in each of the three prognostic categories. A value of 20% is used for patients who successfully receive transplants after the onset of the accelerated phase. The analysis allows assessment of the risk of delaying transplantation for a finite time in patients with CML. The importance of the method rests in its consideration of multiple variables, including the peritransplant mortality, transplant projected survival before and upon entering the accelerated phase, age, prognostic group, and other risk factors. The program permits a change in these parameters as new information or advances in treatment occur. This analysis does not replace the diagnostic deliberations of the clinician. Rather, it provides a numeric framework for prognosis based on the currently available data. The physician in conjunction with the patient, not the algorithm, makes the decisions of whether and when to transplant.

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MATERIALS AND METHODS

Calculation of Chance of Survival

Basic calculation of chance of survival. This analysis determines the chance of survival from the time of diagnosis, that is, the proportion of the original population that achieves a normal life span if marrow transplantation is performed at some time after diagnosis. Figure 1 illustrates a hypothetical survival curve [S(t)] of patients with CML. The horizontal axis indicates years after diagnosis, and the vertical axis indicates the surviving fraction of the original population of patients. In this example approximately 60% of the patients [S(T1)] survive 4 years without transplantation, and the probability of surviving 4 years without transplantation is therefore approximately 0.6.

If at 4 years, the patient is still in the chronic phase of CML, has a histocompatible donor, and receives a marrow transplant, there is, for example, a 70% chance of long-term survival or cure after transplantation, ie, K = 0.7. The combined probability of surviving CML for 4 years and the transplantation procedure at the end of the fourth year equals the product of the survival fraction of the transplant (K) and the fractional survival at 4 years [S(T1)]; thus, K[S(T1)] = 0.7 x 0.6 = 0.42 or 42%.

Correction for salvage transplantation during the accelerated phase prior to T1. A fraction of patients, L, who develop accelerated disease during the 4-year period can be salvaged by marrow transplantation at the time that CML progresses. Up to T1, the fraction of the original population that develops accelerated disease is [1 – S(T1)], and at T1 it is [1 – S(T1)] (Fig 2). Thus, if L = 0.3 or 30% and 1 – S(T1) = 0.4, then the product of 1 – S(T1) and L or 0.12 should be added to the survival of patients who received transplants successfully at 4 years, making the chance of survival for all CML patients with a marrow donor 54%. Thus, the chance of survival calculation, which includes both elective transplantation at
expectancy without salvage. This Figure represents a hypothetical example. Bone marrow transplantation is performed at time \( T_1 \) and transplantation during the accelerated phase of the disease prior to \( T_1 \). The chance of survival is equal to \( KS(T_1) \). The chance of surviving CML for 4 years and the transplantation procedure is \( KS(T_1) \). The chance of survival is equal to \( KS(T_1) \) plus \( L[1 - S(T_1)] \), which represents the correction for salvage transplantation during the accelerated phase of the disease prior to \( T_1 \) (Fig 2). The mathematical representation of the area under each portion of the survival curve is necessary for the calculation of the mean life expectancy. The derivation of these calculations is presented in the text.

\[
\text{Chance of survival beyond } T_1 = KS(T_1) + L[1 - S(T_1)]. \tag{1}
\]

**Calculation of Mean Life Expectancy**

**Basic calculation of mean life expectancy.** The calculation of mean life expectancy, that is, the product of the proportion of patients cured and the number of surviving years, provides an alternative index for prognosis and timing of marrow transplantation. We have chosen 70 years of age as the normal life span, and \( T \) is equal to 70 years minus the patient's age. To calculate the life expectancy with transplantation at time \( T_1 \), we compute the area under the curve in Fig 1 up to time \( T_1 \). Added to this quantity is the area under the curve equal to the transplant survival fraction, \( KS(T_1) \) multiplied by \( T - T_1 \). Thus,

\[
\text{Life expectancy (years)} = \int_0^{T_1} S(t) dt + KS(T_1)(T - T_1). \tag{2}
\]

The calculation of the integral up to \( T_1 \) is most conveniently done by drawing a smooth curve through the survival data points (without transplantation) and reading the height of the curve at small, equal time intervals. The area within an interval is the width of the interval multiplied by the average of the height on the left and right edges of the interval. The height of the right edge of the interval ending at \( T_1 \) is \( S(T_1) \) (Fig 3).

