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What is the significance of necrosis following neoadjuvant chemotherapy in osteosarcoma?

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It is generally accepted that the percentage necrosis following neoadjuvant chemotherapy in osteosarcoma is one of the most important prognostic factors for survival. A level of 90% is generally accepted as the cut off between 'good' and 'bad' response, but there is some lack of clarity as to whether this can be further refined by more accurate assessment of necrosis. The aim of this study was to investigate whether or not more accurate assessment of necrosis offered additional prognostic information.

Method: For many years our unit has recorded the actual % necrosis in patients who underwent surgical resection of osteosarcoma following neoadjuvant chemotherapy. All patients with non-metastatic limb osteosarcoma who underwent neoadjuvant chemotherapy and had >2years follow up were included in the analysis. Initially the % necrosis was scored as follows (100%, 99%, 95-98%, 91-95%; 90%, 80-89%, 50-79%, <50%). Gradually groups were merged until statistical significance was identified. 498 patients were included in the final analysis.

Results: On initial analysis it was apparent that there was a clear cut off below 90% with all patients doing worse. Patients with 90% necrosis had slightly better survival than those with 91-95% which was virtually the same as 95-98%, so these three groups were lumped together (90-98%). Patients with 99% necrosis had slightly better survival than those with 100% but these two groups were lumped together. The best classification was thus as follows - <89%, 90-98%, 99-100%. Using this criteria in a Cox model showed that the chances of survival were:

99-100% = 84% survival at 5 years (HR 0.26, CI 0.13-0.51)

90-98% = 68% survival at 5yrs (HR 0.45, CI 0.29 – 0.68)

<89% = 46% survival at 5 years (HR 1)

Conclusion: The actual % necrosis gives a useful idea of prognosis in patients with osteosarcoma.

Importantly, this study confirms the poor outcome for all patients with <90% necrosis but in this series 90% necrosis was equivalent to necrosis up to 98%. The best response was in those with 99 or 100% necrosis and these patients had nearly a four times better chance of cure than those patients with <90% necrosis.

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