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

By George B. Segel, William Simon, and Marshall A. Lichtman

The prognosis for patients with chronic myelogenous leukemia (CML) treated with chemicals or radiation has not changed substantially over the past 50 years and more than 70% within about 5 years of diagnosis. The advent of marrow transplantation from allogeneic sibling donors has led to an increase in the proportion 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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The combined expectancy without salvage. This Figure represents a hypothetical example. Bone marrow transplantation is performed at time $T_1$ and transplantation if accelerated disease develops before $T_1$, is as follows:

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

(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,

$$\text{Life expectancy (years)} = \int_0^{T_1} S(t) dt + KS(T_1) \cdot (T - T_1).$$

(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...
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:

\[
 S'(t) = 1 - \left[ 1 - S(t) \right] (1 - L) - S(t) + L \left[ 1 - S(t) \right]
\]  

(3)

and add \([S'(T_1) - S(T_1)](T - T_1)\), which is the increment in survival rate resulting from transplantation in the accelerated phase.

**Life expectancy**

\[
 \int_{T_1}^{T} S'(t) \, dt + [K S(T_1) + S(T_1) - S(T_1)](T - T_1)
\]

(4)

\[
 \int_{T_1}^{T} S'(t) \, dt - \int_{T_1}^{T} [S(t) + L [1 - S(t)]] \, dt
\]

\[
 = LT_1 + (1 - L) \int_{T_1}^{T} S'(t) \, dt
\]

(5)

\[
 KS(T_1) + S(T_1) - S(T_1) = KS(T_1) + L [1 - S(T_1)]
\]

(6)

**Life expectancy**

\[
 LT_1 + (1 - L) \int_{T_1}^{T} S(t) \, dt + (T - T_1) \left[ L + (K - L)S(T_1) \right]
\]

(7)

**Life expectancy (years)**

\[
 LT + (K - L)S(T_1) (T - T_1) + (1 - L) \int_{T_1}^{T} S(t) \, dt.
\]

(8)

This latter result appears complicated because the acute-phase transplantation can occur at any time within \( T_1 \) 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'-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.
rate of salvage for transplant recipients during the accelerated phase 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 of CML. The CLE/NLE ratio 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.

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, myeloblasts in the blood and bone marrow, and thrombocytopenia or thrombocytosis as indicators of prognosis. The Philadelphia chromosome and myelofibrosis 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, Ph-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

<table>
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<th>Transplantation Time</th>
<th>Calculated Life Expectancy (yr)</th>
<th>CLE/NLE (%)</th>
<th>Chance of Survival (%)</th>
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<td>20.5</td>
<td>41.0</td>
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TIMING OF MARROW TRANSPLANTATION IN CML

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.

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, ie, 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). A value of 20% was used in this analysis for the salvage of patients who were transplanted after onset of the accelerated phase.

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
Transplant Registry series had a higher projected survival for transplantation of older patients (52% v 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


4. Thomas ED, Clift RA, Fefer A, Appelbaum FR, Beatty P, Bensinger WI, Buckner CD, Cheever MA, Deeg HJ, Doney K,
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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 "#{149}#{149}#{149}#{149}....................
60 PRINT "
70 PRINT " ####### TIMING OF BONE MARROW TRANSPLANTATION IN CML #######
80 PRINT "
90 PRINT " ####### G.B. SEGEL W. SIMON AND M.A. LICHTMAN #######
100 PRINT "
110 PRINT " ####### UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE #######
120 PRINT " ROCHESTER, NEW YORK 14642 #######
130 PRINT "
140 PRINT "
150 PRINT: PRINT: PRINT: PRINT: PRINT
160 PRINT "PRESS ANY KEY TO CONTINUE"
170 AS=INKEY$: IF AS="" THEN 170
180 CLS
190 FOR M=0 TO 10: READ S(M, 1): NEXT M
200 FOR M=0 TO 10: READ S(M, 2): NEXT M
210 FOR M=0 TO 10: READ S(M, 3): NEXT M
220 PRINT "SURVIVAL PREDICTION FOR CML PATIENTS TREATED WITH BONE MARROW TRANSPLANT"
230 PRINT
240 PRINT
250 PRINT
260 INPUT "ENTER PATIENT'S AGE (YEARS) ": AGE
270 IF AGE >50 GOTO 2030
280 CLS: PRINT
290 INPUT "ENTER TOTAL MEAN LIFE SPAN (NORMAL=70) (YEARS) ": DAGE
300 PRINT
310 T=DAGE–AGE: PRINT: PRINT: CLS
320 PRINT
330 INPUT "PROJECTED SURVIVAL VIA TRANSPANTATION (%) ": K
340 SURV=K
350 K=K/100
360 INPUT "PROJECTED SALVAGE VIA TRANSPANTATION IN ACCELERATED/BLASTIC PHASE (%) ": L
370 SALV=L
380 CLS
APPENDIX (Continued)