**Correction for salvage transplantation during accelerated phase prior to \( T_1 \).** Life expectancy from the time of diagnosis to \( T_1 \) has been calculated for the various values of \( T \) and \( T_1 \). In this example we assume that patients survive to \( T_1 \) in the chronic phase of CML. If, however, the disease accelerates during this time, there is still the possibility of a cure using marrow transplantation. This survival fraction, \( L \), should be included in the calculation of life expectancy. The fraction of patients in whom accelerated disease develops up to time \( t \), within the time \( T_1 \), is \( [1 - S(t)] \) (Fig 2). At any point in time \( t \) up to \( T_1 \), those patients in whom accelerated disease has developed could receive transplants with a probability of success, \( L \), or a probability of failure, \( 1 - L \). Thus, the survival curve \( S(t) \) shown in Figs 1 and 2 is modified as shown by the dotted line \( S'(t) \) in Fig 2 in which the nonsurviving fraction \( 1 - S(t) \) is multiplied by the factor \( 1 - L \), and thus the surviving fraction is increased. Note that the quantity \( 1 - L \) indicates that if \( L \) is equal to 0 there are no successful transplants during the accelerated phase of the disease and there is no change in the survival curve. If \( L \) equals 1, then \( 1 - L \) equals 0, and all of the patients in an accelerated phase would receive transplants successfully, and the new survival curve (dotted lines) would be a horizontal line at the survival fraction equal to 1. In this example, the value for \( L \) is approximately 0.3; that is, 30% of those

![Fig 1](image1.png)

**Fig 1.** Calculation of the chance of survival and mean life expectancy without salvage. This Figure represents a hypothetical survival curve designated \( S(t) \) for patients with CML. In this example, bone marrow transplantation is performed at time \( T_1 \) when the fractional survival from the disease is 0.6. The combined probability of surviving CML for 4 years and the transplantation procedure is \( KS(T_1) \). The chance of survival is equal to \( KS(T_1) \) plus \( L[1 - S(T_1)] \), which represents the correction for salvage transplantation during the accelerated phase of the disease prior to \( T_1 \) (Fig 2). The mathematical representation of the area under each portion of the survival curve is necessary for the calculation of the mean life expectancy. The derivation of these calculations is presented in the text.

![Fig 2](image2.png)

**Fig 2.** Calculation of the chance of survival and mean life expectancy with salvage. This Figure is similar to Fig 1 and represents a hypothetical survival curve designated \( S(t) \). The mean life expectancy is the product of the proportion of patients cured and the number of surviving years. Thus, the life expectancy with transplantation at time \( T_1 \) is equal to \( \int_0^{T_1} S(t) dt \) plus \( KS(T_1) \) \( (T - T_1) \). The survival curve is corrected for the proportion of patients who are salvaged by transplantation during the accelerated phase of the disease prior to \( T_1 \). The corrected curve is designated \( S'(T_1) \). The derivation of the calculation for mean life expectancy incorporating the salvage transplantation during the accelerated phase of CML is described in the text.

![Fig 3](image3.png)

**Fig 3.** Calculation of the integral up to \( T_1 \). The area of the curve from time 0 to \( T_1 \), \( \int_0^{T_1} S(t) dt \), is calculated by drawing a smooth curve through the survival data points and reading the height of the curve at small time intervals. The area within an interval is the width of the interval multiplied by the mean height of the left and right edges of the interval. The height of the right edge of the interval ending at \( T_1 \) is \( S(T_1) \). The area under the curve after the time of bone marrow transplantation \( T_1 \) is equal to \( KS(T_1)(T - T_1) \) (see text).
patients entering an accelerated phase can be salvaged by treatment with marrow transplantation. The possibility of long-term survival after transplantation during the accelerated phase of disease increases both the chance of survival (see the preceding material) and the calculated life expectancy.

To evaluate life expectancy: Replace $S(t)$ in the integral of equation 2 by:

$$S'(t) = 1 - [1 - S(t)](1 - L) - S(t) + L[1 - S(t)] \quad (3)$$

and add $[S'(T_i) - S(T_i)](T - T_i)$, which is the increment in survival rate resulting from transplantation in the accelerated phase.

