

Survival of Breast Cancer patients receiving adjunctive psychosocial support therapy : a 10-Year follow-up study.

Gellert G.A, Maxwell R.M, and Siegel B.S.

J Clin Oncol 1993;11(1):66-69.

AIM:

The endpoint of the study is survival. The study looks at survival in patients with breast cancer with and without an adjunctive psychosocial program in addition to the regular care.

TRIAL SUMMARY:

This is a retrospective case-control study of 10 years follow-up duration looking at the impact of a psychosocial support system on the survival of breast cancer patients. The study showed a non-significant difference in the survival outcomes of the two groups.

TRIAL DESIGN:

Patient Accrual

It is not mentioned how patients were admitted to the ECaP programme. It is assumed that they were self or physician referred and as such this opens an opportunity to bias.

The use of a 1 case to 3 controls reduces the chance of a statistically significant result (1). In addition the study should be randomised to more cases to controls. This study had 34 patients and 102 controls. No power calculations were quoted in the design of this study. The cases

were matched according to age at diagnosis, race, stage of disease (localised, regional or distant), surgery history (positive or negative), and sequence of malignancy ie whether first primary or second primary etc. It is accepted practise to match cases and controls to known prognostic factors. In this case age is not a prognostic factor per se but a surrogate prognostic factor for menopausal status. While race is a risk factor there is no information that it is a prognostic factor once a diagnosis has been made. Stage of disease is a prognostic factor, but it would have been more accurate to match for TNM stage. It is probably reasonable to match temporally for the time of diagnosis to control for change in society attitudes and for change in treatments over time. For the remaining two factors which are not prognostic factors for breast cancer if they are thought to be important from the point of view of psychological impact on survival then the authors should have presented some data to support this belief, or should at least have given reasons why they believe this is so. Other prognostic factors such as number of nodes, lymphatic and vascular invasion, receptor status are not mentioned(2).

The study protocol does not mention any enquiry regarding psychological assessment or participation in any programme of a psychosocial nature for the control group. As the data was gathered retrospectively, this would not have routinely been included in the notes of most oncology departments at the time, and would not be found on hospital tumour registries which were the source for the controls. Furthermore, the authors of this article do not state whether it was standard practise to document in their history taking, involvement in psychosocial programmes. In conclusion then we have no information on the validity of the statement that this paper examines "the impact of an adjunctive psychosocial support programme on survival". All we may conclude is that this paper examines the impact of the ECaP programme on survival vs no psychosocial programme, or programmes unspecified.

Treatment factors

There is inadequate reporting of treatments received in the two groups. There is no mention of radiotherapy or chemotherapy. Surgery, for which patients are matched is reported as "positive or negative". This is ambiguous.

Followup

There is no mention of the mode of followup, or how the authors intend to correct for a confounding effect of followup in different hospitals and treatment in different hospitals. No effort was made to account for the fact that the care of the cases and controls was not necessarily performed by the same surgeons, radiotherapists and chemotherapists.

Statistical Analysis

The proposed use of life table analysis is appropriate for this type of study. A restricted analysis of only those cases who survived long enough to enter the ECaP programme excluded 24% of the control group and none of the case group. It is not mentioned whether patients were selected for the case group on intention to attend or actual attenders and this could be a source of bias. Either way it possibly indicates poor case-control matching. There are no further details as to who comprised this group ie metastatic patients, and what the causes of death were in this group.

The authors state that differences in treatment modalities were assessed for. They do not state what method was used to assess this statistically and how different treatments were ranked or evaluated for each different clinical scenario.

A relationship between survival and frequency of attendance was further sought. It is unreasonable to do this in the absence of any suggestion of an effect for the group as a whole. In addition, the frequency of 34 attenders was subdivided into 3 groups. It is not stated how many patients were in the 3 groups but the small numbers in each group would make the confidence intervals in each group very large and make the likelihood of a true result very small indeed.

TRIAL CONDUCT:

There were no reports of patients lost to followup in the study. The authors mention that case records of the state registry were used to verify deaths but admit that if patients moved interstate they would be lost from the registry if deceased, and assumed to be alive. No attempt was made to verify their health status with their local doctor, or for verification with hospital records, or with electoral roll or other municipal records. Causes of death as written on the death certificates were taken at face value and no attempt was made to verify this with other case records. No quality control measures were instituted to recheck staging information and histology or of any other demographic factors.

STATISTICAL ANALYSIS:

The authors report the mean ages of the patient populations without giving any idea of the distribution of the ages about the mean. This does not mean that the two groups are comparable.

The use of Kaplan-Meier curves is correct to measure the endpoint of survival. To quote the median survival and mean survival however is misleading(1). In a disease where the survival does not follow a fixed relationship with time and is almost invariably skewed with the highest attrition in the early years, the mean will be skewed towards the top end (later) part of the distribution and the median will be skewed towards the lower end. This says nothing about the distribution about the middle value. The use of standard deviation in this instance is not appropriate as the distribution is skewed. It would be more correct to transform the data and then extract means and standard deviation or median and interquartile ranges. In this situation where the data is low positively skewed, the transformation should be a square root or logarithmic function. It is illogical that the abstract should report mean and median survivals +/- standard deviation (sd), and the results section report mean and median survivals +/- confidence intervals (CI). The wide confidence intervals in this study reflect the small sample size. The use of 10 year survivals are more useful.

