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Title

Physicians' prognostic estimates of survival for patients undergoing allogeneic hematopoietic stem cell transplantation[1]

Running title

Physicians' prognosis estimates

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Summary

Objective: To evaluate the subjective prognosis estimates of physicians given before performing allogeneic HSCT.

Patients / Methods: 140 patients were recruited from the transplant units at the university hospitals in Ulm and Tübingen, Germany. Each patient was to be followed-up on for at least two years. After admission for HSCT, the respective attending physicians were asked „What is your overall prognosis for the patient?" and answered based on a scale from 1 (very good) to 6 (very bad). 136 ratings were evaluable. Kaplan-Meier survival curves and Cox regression models were used to evaluate survival times.

Results: A 1-point less favourable prognosis on the scale correlates to a 50% increase in the mortality risk (Cox-Regression: hazard ratio HR = 1.51, 95%-CI = 1.25 – 1.82, $p < .001$).

Conclusion: The prognosis estimates of the physicians before the transplant procedure are valid. It is still unclear, how the physicians arrive at their individual prognoses. It seems to involve a complex evaluation process, which, however, would have to be empirically verified. More information about this implicit evaluation process might improve the informed consent procedure and could help improve the training of future haematologists.

Keywords

Survival, prognosis, prospective study, informed consent

Introduction

When obtaining informed consent, the attending physicians inform the patients in detail about the transplant procedure before they undergo HSCT. For most patients it is very important to know what their physician thinks about their chances for recovery and they quite often demand to be told. Thus, the physician is often forced to make a statement about the individual patient's prognosis and chances for recovery. So far, there has been little research regarding the accuracy of these statements. Existing studies (e.g. [1-8]) regarding the quality of the physician's prognosis often originate from intensive care units. The results are heterogeneous and include various illnesses, different therapies, and prognosis goals. In summary, the reports seem to indicate that the physician's prognosis correlates with the respective outcome. In addition, some findings show that objective parameters are not necessarily more precise than subjective estimates [3].

There are two studies within the field of HSCT dealing with physicians' prognoses. Dobkin et al. [9] analysed the survival times of 68 pediatric patients who underwent bone marrow transplantations and the physicians' prognoses before the transplantation. The prognoses were based on a rating scale from 0 to 5 and turned out to be a significant prediction tool for the survival time of patients after a bone marrow transplant. Lee et al.[10] interviewed 313 patients and their attending physicians about their prognosis estimates before an allogenic or autologous stem cell transplantation. They were asked to indicate on a 6-point Likert-scale to estimate the individual patient's chances of recovery with and without the bone marrow transplant, and how high they see the risk for the patient to die within one year of the transplantation. The researchers surveyed the 1-year-mortality. Both attending physicians and patients were relatively precise in their prognoses when actual mortality was less than 30%. In groups with higher mortality, the physicians underestimated the mortality chances somewhat, the patients quite significantly. We are not aware of any further research regarding HSCT that scientifically evaluates the subjective prognosis estimates of physicians.

Our own initial research (data collected between 1990 and 1995) gave some indication that transplant physicians were able to predict future outcome (overall survival) in 45 leukemia patients based on a 5-point-Likert-scale ranging from „very

good“ to „very bad“ [11]. A less favourable physician prognosis by one point, was associated with a relative risk of 1.49 (95%-CI = 1.02 – 2.17, p = .04). In 1999 [12], we launched a major psycho-oncology intervention study, aiming at reducing emotional stress and adverse side effects of treatment during the patient's inpatient stay for allogenic HSCT and to improve the patient's quality of life. The psychosocial interventions had, as expected, no influence on the survival times (results not reported here). This study also provided us with the opportunity to investigate the validity of the physician's prognosis.

Patients and Methods

The study was approved by the Ethics committee of Ulm University. From 9/1999 to 12/2001, we recruited 140 patients for the psycho-oncology study from the transplant units at the university hospitals in Ulm and Tübingen. Each patient was to be followed-up on for at least two years.

Patients

The majority of the 140 examined patients are male (59%). The average participant in the sample is 41 years old (range 18 – 61). Nearly 80% of them are in a steady relationship, about 70% have children, and most of them manage their own household (80%). About 40% of the patients have been educated at school for 9 years, a third for 10 years, and a quarter for 13 years. Nearly 50% of the patients were treated for acute leukemia. About 20% were diagnosed with CML. 15% received the transplant due to malignant lymphoma. Two thirds of the patients received peripheral blood stem cells, and one third received bone marrow. Half of the donors are related to the recipients. Only in about 10% of the cases, the HSCT was carried out without HLA-identical donors. The patients were treated in accordance with customary standards.

Measuring Method

After the patients were admitted for HSCT and after having given their informed consent, the respective attending physicians of the transplant unit were asked to make a prognosis based on a scale from 1 to 6:

„What is your overall prognosis for the patient?
very good 1 - 2 - 3 - 4 - 5 - 6 very bad“

This scale is based on the established and in Germany well-known marking system of German schools.

Statistical Evaluation

We calculated the normal descriptive statistics. Comparisons of arithmetic means were carried out using t-tests or simple variance analyses. The survival time of a patient (overall survival) is calculated in days after HSCT up to the day the patient died or the last documented contact of the patient with the transplant centre. We used the Kaplan-Meier survival curves and Cox regression models to evaluate survival times and SPSS software for Windows (Version 11.0.1; SPSS Inc., Chicago, Ill.) for the evaluation.