Life expectancy $= \int_0^{T_i} S'(t) dt$

$$+ [KS(T_i) + S'(T_i) - S(T_i)](T - T_i) \quad (4)$$

$$\int_0^{T_i} S'(t) dt = \int_0^{T_i} [S(t) + L[1 - S(t)]] dt$$

$$= LT_i + (1 - L) \int_0^{T_i} S(t) dt \quad (5)$$

$$KS(T_i) + S'(T_i) - S(T_i) = KS(T_i) + L[1 - S(T_i)] \quad (6)$$

Life expectancy $= LT_i + (1 - L) \int_0^{T_i} S(t) dt$

$$+ (T - T_i) [L + (K - L)S(T_i)] \quad (7)$$

Life expectancy (years) $= LT + (K - L)S(T_i)(T - T_i)$

$$+ (1 - L) \int_0^{T_i} S(t) dt. \quad (8)$$

This latter result appears complicated because the acute-phase transplantation can occur at any time within $T_i$ and because the factor $L$ already includes the transplantation risk. However, the computation is easily done using the computer program listed in the attached Appendix.

RESULTS AND DISCUSSION

We have established a mathematic analysis in which two prognostic indexes can be calculated for a group of patients with $Ph^1$-positive CML: the chance of survival, ie, chance of living a normal life span, and the mean life expectancy for a CML patient. Without marrow transplantation, life expectancy is limited, and patients die at rates shown in Fig 4 for each of three prognostic groups (see the following). For those patients with a histocompatible donor, marrow transplantation provides the potential for cure. The object of this analysis is to permit a more precise assessment of how long a patient can delay transplantation without incurring undue risk. The mathematic calculation considers the age of the patient, the prognostic category of the patient's disease, the projected survival rate for allogeneic marrow transplantation, and the projected salvage of patients by transplantation in whom accelerated disease develops.

Calculated Life Expectancy

All eligible patients with CML require transplantation to permit the possibility of normal life expectancy. The projected survival for allogeneic marrow transplantation in CML patients taken from data published by the Seattle group is 55%, by the UCLA group is 70%, and by the International Bone Marrow Transplant Registry is 65%. These results include patients from 5 to 50 years of age without regard for prognostic factors. The projected salvage rates of patients transplanted after developing accelerated disease or blast crisis are, respectively, 15% and 15% in the Seattle study, 35% and 10% in the UCLA study, and 40% and 10% in the International Bone Marrow Transplant Registry study.

In the following analysis we have determined the calculated life expectancy for a cohort of 20-year-old patients, assuming a 65% projected survival after transplantation in chronic phase and a 20% projected survival after transplantation in the accelerated or blastic phase of CML as being representative of the published studies. The maximum calculated mean life expectancy is 0.65 of the normal life expectancy of a 20-year-old, in this case the remaining 50 years (70 20 years). Thus the calculated mean life expectancy is 32.5 years if the patients receive transplants at the time of diagnosis (Fig 5). This calculated life expectancy decreases as transplantation is delayed from the time of diagnosis (lower curve). When the calculation is adjusted for a 20% projected survival for patients who received transplants during the accelerated phase or blast crisis, the overall slope of the curve is more shallow (Fig 5).

Table 1 shows the data for the upper curve of Fig 5, ie, calculated life expectancy with a 65% projected survival after transplantation in the chronic phase and a 20% projected survival with transplantation in the accelerated phase of CML. We have calculated two types of prognostic curves from these data to assess the impact of delay in transplantation. The first is a ratio of the calculated mean life expectancy to the normal life expectancy (CLE/NLE) expressed as a percentage (Table 1). The second is the chance of survival, which is calculated at a given time as the sum of the proportion of patients “cured” by allogeneic transplantation during chronic and accelerated phases of CML.
Fig 5. Calculated mean life expectancy without and with a 20% rate of salvage for transplant recipients during the accelerated or blastic phases of CML. The calculated mean life expectancy is shown for a cohort of 20-year-old patients with a 65% survival after bone marrow transplantation and a 20% salvage rate for transplantation during the accelerated or blastic phase if this occurs prior to the time chosen for transplantation, T. The initial point on the curve, 32.5 years, represents the maximal life expectancy if transplantation is performed at the time of diagnosis. In this case it is 0.85 of the normal life expectancy of a 20-year-old, i.e., the remaining 50 years (70 − 20).