If further comparison of these two measures were required, then two independent medians can be compared with the Wilcoxon rank sum test (or Mann-Whitney U test or Kendalls S test), or the transformed means can be compared with a paired t test.

RESULTS ANALYSIS:

The authors report disease states as localised, regional and distant is difficult to interpret. The authors should have either defined these states, or given the staging in more detail. If there were in fact patients with localised, nodal and metastatic disease then this gives a very heterogeneous group of patients. Even were this group to show no difference in the survivals between each cohort, the null result is impossible to interpret in the context of clinical knowledge to date as the group has such a wide range of prognoses. It would have been better to have chosen a group of patients with metastatic disease only, resulting in shorter periods of followup, an earlier result, and a better chance of having a result that can be interpreted in the light of other studies if there is a null result. The matching of histology was complete in only 60% and the authors state that the remaining patients were assessed by an histopathologist (blinded) with regards to matching for prognosis. They give no scoring system for matching these patients, and I know of no prognostic staging scores that can be that accurate. It would have been better science to either reference their scoring system, or to give more details about the actual histology and the way they were matched.

The authors go on to say that "no significant differences were found between groups in the percentages who received the three most frequent combinations of treatment. Therefore, neither histological type nor matching variables should confound the effect of the program, if any on survival." With regard to this the actual treatment received is not documented, the statistical test used to examine the differences in the two groups is not stated, and the actual results of this analysis is not given in the text. For all of this passage in the text comparing patient groups, the authors would have set it out more clearly in a table, with appropriate referencing to statistical methods in the text and as footnotes to the table.

The use of an unadjusted analysis and a restricted analysis both showed no statistical difference between the survival curves. The restricted analysis should not have been done given that the p value was 0.1 for the unadjusted analysis it is unlikely that any subanalysis would show a difference unless a large number of patients were excluded. For the same reasons, subanalysis on ECaP attendance and frequency of treatment were unlikely to show a difference.

The authors state that from review of death certificates, all deaths were due to breast cancer, but also say that 2 deaths were of unknown causes. This is a contradiction. Death certificates are notoriously unreliable as a cause of death, and further efforts should have been taken to assure that the patients did die with metastatic disease, if not of breast cancer.

CONCLUSIONS:

The conclusion of this study was that breast cancer patients in a psychosocial support programme did not live longer than non-participants.

I feel that no conclusions from this study can be made because the methodology of the study is so poor. The authors consider one reason this study did not show a difference in survival is that the programme is different from the previous programme which did show a difference. The authors state that confounding due to self-selection bias, referring physician bias, could occur and go on to conclude that the data cannot exclude the possibility that the ECaP programme did not have a beneficial impact on survival but that the participants were not exceptional with regards to survival, and that large prospective studies are warranted.

PRESENTATION:

The presentation of the abstract is clear, and the introduction presents the background data well. The graphs are not Kaplan-Meier plots, although the labelling is adequate. The title is appropriate for the intent of the study.

ETHICS:

One of the authors is a well known popular author who has published extensively in the popular lay press on the impact of attitudes on survival in cancer patients. Accordingly, I doubt that this author is unbiased. This study type is difficult to carry out as a retrospective study unless the department routinely and constantly at followup documents the psychological status of their patients. It is unknown whether the control group were receiving any type of psychosocial support. It is easier to do this type of study where the information is collected prospectively. There appears to have been no consent obtained from the patients for this study which is an omission. I believe that this study is unethical from the perspective that the authors seek to confirm a previously held viewpoint, that the research has not been designed with the end result in mind, and that the results of the study with a null result are uninterpretable because of the poor study design.

RECOMENDATIONS:

I would not publish this study. I do not think that this study can be improved to a point where it is acceptable to publish.

The comments I would make to the authors are :

1. The study has been designed with insufficient power to show a difference.
2. The use of a broad range of different stages of disease makes clinical interpretation of the survival curves impossible. It would be more informative if there were enough patients in each stage subgroup for a separate analysis. This study would be better if just patients with metastatic disease at presentation were included. This would have resulted in shorter followups and a quicker result. It would also mean that the survivals in the study could be compared with survivals of patients with metastatic disease in other centres.
3. The patient selection is haphazard, and there is no information on other psychosocial support received by both the control group and the ECaP group.
4. The information on patient matching and histologies would be easier to read in a table.
5. More information about the patient characteristics should be given eg age range. The results would be better documented in a table.
6. More detailed information on stage should be presented.
7. Other treatment received should be documented in more detail
8. The graphs should be drawn properly.
9. Survival results should be presented as 5 and 10 year survivals, not median and mean survivals.
10. More attempts to confirm the status of patients not under review by the department should have been made such as following up status with the family doctor or surgeon. Electoral rolls or civic records may have been another way of finding patients.

SUMMARY:

This is a retrospective study of the effect of patient participation in a psychological support programme. It is poorly designed and shows no difference between the patient groups studied. The results are not justified and the errors in patient selection are so great that the conclusions cannot be made on the basis of the results. I would not change my clinical practise on the basis of this study.

BIBLIOGRAPHY:

1. Daly L.E, Bourke G.J, McGilvray J. Interpretation and uses of medical statistics. 4th Edn. 1996:Blackwell Science Ltd.
2. Perez C.A, Brady L.W. Principles and Practice of Radiation Oncology. 2nd Edn. 1992, J.B.Lippincott Company.