Complementary Therapies in Medicine 27 (2016) 65–67

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevierhealth.com/journals/ctim

Short communication

Re-analysis of survival data of cancer patients utilizing additive homeopathy

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ARTICLE INFO

Article history:
Available online 7 June 2016

Keywords:
Additive homeopathy
Cancer
Immortal time bias
Landmark

ABSTRACT

In this short communication we present a re-analysis of homeopathic patient data in comparison to control patient data from the same Outpatientś Unit "Homeopathy in malignant diseases" of the Medical University of Vienna. In this analysis we took account of a probable immortal time bias. For patients suffering from advanced stages of cancer and surviving the first 6 or 12 months after diagnosis, respectively, the results show that utilizing homeopathy gives a statistically significant ($p<0.001$) advantage over control patients regarding survival time. In conclusion, bearing in mind all limitations, the results of this retrospective study suggest that patients with advanced stages of cancer might benefit from additional homeopathic treatment until a survival time of up to 12 months after diagnosis.

In a previous study[1] survival time of cancer patients with homeopathic add-on therapy was compared to survival time distributions reported in the relevant literature for patients with conventional cancer therapy. In this short communication we present a re-analysis of the same homeopathic patient data as the patients described in the previous study in comparison to control patient data from the same Outpatient's Unit "Homeopathy in malignant diseases" of the Medical University of Vienna. In this re-analysis we took account of a probable immortal time bias.[2]

Control patient data were obtained for all patients with the same cancer types as those in the homeopathy group and diagnoses from July 2005 to June 2006. This time frame is shorter than that of the homeopathic patients (first consultation between March 2004 and March 2008). Survival times were updated for 14 homeopathic patients who had still been alive (censored) at the time of the previous analysis.

Survival time for each patient is defined as time from diagnosis to death or lost to follow-up. In patients with metastasized renal cell carcinoma (mRCC) or metastasized sarcoma (mSARC) survival time starts from time of diagnosis of metastases (this has been omitted to be reported in the previous calculation[1]). For the control group Table 1 shows median and quartiles of survival estimated from Kaplan-Meier curves to describe the survival distribution in each stage specific tumor type. In addition, 95% confidence intervals for median survival are added for the comparison with results reported in the literature and used in the previous analysis.[1]

It is important to note that patients who have died soon after cancer diagnosis were 'prevented' from trying the homeopathic add-on therapy. This so-called 'immortal time bias' was to be taken into account by adequate statistical methods.[3] Since it has to be assumed that the waiting time (i.e. the time from diagnosis to the first homeopathic visit) is informative for the overall survival, common delayed-entry methods are insufficient and thus the landmark approach was used.[4] In this method, for various landmark times, only patients are included whose survival or censoring date is beyond the landmark; in addition, patients who started the homeopathic treatment after the landmark are counted as control patients (i.e. the control group comprises patients without homeopathic treatment until the landmark while still having the option of homeopathy after the landmark). The reported survival estimates do not allow for a counterfactual interpretation but have to be interpreted as referring to a group of patients with different waiting times.[4] For each landmark a Cox proportional-hazards model has been estimated using age and sex as adjustment variables and the stage specific tumor type as stratification factor to allow for tumor and stage specific baseline hazards. The proportional-hazards assumption was checked using weighted Schoenfeld residuals. Two-sided p-values ≤ 0.05 were regarded as indicating statistical significance. Calculations were done using SAS 9.4 while graphics were produced using R 3.0.3.