Fig 6. CLE/NLE ratio and chance of survival. These prognostic curves assess the impact of delay from the time of diagnosis to bone marrow transplantation on the prognosis in patients with CML who have a histocompatible donor. The curves represent data for a cohort of 20-year-old patients with a 65% survival after transplantation in the chronic phase and a 20% success of transplantation in the accelerated or blastic phase of CML. The CLE/NLE is the ratio of the calculated mean life expectancy to the normal life expectancy expressed as a percentage. The chance of survival is calculated at a given time as the sum of the proportion of patients cured by allogeneic transplantation during the chronic and accelerated phases of CML.

Table 1. Calculated Life Expectancy for 20-Year-Old Patients in Prognostic Group 2 With a 65% Projected Survival After Transplantation in Chronic Phase and a 20% Projected Salvage After Transplantation in Accelerated Phase or Blast Crisis

<table>
<thead>
<tr>
<th>Transplantation Time</th>
<th>Calculated Life Expectancy (yr)</th>
<th>CLE/NLE (%)</th>
<th>Chance of Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>32.5</td>
<td>65.0</td>
<td>65.0</td>
</tr>
<tr>
<td>0.5</td>
<td>32.2</td>
<td>64.4</td>
<td>64.1</td>
</tr>
<tr>
<td>1</td>
<td>31.7</td>
<td>63.4</td>
<td>62.7</td>
</tr>
<tr>
<td>1.5</td>
<td>30.3</td>
<td>60.7</td>
<td>59.6</td>
</tr>
<tr>
<td>2</td>
<td>28.7</td>
<td>57.5</td>
<td>56.0</td>
</tr>
<tr>
<td>2.5</td>
<td>27.1</td>
<td>54.3</td>
<td>52.4</td>
</tr>
<tr>
<td>3</td>
<td>25.5</td>
<td>51.1</td>
<td>48.8</td>
</tr>
<tr>
<td>3.5</td>
<td>23.5</td>
<td>47.1</td>
<td>44.3</td>
</tr>
<tr>
<td>4</td>
<td>22.2</td>
<td>44.4</td>
<td>41.1</td>
</tr>
<tr>
<td>4.5</td>
<td>21.2</td>
<td>42.5</td>
<td>38.9</td>
</tr>
<tr>
<td>5</td>
<td>20.5</td>
<td>41.0</td>
<td>37.1</td>
</tr>
</tbody>
</table>

Influence of Prognostic Group

A variety of variables has been correlated with prognosis in CML. The data supporting an association between historic factors and prognosis are weak. However, there is substantial support for liver and spleen size, 7,11,12 myeloblasts in the blood, 5,11,12 and bone marrow, 6,11,12 basophilia, 7,11,12 and thrombocytopenia or thrombocytosis, 5,7,11,12 as indicators of prognosis. The Philadelphia chromosome 6,7,11,12 and myelofibrosis 11,12 also are prognostic findings.

Tura and his co-workers established the relationship of six clinical features to overall prognosis. These include spleen size, liver size, blood progranulocytes and myeloblasts, total white count, and platelet count. Three prognostic groups were established from these data. The best prognostic group had no or one negative prognostic feature, the intermediate group had two or three negative prognostic features, and the worst prognostic group had four or more negative prognostic features. These data were developed from two series of patients with CML, one containing 116 patients and the other containing 139 patients. A similar prognostic grouping was established by Sokal and co-workers, who analyzed data from 813 chronic-phase, Ph1-positive patients with CML who were studied at six medical centers. In this study the prognostic factors were determined using Cox’s proportional hazard model for covariant analysis. Sokal and co-workers developed a hazard ratio function based on the age of the patient, the size of the spleen, the platelet count, and the percentage of blasts in the blood. We have chosen to use
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Sokal and co-workers' calculation of the hazard ratio function so that the prognostic group can be determined from the patient characteristics. This calculation is incorporated into the computer program.