390   L=L/100
400   INPUT "DO YOU WANT TO ENTER PROGNOSTIC GROUP OR PATIENT PARAMETERS?"
410   IF W$="PG" THEN 590
420   IF W$="pg" THEN 590
430   PRINT
440   PRINT "PARAMETERS TO DETERMINE PROGNOSTIC GROUP": PRINT: PRINT
450   INPUT "SPLEEN SIZE (CENTIMETERS BELOW LEFT COSTAL MARGIN) ";SPL: PRINT
460   INPUT "PLATELET COUNT (X 1000) ";PLT: PRINT
470   INPUT "PERCENTAGE OF BLASTS"
480   A=EXP((.0116)*(AGE-43.4))
490   B=(.0345)*(SPL-7.51))
500   C=((.1 88).(((PLT/700)'2)-(.-563)))
510   D=-(.869999E -.02) (BLAST-2.1))
520   FCT=A+B+C+D
530   IF FCT<.78 THEN P= 1
540   IF FCT-.78 THEN P=2
550   IF (FCT>.78) AND (FCT<1.3) THEN P=2
560   IF FCT=1.3 THEN P=3
570   IF FCT>.1.3THEN P-.3
580   CLS: GOTO 600
590   PRINT: INPUT "PROGNOSTIC GROUP- ";P
600   PRINT "FACTOR < 1 FOR DECREASING TXP CURE WITH DELAY (ENTER 1.0 IF NO DECREASE) ";F
610   F=F-.5
620   INPUT "FILENAME FOR RESULTS ";D$: CLS
630   OPEN D$ FOR OUTPUT AS #1
640   PRINT#1, "OUTPUT FILE ";D$:
650   PRINT "AGE = ",AGE
660   PRINT "MEAN LIFE SPAN= ",DAGE
670   PRINT "RELATIVE RISK = "; FCT
680   PRINT "PROGNOSTIC GROUP= "; P
690   IF FCT-O GOTO 720
700   PRINT "RELATIVE RISK = "; FCT
710   PRINT "PROGNOSTIC GROUP= "; P
720   PRINT "SURVIVAL AFTER TRANSPLANT= ";K*100; "%"
730   PRINT "SURVIVAL AFTER TXP = "; K*100; "%"
740   PRINT "SALVAGE AFTER TRANSPLANT= ";L*100; "; %"
750   PRINT "SALVAGE AFTER TXP = "; L*100; "%;"
760   PRINT "FACTOR FOR DECREASING TXP CURE WITH DELAY "; F*2; " PER YR"
770   PRINT "FACTOR FOR DECREASING TXP CURE WITH DELAY "; F*2; " PER YR"
780   PRINT "CALC LIFE EXP";
790   PRINT "CALC LIFE EXP"
800   PRINT "CALC LIFE EXP"
810   PRINT "CALC LIFE EXP"
820   PRINT "CALC LIFE EXP"
830   PRINT "CALC LIFE EXP"
840   PRINT
850   SAL=0
860   FOR T=0 TO 5 STEP .5: REM TIME OF TRANSPLANT
870   J=T/.5
880   IF J=0 THEN 900
890   GRAL=GRAL + (S(J,P)) + S(J-1,P))*.25
900   MYEXP=(1-L)*GRAL + L*T+(T-T1)*S(J,P)*(K-L)
910   TN=70-AGE
920   R=(MYEXP/TN)*100
930   C=((K+(S(J,P)))+(L*1-(S(J,P))))*100
940   IF MYEXP<T1 THEN R=0
950   IF W$="T1 THEN GOTO 990
960   PRINT T1, MYEXP, R; "; C; "%
970   PRINT T1, MYEXP, R, C
980   GOTO 1010
990   PRINT T1, MYEXP, R, C; "%
1000 PRINT#1, MYEXP, R, C
1010
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 T