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http://dx.doi.org/10.1016/j.ctim.2016.06.001
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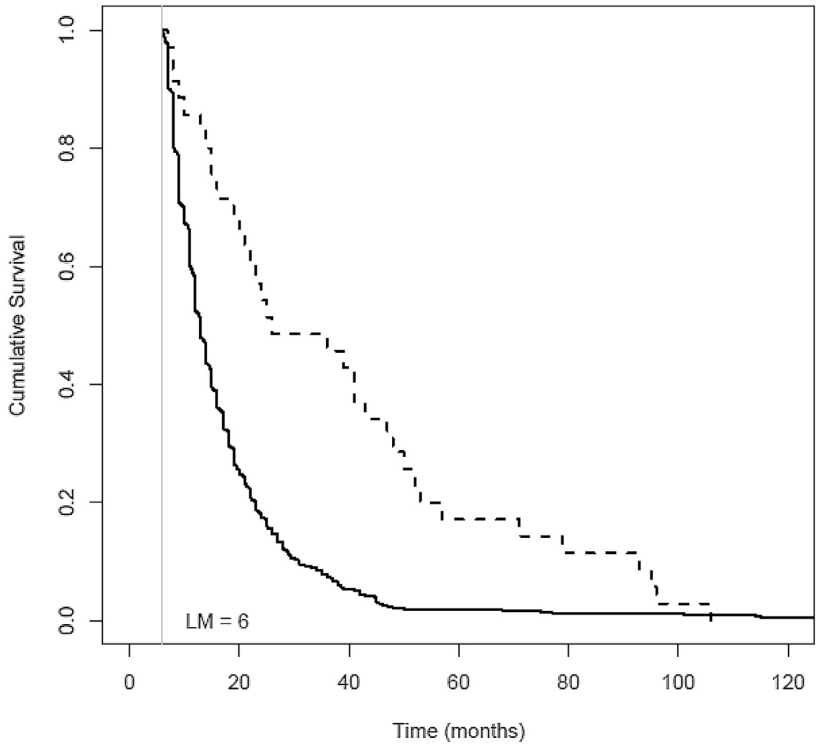

Fig. 1. Survival estimates using a landmark (LM) at 6 months for Per-protocol analysis.

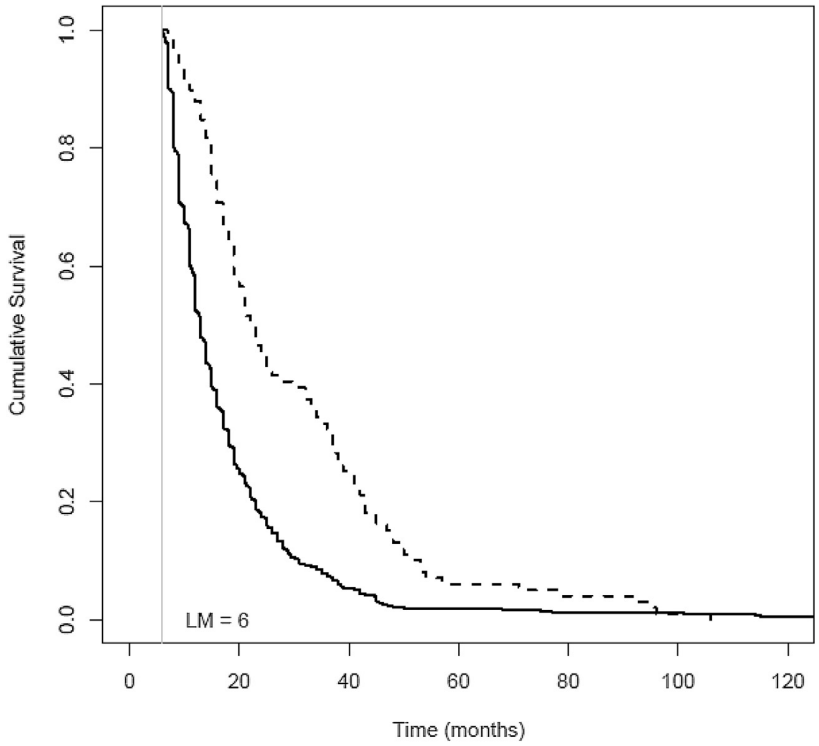

Fig. 2. Survival estimates using a landmark (LM) at 6 months for Intention-to-treat analysis.