Evaluation of a 20-year-old patient with chronic-phase CML is shown in Fig 7. The projected survival after marrow transplantation is 65%, and the projected salvage by transplantation in the accelerated phase is 20%. The ratio CLE/NLE is shown for the three prognostic groups. The initial points represent transplantation at the time of diagnosis and cannot be greater than the projected survival for transplantation in the chronic phase, i.e., 65%. For the first and second prognostic groups the analysis indicates that the CLE/NLE ratio is unchanged and thus marrow transplantation could be delayed for 1 year with little additional risk. In contrast, the CLE/NLE ratio for patients in the third prognostic group begins to fall sharply 6 months after the time of diagnosis. This analysis indicates that the least risk would be incurred if marrow transplantation was performed immediately for patients in the worst prognostic group.

Influence of Patient Age

Younger patients fare better after marrow transplantation. Of 34 transplant recipients under the age of 30 in Seattle, the projected survival was 58%, whereas of 33 patients over the age of 30 years, the projected survival was 40%. In patients accumulated from 36 centers by the International Bone Marrow Transplant Registry, projected survival was 82% in 14 patients under 25 years of age and 52% in 25 patients over 25 years of age. We have determined the CLE/NLE ratio for two hypothetical patients aged 20 and 40 years in each of the three prognostic categories using the percent survival by age group from Seattle and the International Bone Marrow Transplant Registry (Figs 8 and 9).

Influence of Patient Age

For patients aged 20 years in prognostic categories I and II, a delay of 1 year prior to transplantation posed little additional risk to overall survival, in contrast to those patients in prognostic group III where the CLE/NLE ratio fell at an accelerated rate after 6 months (Fig 8). The result was similar in the analysis of the data from Seattle or the International Bone Marrow Transplant Registry.

For those patients 40 years of age, it was no longer clear that transplantation for group III patients should be undertaken within the first 6 months (Fig 9). In the Seattle series, the CLE/NLE ratio did not decrease significantly until 1 year following diagnosis. The International Bone Marrow

Fig 7. Influence of prognostic group on the CLE/NLE ratio. The CLE/NLE is the ratio of the calculated mean life expectancy to the normal life expectancy expressed as a percentage. In this analysis the prognostic group was determined from a hazard ratio function based on the patient's age, spleen size, platelet count, and the percentage of blasts in the blood as described by Sokal et al. The curves represent data for a cohort of 20-year-old patients with a 65% survival after transplantation in the chronic phase and a 20% success of transplantation in the accelerated or blastic phase of CML.

Fig 8. Influence of patient age on the CLE/NLE ratio in a 20-year-old cohort. The CLE/NLE is the ratio of the calculated mean life expectancy to the normal life expectancy expressed as a percentage. In this analysis the CLE/NLE ratio was calculated for the three prognostic groups using the published success rates for transplantation from Seattle and from the International Bone Marrow Transplant Registry (IBMTR). This Figure may be compared with Fig 9, which provides a similar analysis for 40-year-old patients.
Transplant Registry series had a higher projected survival for transplantation of older patients (52% vs 40%). The increased projected survival for transplantation results in a slightly more rapid decrease in the CLE/NLE ratio in group III patients reported by the International Bone Marrow Transplant Registry. Although transplantation should eventually be performed to achieve a normal life span in any of the patients, its delay may be justified when one considers the patient’s age and the projected survival with transplantation.

Other Risk Factors

Our analysis is based on the assumption that the delay in transplantation does not diminish the success of the procedure. There is a suggestion in studies performed in Seattle that there may be a decreased efficacy of transplantation as the duration of chronic phase of CML increases. A risk of this type could be incorporated into the analysis if this observation is substantiated. The computer program includes the option for inserting a factor less than 1 to indicate decreased projected survival for transplantation with increasing duration of chronic phase. If, for example, a 1-year delay results in only 80% of the projected survival for a transplantation performed at the time of diagnosis, a factor of 0.8 rather than 1.0 could be entered, and the CLE/NLE ratio would decrease as transplantation is delayed.

A second assumption is that successful transplantation results in a normal life span. Since no data are available, we have used a life span of 70 years for the purpose of analysis. If future clinical studies indicate a shortened life span after transplantation, a value less than 70 years can be entered into the program. We have conducted an analysis at a life span of 60 years for transplant recipients, and little change was observed in the shape of the CLE/NLE ratio curves, although a shortened life span tends to make early transplantation less desirable.