1070  PRINT
1080  PRINT "TO CONTINUE TOUCH ANY KEY"
1090  A$ = INPUT$: IF A$ = "" THEN 1100
1100  CLOSE #1
1110  CLS: CLOSE ALL
1120  DEFNG A-Z
1130  OPEN #1 FOR INPUT AS #1
1140  COUNT = 0
1150  SCREEN 2.0 : KEY OFF
1160  INPUT "DO YOU WANT TO ENTER MORE DATA? (Y OR N)" ; AN$
1170  IF (INSTR(A$, "TIME") = 0) THEN 1300
1180  XMAX = 10 'ESTABLISH X&Y AXES-
1190  YMAX = 100
1200  GOSUB 1300 'INPUT DATA
1210  'ESTABLISH X&Y AXES
1220  'DRAW X&Y AXES
1230  'DRAW DATA POINTS
1240  A$ = INPUT$: IF A$ = "" 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$, "TIME") = 0) THEN 1300
1320  COUNT = COUNT + 1
1330  IF EOF(1) THEN 1360
1340  INPUT #1, TXP(COUNT), CALC(COUNT), CLE(COUNT), CHANCE(COUNT)
1350  GOTO 1320
1360  RETURN
1370  XMAX = 10 'ESTABLISH X&Y AXES-
1380  YMAX = 100
1390  RETURN
1400  'DRAW LABELS AND AXES-
1410  LINE (FNX(0), FNY(YMAX)) - (FNX(0), FNY(0))
1420  LINE -(FNX(XMAX), FNY(0))
1430  LOCATE 3,10: PRINT "CLE/NLE IF NO DISEASE"
1440  LOCATE 3,1: PRINT "YMAX;"
1450  LOCATE 7,2: PRINT "PER;"
1460  LOCATE 8,2: PRINT "CENT;"
1470  LOCATE 13,1: PRINT "YMAY/2;"
1480  LOCATE 24,4: PRINT "XMAX/2;"
1490  LOCATE 24,7: PRINT "XMAX;"
1500  LOCATE 25,36: PRINT "Y YEARS AFTER DX;"
1510  LOCATE 1,36: PRINT "D$"
1520  LOCATE 5,42: PRINT "CLOSED SYMBOLS: CLE/NLE"
1530  LOCATE 6,42: PRINT "OPEN SYMBOLS: CHANCE OF SURVIVAL"
1540  LOCATE 10,48: PRINT "MEAN LIFE SPAN - ; DAGE"
1550  LOCATE 11,46: PRINT "RELATIVE RISK - ; FCT"
1560  LOCATE 13,46: PRINT "PROGNOSTIC GROUP - ; P"
1570  IF FCT = 0 THEN 1580
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))
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  'DRAWS SQUARES---------
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 = 2 TO COUNT  'DRAWS LINE---------
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 = 2 TO COUNT  'DRAWS LINE---------
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
2000 DATA .1,.9,.97,.93,.88,.84,.78,.72,.66,.61,.55
2010 DATA 1,.98,.95,.88,.80,.72,.64,.54,.47,.42,.38
2020 DATA 1,.97,.74,.63,.50,.39,.29,.21,.16,.12
2030 CLS: PRINT "PATIENT NOT ELIGIBLE FOR TRANSPLANT IF AGE > 50 YEARS!": END

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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