ELSEVIER

Sign of the Zodiac as a Predictor of Survival for Recipients of an Allogeneic Stem Cell Transplant for Chronic Myeloid Leukaemia (CML): An Artificial Association

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ABSTRACT

Background. Astrological or Zodiac (star) sign has been shown to be a statistically significant factor in the outcome of a variety of diseases, conditions, and phenomena.

Methods. To investigate its relevance in the context of a stem cell transplant (SCT), we examined its influence in chronic myeloid leukaemia, a disease with well-established prognostic factors. Data were collected on 626 patients who received a first myeloablative allogeneic SCT between 1981 and 2006. Star sign was determined for each patient.

Results. Univariate analyses comparing all 12 individual star signs showed considerable variation of 5-year probabilities of survival, 63% for Arians, to 45% for Aquarians, but without significance ($P = .65$). However, it was possible to pool together star signs likely to provide dichotomous results. Thus, grouping together Aries, Taurus, Gemini, Leo, Scorpio, and Capricorn (group A; $n = 317$) versus others (group B; $n = 309$) resulted in a highly significant difference (58% vs 48%; $P = .007$). When adjusted for known prognostic factors in a multivariate analysis, group B was associated with an increased risk of mortality when compared with group A (relative risk [RR], 1.37; $P = .005$).

Conclusion. In this study, we show that, providing adequate care is taken, a significant relationship between patient star sign and survival post SCT for CML can be observed. This is, however, a completely erroneous result, and is based on the pooling together of observations to artificially create a statistically significant result. Statistical analyses should thus be carried out on *a priori* hypotheses and not to find a meaningful or significant result.

THE ASSOCIATION of astrological star sign (zodiac) with health and health care outcomes has previously been investigated in numerous studies,[1–10] and has been shown to be a significant factor in the determination of a variety of diseases and conditions, including schizophrenia,[1] gastrointestinal (GI) hemorrhage,[2] upper limb fractures,[2] fertility,[3] and suicidal disposition.[4,5] In addition, a report by Doblhammer and Vaulpel[11] showed that lifespan is associated with an individual's month of birth. Thus, there is clear potential for studying the relationship between date of birth and outcome. To investigate the relevance of this factor in the context of stem cell transplantation (SCT), we examined the influence of date of birth using the surrogate marker of zodiac star sign in a cohort of patients with chronic myeloid leukemia (CML). This disease has well-established and validated prognostic factors that are incorporated in the EBMT/Gratwohl scoring system,[12] and is thus an excellent model for teasing out potential new factors.

PATIENTS

All patients >16 years old (median, 33; range, 16–59) who underwent myeloablative allogeneic SCT for CML between 1981 and 2006 were included in this study (first chronic phase [$n = 474$], accelerated phase [$n = 95$], blastic phase [$n = 25$], second chronic phase [$n = 32$]). Stem cell donors were either HLA-identical siblings ($n = 364$; 58%) or HLA-matched unrelated donors (MUD; $n = 262$; 42%). Conditioning consisted of total body irradiation and intravenous cyclophosphamide. All patients received graft-versus-host

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0041-1345/10/$–see front matter
doi:10.1016/j.transproceed.2010.07.036

disease prophylaxis, which consisted, in the main, of either cyclosporine (CSA) and methotrexate (MTX) in 314 patients with related donors (86.2%), and CSA and MTX in addition to T-cell depletion for the MUD ($n = 253$; 96.5%).

METHODS

Star sign was determined for each patient based on their date of birth. The primary end point of interest in this study was survival. Survival curves were generated using the Kaplan-Meier method, and the log-rank test used to compare groups. Gratwohl scores were calculated for each patient on the basis of disease stage, donor type, recipient age, donor/recipient gender combination, and interval from diagnosis to transplant, allowing characterisation into 4 distinct groups (Table 1). The prognostic significance of star sign was investigated firstly in univariate analyses, and then in multivariate analyses that included the Gratwohl scoring system and year of transplant. $P < .05$ was considered significant.

RESULTS

The variables incorporated in the Gratwohl scoring system, and their influence on survival, are shown in Table 1. As expected, patients transplanted in an advanced disease phase, from a MUD, with a duration of disease before SCT of >1 year, or age >40 years had inferior survival probabilities. No influence due to recipient/donor gender mismatch was observed. The Gratwohl scoring system predicted well for those patients who were at high risk for poor survival (i.e., high Gratwohl score), but was less able to differentiate the 2 groupings with the lowest scores (hence best survival prognosis). The influence of year of transplant showed that significant improvement has been achieved in the last epoch.