A related assumption is that the projected survival for transplant recipients already incorporates those patients who relapse after transplantation. If late posttransplant relapse reduces the survival further, the new, lower rate can be used in the analysis when this information becomes available. Such late relapse would tend to favor the delay of transplantation.

How To Assess The Computed Data

The model incorporates the impact of a patient’s age, prognostic group, and the success rate of transplantation. The program computes a prognostic parameter, the CLE/NLE ratio, which applies to a group of patients with similar characteristics. The CLE/NLE ratio is a summary statement of the risk of delaying marrow transplantation in CML. The ratio thus provides a specific concept that can be used to weigh treatment alternatives, and a common language for assessment of multiple variables by physicians who care for patients with CML.

The information should be used to integrate the observed variables and aid the physician and patient in the decision of when to transplant. The patient’s and physician’s own personalities and nonmedical factors in the patient’s life will also play a role in the timing of transplantation. The program, however, helps the physician and the patient to make an informed decision.

REFERENCES

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APPENDIX

Program Listing of CMLPROG.BAS

10 REM CMLPROG.BAS: CALC OF BOTH CLE/NLE AND CHANCE OF SURVIVAL
15 WIDTH 80
20 DIM S(10, 3): SCREEN 0, 0, 0: COLOR 7, 1, 1: KEYOFF: CLS
30 DIM TXP(20), CALC(20), CLE(20), CHANCE(20)
40 PRINT: PRINT: PRINT: PRINT: PRINT
50 PRINT "***************
60 PRINT "TIMING OF BONE MARROW TRANSPLANTATION IN CML**********
70 PRINT "G.B. SEGEL W. SIMON AND MA. LICHTMAN
80 PRINT "UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE ROCHESTER, NEW YORK 14642
90 PRINT "PRESS ANY KEY TO CONTINUE"
100 CLS
110 FOR M=0 TO 10: READ S(M, 1): NEXT M
120 FOR M=0 TO 10: READ S(M, 2): NEXT M
130 FOR M=0 TO 10: READ S(M, 3): NEXT M
140 PRINT "SURVIVAL PREDICTION FOR CML PATIENTS TREATED WITH BONE MARROW TRANSPLANT"
150 PRINT: PRINT: PRINT: PRINT
160 PRINT "ENTER PATIENT’S AGE (YEARS) "; AGE
170 IF AGE > 50 GOTO 2030
180 CLS: PRINT
190 FOR M=0 TO 10: READ SIM(1): NEXT M
200 FOR M=0 TO 10: READ SIM(2): NEXT M
210 FOR M=0 TO 10: READ SIM(3): NEXT M
220 PRINT "SURVIVAL PREDICTION FOR CML PATIENTS TREATED WITH BONE MARROW TRANSPLANT"
230 PRINT: PRINT: PRINT: PRINT
240 PRINT: PRINT
250 PRINT: PRINT
260 INPUT "ENTER PATIENT’S AGE (YEARS) "; AGE
270 IF AGE > 50 GOTO 2030
280 CLS: PRINT
L=L/100

INPUT "DO YOU WANT TO ENTER PROGNOSTIC GROUP OR PATIENT PARAMETERS?";
(PG FOR PROGNOSTIC GROUP OR RETURN FOR PATIENT PARAMETERS)"; W$

