Title

Impact of Surgical Margin on Survival in Extremity Soft Tissue Sarcoma: A Systematic Review and Meta-analysis

Authors

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Background

A correct understanding of the prognostic effect of the surgical margin is essential in extremity soft tissue sarcoma (STS). If the status of surgical margin has by itself a significant impact on survival, wider surgical margins would be needed, and larger functional sequelae justified. However, if the status of surgical margin does not affect survival, closer surgical margins with a lower loss of function may be advantageous.

The impact of surgical margin status on survival in extremity STS remains to be clearly defined. Although surgical margin status is thought to be of prognostic importance for local recurrence, its effect on metastasis and survival remains controversial in extremity STS. Relatively large, retrospective studies exploring the impact of surgical margin status on survival have produced widely varying findings.

Questions

We conducted a systematic review and meta-analysis to determine the impact of surgical margin status on survival in extremity STS.

Methods

A literature search of the National Library of Medicine and National Institutes of Health (PubMed), EMBASE, and Cochrane Controlled Trials Register (CENTRAL) electronic database and by hand searching reference lists of original studies was performed independently by 2 authors. We searched the studies with the following text words and/or Medical Subject Heading(MeSH) terms: “neoplasm” or/and “sarcoma” and/or “connective tissue” and/ or “soft tissue” “extremity” and/or “extremity“ and/or “surgical margin”.

Studies meeting the following criteria were analyzed for inclusion in the study: (1) published as an original article, (2) exposure of interest was surgical margin status, (3) outcome of interest was 5yr survival rate (4) data of event number or hazard ratio (HR) with corresponding 95 % confidence intervals (CIs).

The quality of each study was assessed independently by two authors using the Newcastle–Ottawa Scale (NOS). Heterogeneity was assessed using Higgins I^2, which measures the percentage of the total variation across studies that is due to heterogeneity rather than chance. The random effects model was used for data with substantial heterogeneity in order to obtain a meaningful confidence interval for the effect. For identifying publication bias, Egger’s test and Begger’s funnel plot were used.

Results

A total of 719 potentially relevant studies were identified based on the above search terms. All of the studies retrieved from the databases were independently evaluated. After the titles and abstracts were previewed, 29 identified studies concerning surgical margin status of extremity STS were further evaluated. Upon further review, 18 reports were excluded: Fourteen were eliminated due to inadequate data for meta-analysis; four were duplicate reports on the same population. Finally, 11 studies were included for analysis.

Selected studies, reporting a total of 4,115 cases of extremity STS, were published between 1994 and 2012. All of eligible studies were observational cohort studies and sample sizes ranged from 48 to 1261 patients. Seven

studies reported no significant association between surgical margins status and survival. Four of 11 studies reported data on association between surgical margin status and survival.

Meta-analysis of 11 studies showed that positive surgical margin predicted poor 5-year overall survival (OS) compared to patients with negative surgical margin in a random-effects model with moderate heterogeneity among studies (SHRs = 1.46, 95 % CI 1.11–1.91; test for heterogeneity $p<0.005$, $I^2 = 59.75$ %) (Fig. 1). The mean NOS was 7 and there was no publication bias in the present meta-analysis (Fig. 2).

Conclusions

This meta-analysis supports the hypothesis that positive surgical margin is poor prognostic factor for survival in extremity STS.