For patients suffering from advanced stages of cancer and surviving the first 6 or 12 months after diagnosis, respectively, the new results show that utilizing homeopathy gives a statistically significant ($p < 0.001$) advantage over control patients regarding survival time. This result is consistent for patients with at least 3 visits using per-protocol analysis (Table 2, Fig. 1), and when 64 patients with up to 2 visits were included for an Intention-to-treat-analysis (Table 3, Fig. 2). The instantaneous risk of death (i.e. the hazard) is approximately divided in half.

While the presented analysis accounted for differences in age, sex and tumor type between the two groups further potential confounding factors were not incorporated, since these were not

Table 1
Medians + quartiles of control patients. N: Number of controls; Q1, Q3: 1st and 3rd quartile of survival distribution; LCL, UCL: lower and upper limit of 95% confidence interval for median, median (Lit.): medians as reported in the literature.[1] GBM: Glioblastoma, MRCC: metastasized renal cell carcinoma, MSARC: metastasized sarcoma, CCC: cholangiocellular carcinoma, PC: Pancreatic carcinoma, PC I to III: PC stage I to III, PCmet: PC stage IV metastasized, NSCLC: Non-small-cell lung-carcinoma stage III and IV, SCLC: Small-cell-lung carcinoma, SCLCext: SCLC extended disease, SCLClim: SCLC limited disease.

Tumor type	N	Median survival	Q1	Q3	LCL	UCL	Median (Lit.)
GBM	244	8.8	4.1	17.9	6.9	10.9	13
MRCC	56	34.0	25.5	38.5	28.0	36.0	35
MSARC	66	11.0	8.0	13.0	9.0	12.0	12
CCC	43	10.0	8.0	12.0	9.0	11.0	10
PC I to III	68	20.5	14.5	24.0	18.0	22.0	22
PCmet	77	8.0	7.0	9.0	7.0	8.0	8
NSCLC_III	46	14.0	12.0	17.0	12.0	15.0	15
NSCLC_IV	51	9.0	8.0	12.0	8.0	11.0	10
SCLCext	35	8.0	7.0	11.0	8.0	9.0	10
SCLClim	39	15.0	13.0	18.0	14.0	17.0	16

Table 2
Results of landmark models for Per-protocol analysis (homeopathy patients with at least 3 visits). N: number of patients at risk at landmark time, HR: hazard ratio, CI: 95% confidence interval.

Landmark time (months)	N (controls)	N (homeopathy)	HR	CI	p-value
6	607	35	0.35	0.24–0.52	<0.001
12	310	38	0.48	0.31–0.74	<0.001
24	98	27	0.85	0.49–1.50	0.580
36	40	21	0.97	0.46–2.01	0.925

available for the retrospective control cohort: type of conservative treatment, socio-economic factors, education, intelligence, income, perceptions, and hopes and ideas of cancer patients. Since the comparison is not based on randomized allocation of the homeopathic add-on but comes from observational data ignoring these confounders might result in

over-estimation of effects. Another limitation is that the two patient groups refer to time periods of different length; the validity of the new results thus relies on the assumption that the included control patients are representative for all control patients in the recruitment period of the homeopathic patients since the standard of care has not changed in this period. In conclusion, bearing in mind all limitations, the results of this retrospective study suggest that patients with advanced stages of cancer might benefit from additional homeopathic treatment until a survival time of up to 12 months after diagnosis. The re-analysis lead to similar qualitative conclusions as the previous calculation.[1] These results encourage performing a prospective study.

Table 3
Results of landmark models for Intention-to-treat analysis (including homeopathy patients with less than 3 visits). N: number of patients at risk at landmark time, HR: hazard ratio, CI: 95% confidence interval.

Landmark time (months)	N (controls)	N (homeopathy)	HR	CI	p-value
6	607	99	0.41	0.32–0.53	<0.001
12	310	95	0.59	0.44–0.80	<0.001
24	98	52	0.93	0.60–1.44	0.755
36	40	36	1.26	0.68–2.34	0.460

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