IF W$="PG" THEN 590
IF W$="pg" THEN 590
PRINT
PRINT "PARAMETERS TO DETERMINE PROGNOSTIC GROUP": PRINT: PRINT
INPUT "SPLEEN SIZE (CENTIMETERS BELOW LEFT COSTAL MARGIN)"; SPL: PRINT
INPUT "PLATELET COUNT (X 1000)"; PLT: PRINT
INPUT "PERCENTAGE OF BLASTS"; BLAST
A=EXP ((.0116)*(AGE – 43.4))
B=-(.0345)*(SPL – 7.51))
C=((.188)+((PLT/700)^2) – (.563))
D=-(8.869999E -02)*(BLAST – 2.1))
FCT=A+B+C+D
IF FCT<.78 THEN P=.1
IF FCT=.78 THEN P=2
IF (FCT>.78) AND (FCT<1.3) THEN P=2
IF FCT=1.3 THEN P=3
IF FCT>1.3 THEN P=.3
CLS: GOTO 600
PRINT: INPUT "PROGNOSTIC GROUP"; P
INPUT "FACTOR < 1 FOR DECREASING TXP CURE WITH DELAY (ENTER 1.0 IF NO DECREASE)"; F
F=F+.5
F=F+.5
INPUT "FILENAME FOR RESULTS" ; D$; CLS
OPEN D$ FOR OUTPUT AS #1
PRINT#1, "OUTPUT FILE" ; D$
PRINT "AGE= " ; AGE
PRINT "MEAN LIFE SPAN= " ; DAGE
IF FCT=0 GOTO 720
PRINT "RELATIVE RISK = " ; FCT
PRINT "PROGNOSTIC GROUP = " ; P
PRINT "SURVIVAL AFTER TRANSPLANT = " ; K*100; "%
PRINT "SURVIVAL AFTER TXP = " ; L*100; "%
PRINT "SALVAGE AFTER TRANSPLANT = " ; L*100; "%
PRINT "FACTOR FOR DECREASING TXP CURE WITH DELAY " ; F*2; " PER YR"
PRINT "FACTOR FOR DECREASING TXP CURE WITH DELAY " ; F*2; " PER YR"
PRINT "CACLE LIFE EXP" ; CLE/NLE ; "CHANCE OF SURV"
FOR Ti .=0 TO 5 STEP .5: REM TIME OF TRANSPLANT
J=T1/.5
IF J=0 THEN 900
K=(1-L)*T1
K=(1-L)*T1
L=MYEXP=(I-K)*T1
L=MYEXP=(I-K)*T1
R=GRAL=+MYEXP*(1-L)*T1
R=GRAL=+MYEXP*(1-L)*T1
S=+(S(J,P)+S((J-1),P))*25
S=+(S(J,P)+S((J-1),P))*25
T=T1+T

APPENDIX (Continued)
APPENDIX (Continued)

1020 K = F + K
1030 IF K < 0 THEN K = 0
1040 L = F + L
1050 IF L < 0 THEN L = 0
1060 NEXT T1
1070 PRINT
1080 PRINT "TO CONTINUE TOUCH ANY KEY"
1090 A$ = INKEY$: IF A$ = "" THEN 1100
1100 CLOSE #1
1110 CLS: CLOSE ALL
1120 OPEN A-Z FOR INPUT AS #1
1130 COUNT = 0
1140 SCREEN 2.0: KEY OFF
1150 DEF A-Z
1160 OPEN D$ FOR INPUT AS #1
1170 XMAX = 10
1180 DEF FNX(X) = 60 + X/550/XMAX
1190 DEF FNY(Y) = 16 + (YMAX - Y) / 160 / YMAX
1200 GOSUB 1300 'INPUT DATA ------------------------
1210 GOSUB 1370 'ESTABLISH X&Y AXES -------------
1220 GOSUB 1400 'DRAW X&Y AXES------------------
1230 GOSUB 1690 'DRAW DATA POINTS----------------
1240 A$ = INKEY$: IF A$ = " " THEN 1240
1250 CLOSE #1
1260 SCREEN 0,0,0: COLOR 7, 1, 1: CLS: KEY OFF
1270 INPUT "DO YOU WANT TO ENTER MORE DATA? (Y OR N) " ; AN$
1280 IF (AN$ = "Y") OR (AN$ = "y") THEN CLS: RUN
1290 END
1300 INPUT#1, A$ 'INPUTDATA
1310 IF (INSTR(A$, "TIME") = 0) GOTO 1300
1320 COUNT = COUNT + 1
1330 IF EOF(1) THEN 1360
1340 INPUT#1, TXP(COUNT), CALC(COUNT), CLE(COUNT), CHANCE(COUNT)
1350 GOTO 1320
1360 RETURN
1370 XMAX = 10 'ESTABLISH X&Y AXES----------------
1380 YMAX = 100
1390 RETURN
1400 'DRAW LABELS AND AXES----------------------
1410 LINE (FNX(0), FNY(YMAX)) - (FNX(0), FNY(0))
1420 LINE (FNX(XMAX), FNY(0))
1430 LOCATE 3, 10: PRINT "------";
1440 LOCATE 3, 21: PRINT "CLE/NLE IF NO DISEASE"
1450 LOCATE 3, 1: PRINT YMAX;
1460 LOCATE 7, 2: PRINT "PER-";
1470 LOCATE 8, 2: PRINT "CENT";
1480 LOCATE 13, 1: PRINT YMAX/2;
1490 LOCATE 24, 41: PRINT XMAX/2;
1500 LOCATE 24, 75: PRINT XMAX;
1510 LOCATE 25, 36: PRINT "YEARS AFTER DX";
1520 LOCATE 1, 36: PRINT D$;
1530 LOCATE 5, 42: PRINT "CLOSED SYMBOLS: CLE/NLE"
1540 LOCATE 6, 42: PRINT "OPEN SYMBOLS: CHANCE OF SURVIVAL"
1550 LOCATE 10, 48: PRINT "AGE = "; DAGE
1560 LOCATE 11, 46: PRINT "MEAN LIFE SPAN = "; DAGE
1570 IF FCT = 0 THEN 1590
1580 LOCATE 12, 46: PRINT "RELATIVE RISK = "; FCT
1590 LOCATE 13, 46: PRINT "PROGNOSTIC GROUP = "; P
1600 LOCATE 14, 46: PRINT "SURVIVAL AFTER TXP = "; SURV; "%
1610 LOCATE 15, 46: PRINT "SALVAGE AFTER TXP = "; SALV; "%
1620 LOCATE 16, 46: PRINT "DELAY FACTOR = "; F. 2
1630 FOR Y = 0 TO YMAX STEP YMAX/10
1640 LINE (58, FNY(Y)) - (62, FNY(Y))
1650 NEXT Y
APPENDIX (Continued)