Results

For four patients, the physician's prognosis was not available. The frequency distribution of the prognosis estimates is illustrated in table 1. The mean was at 3.1 (median 3.0) with a standard deviation of 1.23. The entire scale spectrum was utilized. The two most extreme categories were rarely used. Based on this distribution, it made sense to always combine two levels of the ranking scale.

Table 1: Physician's prognoses – Frequency distribution for raw data and grouped values

Prognosis	1	2	3	4	5	6	Total
Frequency	6	49	33	27	17	4	136
%	4.4	36.0	24.3	19.9	12.5	2.9	100.0
Prognosis Group	good		medium		poor		
Frequency	55		60		21		136
%	40.4		44.2		15.4		100.0

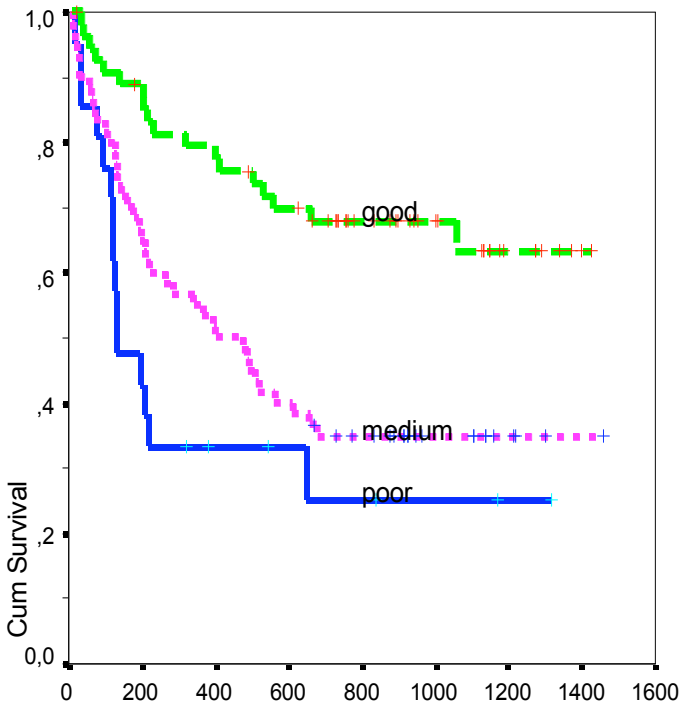
The correlation between the physician's prognosis and survival time after HSCT is highly significant. A 1-point less favourable prognosis on the scale correlates to a 50% increase in the mortality risk (Cox-Regression: hazard ratio HR = 1.51, 95%-CI

= 1.25 – 1.82, p < .001). Table 2 depicts the average survival times for the respective prognosis groups. Illustration 1 shows the Kaplan-Meier survival curve.

Table 2: Number and percentage of patients, who died, survival times (days post HSCT): mean, 95%-confidence interval for the mean, and median for grouped prognosis estimates

Prognosis group	good (n=55)	medium (n=60)	poor (n=21)
deaths (%)	18 (32.7)	39 (65.0)	15 (71.4)
Mean	1041	672	460
95% CI	893-1189	520-823	231-690
Median	(not defined)	402	132

Figure 1: Kaplan-Meier Survival rates for grouped prognosis estimates



(log rank = 18.4, df = 2, p = .0001)

Discussion

For the sample we researched, the prognosis estimates of the physicians before the transplant procedure - operationalized as overall survival after HSCT - are valid. The four patients with the least favourable prognosis (6) died within 200 days after HSCT. A 1-point less favourable prognosis correlates to a hazard ratio of 1.51 and thus corresponds with the results of our earlier study (HR = 1.49). The study by Dobkin et al. [9] with a scale in reverse to ours, indicates that a 1-point more favourable prognosis relates to a decrease in relative risk of 0.62, which would translate into an increased relative risk of HR = 1 / 0.62 = 1.61 (95%-CI = 1.03 – 2.50) of a less favourable prognosis by one point. Unfortunately, there is no corresponding information in the study by Lee et al. [10].
There were always several attending physicians on duty at the three transplant units during the time the data was obtained. In all centres, there appear to be equally good prospects and results for individual prognoses. But because subjective prognosis was not the main topic of the study, the results only have explorative significance.

It is still unclear, how the physicians arrive at their individual prognoses. For individual clinical pictures, it is possible to calculate prognostic indices based on objective factors, e.g. with CML [13] or lymphoma [14]. Recently, researchers also suggested a HCT-specific comorbidity index [15]. We did not determine these indices in our study and thus, the physicians' prognosis estimates might only reflect these characteristics.

This contradicts the informal statements by the physicians participating in this study. They indicated that they base their individual prognoses primarily on experience and a 'gut-feeling' in the sense of implied knowledge. Of course, explicit knowledge of the patient's data (such as previous therapies, comorbidity, drug intolerance, etc.) and prognosis statistics would also play a part in their conclusions. They were not able to explain, however, how they evaluate this objective data and combine it with their hematological experience. Thus, it is difficult to determine to what extent the respective objective factors (hard facts) and the intuitive factors based on clinical experience (soft facts) lead to an individual prognosis. It seems to involve a complex evaluation process, which, however, would have to be empirically verified.

Future research could examine which factors lead to certain subjective prognosis estimates and to what extend the clinical experience and expertise of the evaluating physician is responsible for the quality of the prognosis. In addition, it could be systematically investigated, if after consideration of known objective data, subjective prognosis estimates further influence the prognosis.

More information about this implicit evaluation process might be of clinical importance. It might be easier for the physician to create a more transparent informed consent procedure for the patient with regard to the individual prognosis and thus to improve the informed consent procedure. A systematic description of the extensive implicit experience regarding hard and soft data and its weighting could help improve the training of future haematologists.

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