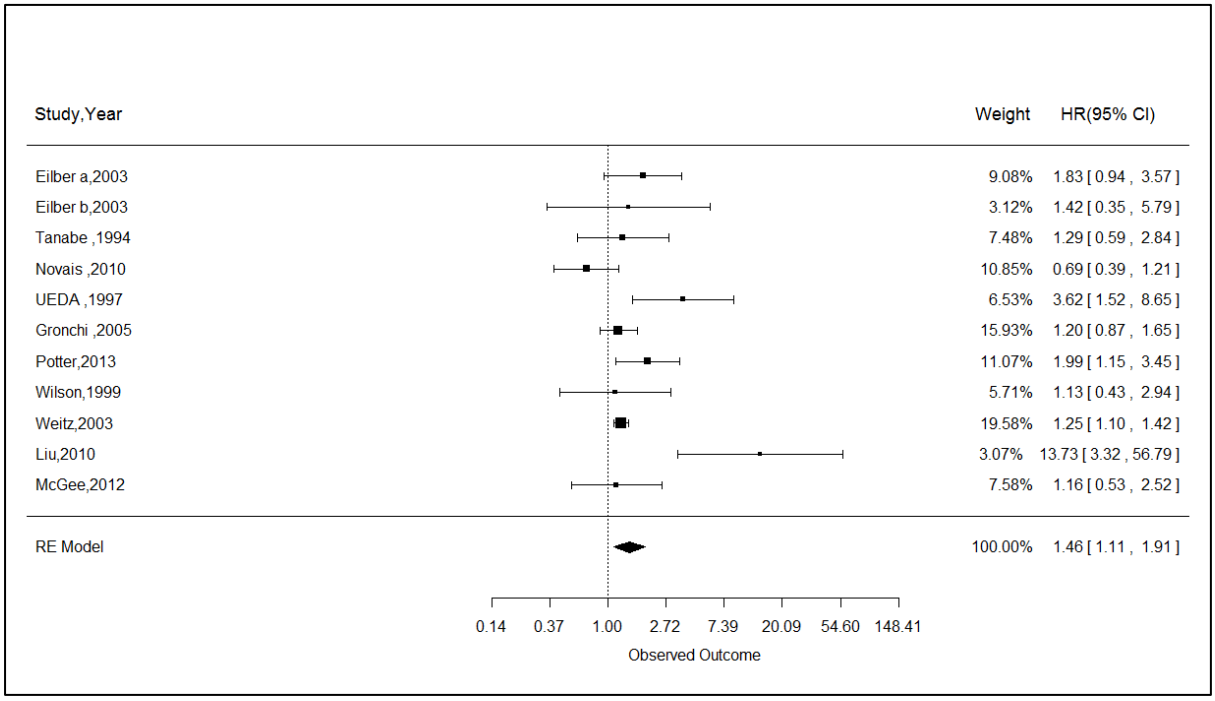

Fig.1 Forest plot of a meta-analysis of 11 studies. Diplayed are 5-year survival data with hazards ratio (HR) and 95% confidence intervals (CIs).

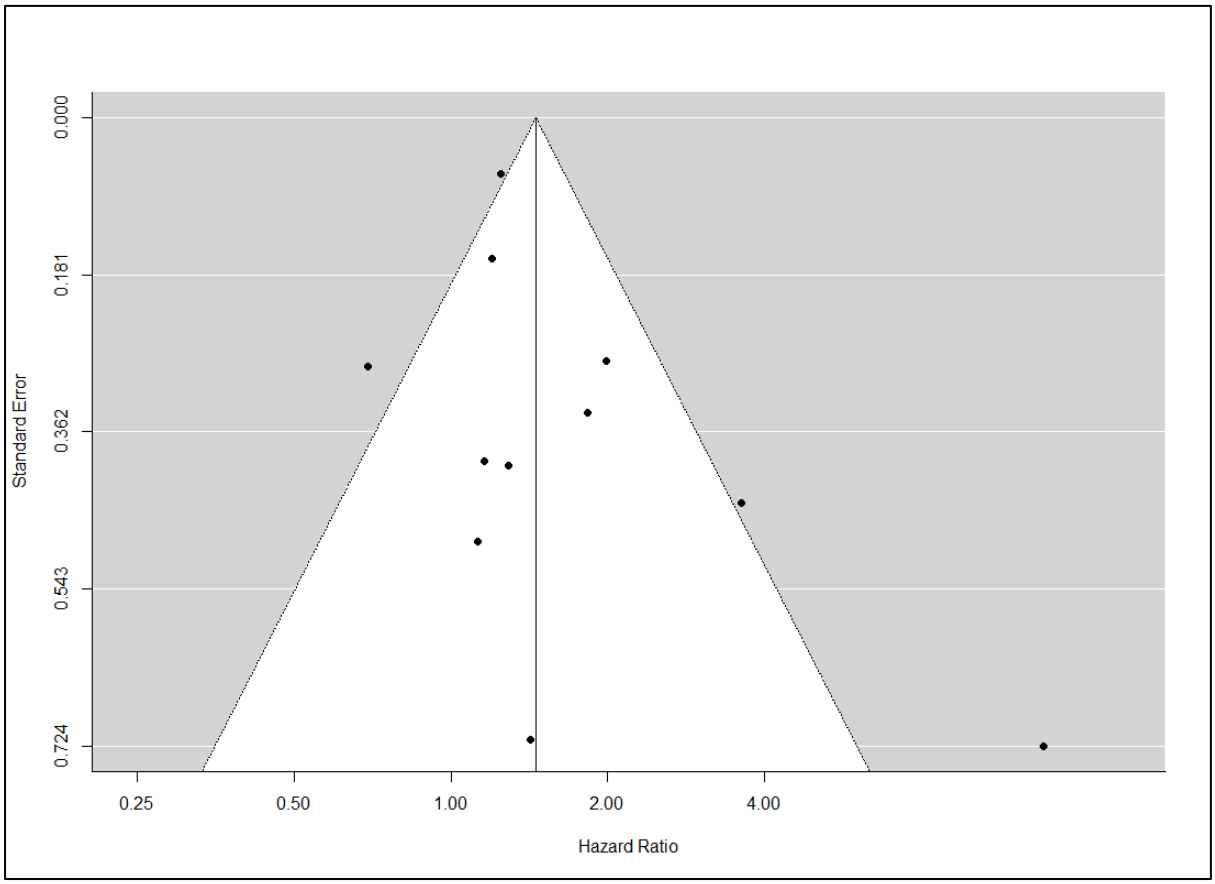

Fig.2 Funnel plot of publication bias for studies included in the meta-analysis.