1660 FOR X = 0 TO XMAX STEP XMAX/10
1670 LINE (FNX(X), 174) – (FNX(X), 178)
1680 NEXT X : RETURN

1690 COUNT = COUNT – 1
1700 FOR I = 1 TO COUNT
1710 X = TXP(I)
1720 Y = CLE(I)
1730 IF CLE(I) = 0 THEN GOTO 1750
1740 LINE (FNX(X) – 2, FNY(Y) – 2) – STEP(4, 4), 1, BF
1750 NEXT I

1760 I = 0
1770 FOR I = 1 TO COUNT
1780 X1 = TXP(I)
1790 X2 = TXP(I – 1)
1800 Y1 = CLE(I)
1810 Y2 = CLE(I – 1)
1820 IF Y1 = 0 GOTO 1840
1830 LINE (FNX(X1), FNY(Y1)) – (FNX(X2), FNY(Y2))
1840 NEXT I

1850 I = 0
1860 FOR I = 1 TO COUNT
1870 X = TXP(I)
1880 Y = CHANCE(I)
1890 LINE (FNX(X) – 2, FNY(Y) – 2) – STEP(4, 4), B
1900 NEXT I
1910 FOR I = 1 TO COUNT
1920 X1 = TXP(I)
1930 X2 = TXP(I – 1)
1940 Y1 = CHANCE(I)
1950 Y2 = CHANCE(I – 1)
1960 LINE (FNX(X1), FNY(Y1)) – (FNX(X2), FNY(Y2))
1970 NEXT I
1980 RETURN

1990 ' DATA I,.99,.97,.93,.88,.84,.78,.72,.66,.61,.55
2000 DATA 1,.98,.95,.88,.80,.72,.64,.54,.47,.42,.38
2010 DATA 1,.97,.87,.74,.63,.50,.39,.29,.21,.16,.12
2020 DATA 1,.99,.97,.93,.88,.84,.78,.72,.66,.61,.55
2030 DATA 1,.98,.95,.88,.80,.72,.64,.54,.47,.42,.38
2040 DATA 1,.97,.87,.74,.63,.50,.39,.29,.21,.16,.12

The authors will provide a copy of this program to interested readers who supply a blank 5½” magnetic disk that will run on IBM-compatible computers.
Variables influencing the timing of marrow transplantation in patients with chronic myelogenous leukemia

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