Table 1. Probabilities of Survival at 5 Years After SCT for Standard Risk Factors

Parameter	*n*	Probability of Survival	*P*
Patient age (y)			.094
<20	32	54.9	
20–40	408	56.7	
>40	186	45.6	
Disease stage at SCT			>.0001
First CP	474	60.9	
AP	95	37.4	
Second CP/BC	57	15.8	
Duration of disease pre-SCT (y)			.0002
<1	241	64.6	
≥1	384	46.4	
Donor type			.004
Identical sibling	364	58.4	
MUD	262	46.3	
Patient/donor gender match			.40
Male/female	143	53.3	
Other	481	53.5	
Transplant era			.002
2/81–5/89	155	48.4	
6/89–11/93	156	47.4	
12/93–6/98	157	51.5	
7/98–9/06	158	66.9	
Gratwohl score			.0004
0–1	85	72.4	
2	175	69.5	
3	185	48.8	
4–7	178	33.1	

Table 2. Probabilities of Survival at 5 Years After SCT for Zodiac Star Signs

Parameter	*n*	Probability of Survival	*P*
Star sign (calendar dates D/M)			.65
Aries (21/3–19/4)	44	62.9	
Taurus (20/4–20/5)	43	58.1	
Gemini (21/5–20/6)	54	56.8	
Cancer (23/7–22/8)	63	48.8	
Leo (23/7–22/8)	59	57.3	
Virgo (23/8–22/9)	54	46.3	
Libra (23/9–22/10)	54	51.0	
Scorpio (23/10–21/11)	56	59.6	
Sagittarius (22/11–21/12)	54	48.1	
Capricorn (22/12–19/1)	61	56.3	
Aquarius (20/1–18/2)	35	44.5	
Pisces (19/2–20/3)	49	49.7	
Star sign groups			.007
Group A (Aries, Taurus, Gemini, Leo, Scorpio, Capricorn)	317	58.3	
Group B (Cancer, Virgo, Libra, Sagittarius, Aquarius, Pisces)	309	48.1	

Univariate analysis comparing all 12 individual star signs showed considerable variation with respect to their probability of survival at 5 years; however, there was no significant overall difference ($P = .65$; Table 2). The comparison of the 5-year survival probabilities for Arians (63%) and Aquarians (45%) was of borderline nonsignificance ($P = .071$; Fig 1). When grouped according to their elements, fire-vital (Aries, Leo, Sagittarius), earth-physical (Taurus, Virgo, Capricorn), air-mental (Gemini, Libra, Aquarius), and water-emotional (Cancer, Scorpio, Pisces), no statistical difference was observed ($P = .75$). However, it was possible, using observational methods, to pool together star signs

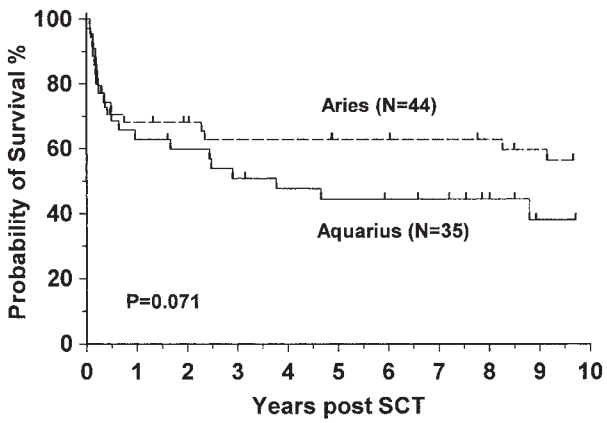

Fig 1. Probabilities of survival after SCT for patients born under the star signs Aries and Aquarius.

likely to provide dichotomous results. Thus, grouping together Aries, Taurus, Gemini, Leo, Scorpio, and Capricorn (group A; $n = 317$) versus others (group B; $n = 309$) resulted in a highly significant difference (58% vs 48% at 5 years; $P = .007$; Fig 2).

When adjusted for Gratwohl score and transplant era in a Cox proportional hazards regression analysis, patients with star signs in group B were associated with an increased risk of mortality when compared with group A (relative risk [RR], 1.37; $P = .005$; Table 3). The influence of patient star sign was thus confirmed in this large cohort of transplant patients.

DISCUSSION

This study was devised to investigate the influence of a controversial parameter on survival after SCT. For this investigation to have a sound basis, it was important to use a disease model with well-established prognostic factors; thus our choice of CML. Our initial investigation failed to find any significant relationship between star sign and survival. However, by pooling together those star signs with the best outcomes versus those with the poorest, a robust result was obtained, even when adjusted for by established prognostic factors. However, this 'significant' result was obtained on the basis of a flawed scientific method-namely, the pooling together of groups with no scientific communality, for the explicit reason of achieving significance. The problem with such an approach is that the post hoc intervention of grouping eliminates the element of chance, which is precisely the basis for the statistical test in the first instance.

The pooling or grouping of data is admissible in the case of adjacent categories, and if there is scientific justification. When dealing with continuous variables, the interpretation of results is often considerably easier if the values are 'reduced' to groups with established cutoff values. However, the seeking of a cutoff value that provides a statistically significant difference is inappropriate. Herein lies the root of the problem: studies that show significant results are considerably more likely to be published than those that have negative findings. Not only does this cause an underrepresentation of studies that show no differences in treatment groups, actual treatment efficacies may be overstated.[13]

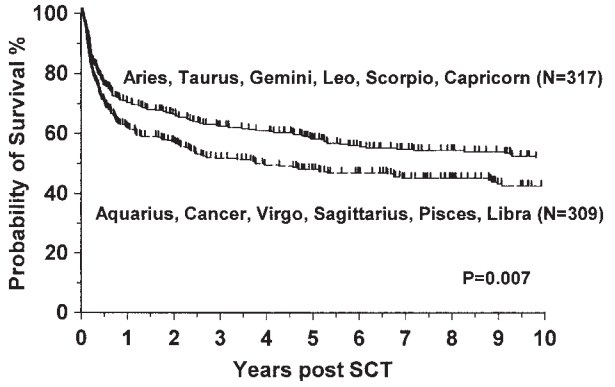

Fig 2. Probabilities of survival after SCT for patients born under the different star sign groupings.

Table 3. Multivariate Analysis of Survival

Variable	*n*	Relative Risk	CI 95%	*P*
Gratwohl score				
0–1	85	1.00		
2	175	1.13	0.7–1.8	.59
3	185	1.94	1.3–2.9	.002
4–7	178	3.47	2.3–5.2	.001
Transplant era				
2/81–5/89	155	1.00		
6/89–11/93	156	0.77	0.58–1.02	.072
12/93–6/98	155	0.62	0.46–0.84	.002
7/98–9/06	157	0.45	0.32–0.64	.0001
Zodiac sign				
Group A	316	1.0		
Group B	307	1.37	1.1–1.7	.005

The trawling and reanalysis of data to find significant results is not a new concept, and was demonstrated in the ISIS-2 trial, where multiple testing of subgroups resulted in significant results of dubious scientific merit.[15] In an interesting publication by Gelman and Stern,[16] the authors argue that our obsession with significance and nonsignificance overshadows the practical implications of the research findings. Large changes in significance levels may correspond with small, nonsignificant changes in the underlying quantities or outcomes.

To counteract the publication bias problem in the field of clinical trials, two initiatives have been undertaken. In 2000, the US National Institutes of Health (NIH) established clinicaltrials.gov, a publicly accessible database of trials and then in 2005, the International Committee of Medical Journal Editors began requiring that trials be registered in a public database prior to enrolling the first patient, in order to be considered for publication. These measures would appear to be redressing the balance.[14]

In the present study, we have demonstrated that providing adequate care is taken (ie, manipulation of the data), a significant relationship between patient Zodiac sign and survival after SCT for CML can be observed. We can postulate that any pseudoscientific parameter can be manipulated to give a seemingly 'important' result, however implausible. Critical awareness therefore, must be maintained, both with the presentation of significant and nonsignificant results.

REFERENCES

1. Ohaeri JU: The planetary positions and relationships at the dates of birth of a cohort of Nigerian schizophrenics. Afr J Med Med Sci 26:127, 1997

2. Austin PC, Mamdani MM, Juurlink DN, et al: Testing multiple statistical hypotheses resulted in spurious associations: a study of astrological signs and health. J Clin Epidemiol 59:964, 2006

3. Yip PS, Lee J, Cheung YB: The influence of the Chinese zodiac on fertility in Hong Kong SA.

4. Salib E: Astrological birth signs in suicide: hypothesis or speculation? Med Sci Law 43:111, 2003

5. Stack S, Lester D: Born under a bad sign? Astrological sign and suicide ideation. Percept Mot Skills 66:461, 1988

6. Jelinek L, Hottenrott B, Moritz S: When cancer is associated with illness but no longer with animal or zodiac sign: investigation of biased semantic networks in obsessive-compulsive disorder (OCD). J Anxiety Disord 23:1031, 2009

7. May M, Braun KP, Helke C, et al: Lunar phases and zodiac signs do not influence quality of radical cystectomy--a statistical analysis of 452 patients with invasive bladder cancer. Int Urol Nephrol 39:1023, 2007

8. Petrovecki M, Rahelić D, Bilić-Zulle L, et al: Factors influencing medical informatics examination grade--can biorhythm, astrological sign, seasonal aspect, or bad statistics predict outcome? Croat Med J 44:69, 2003

9. Angst J, Scheidegger P. Signs of the zodiac and personality. Soz Praventivmed 21:39, 1976

10. Wolbank S, Prause G, Smolle-Juettner F, et al: The influence of lunar phenomena on the incidence of emergency cases. Resuscitation 58:97, 2003

11. Doblhammer G, Vaupel JW: Lifespan depends on month of birth. Proc Natl Acad Sci USA 98:2934, 2001

12. Gratwohl A, Hermans J, Goldman JM, et al: Risk assessment for patients with chronic myeloid leukaemia before allogeneic blood or marrow transplantation. Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation. Lancet 352:1087, 1998

13. Sena ES, van der Worp HB, Bath PMW, et al: Publication bias in reports of animal stroke studies leads to major overstatement of efficacy. PLoS Biol 8:3, 2010

14. Tuma RS: New law may be having some effect on publication bias. J Natl Cancer Inst 102:290, 2010

15. ISIS-2 (Second International Study of Infarct Survival) Group: Randomized trial of intravenous streptokinase, oral aspirin, both, or neither, among 17187 cases of suspected acute myocardial infarction: ISIS-2. Lancet ii:349, 1988

16. Gelman A, Stern H: The difference between “significant” and “not significant” is not Itself statistically significant. Am Stat 60:328, 2006