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Current Controversies in Cancer

Is Limb Amputation Necessary for Locally Advanced Soft Tissue Sarcomas?

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INTRODUCTION

AMPUTATION in sarcoma surgery is the ultimate effort to achieve local control. Several questions arise. How important is local control? Does it affect survival? How do the results after limb-sparing surgery compare with amputation? Historically, amputation was the mainstay of treatment in locally advanced soft tissue sarcoma, but more recently the attitude of the surgeons, the advances in surgical technique and technical developments and, above all, adjuvant treatments have led to an era of limb salvage. In many centres, only a small percentage of patients with soft tissue sarcoma will receive amputation as part of the primary treatment. Is this going too far? In my opinion, it is.

IS LOCAL CONTROL IMPORTANT?

One of the most controversial issues in surgical oncology today is the relationship between local recurrence and survival. A number of investigators have tried to analyse this. As Barr and associates [1] have pointed out, the statistical methods used in most studies have been inadequate. The most reliable method is to examine the relationship between local recurrence and survival in a prospective randomised trial. However, the difficulties in accruing sufficient numbers of patients in such studies will probably prevent the issue from being settled. Analysing recurrence as a time-dependent factor within a multivariate study allows fairly reliable conclusions. Using this methodology, a significant correlation between local recurrence and survival has been demonstrated [2, 3]. This does not prove causation since recurrence could be an expression of the malignant potential of the tumour rather than determining a poor prognosis. The general opinion

today is that local recurrence may have an impact on survival, although the impact is probably not great. Whether this is true or not, a local recurrence is a very much unwanted event. The consequences may not be lethal but severe enough. The new tumour may cause pain, disability, ulceration and, not least, anxiety and fear in the patient and his relatives. More treatment will be needed, and in some instances unplanned amputations will be necessary. Most investigators agree on the importance of local control, if only to avoid morbidity and suffering.

IS A NEGATIVE SURGICAL MARGIN IMPORTANT?

One important question is whether the hazards of a positive (macro- or microscopically tumour contaminated) surgical margin can be eliminated with adjuvant therapy or is amputation justified to assure a negative margin? The patients in question are those in whom only an amputation would provide a safe negative margin. The answer is that adjuvant therapy cannot compensate for positive surgical margins. There is a consensus amongst most investigators that the quality of the surgical margin is a very important prognosticator for local recurrence [4-10]. If amputation is the only way to guarantee a negative margin, it is justified.

IS LOCAL CONTROL MORE FREQUENT AFTER AMPUTATION THAN LIMB SALVAGE?

The importance of pre-operative staging and grading has been long established [11]. Staging is the base for the surgical procedure which must entail adequate margins of healthy tissue around the tumour. Adhering to such surgical principles, which may or may not imply amputation, results in local recurrence rates of 2-8% without adjuvant therapy [12-16]. These series included varying frequencies of amputations

depending on whether the patient had or did not have inadequate surgery or inadequate biopsy outside a centre before referral. The importance of correctly placed biopsies, if any, cannot be overemphasised. Cytological aspiration can, in a substantial number of cases, replace incisional biopsy and thus make very extensive excisions and some amputations superfluous. This is because the biopsy wound and the biopsy haematoma is contaminated with tumour cells and thus should be included with adequate margins in the specimen to avoid the risk of leaving tumour behind. In soft tissue sarcoma patients with surgery as the primary and only treatment according to the given principles, the amputation rate will stay at 15–20%. The amputees will have a local recurrence rate of 0–6% [4, 15–18].

The reported local recurrence rates after modern limb salvage surgery vary considerably. Studies on combined modality treatment, including postoperative radiotherapy, resulted in local failure in 7–22% [4, 8, 19–23]. In these series, amputation had to be done in 4–15% because of recurrence or complication. Pre-operative radiotherapy which is gaining in use may be more successful. A few reports indicate a recurrence rate of around 10% [22, 24–27]. Brachytherapy has been attempted with local failure rates in the range of 10–18% [28–30]. However, not many reports are available and follow-up time is mostly short. Further, this kind of treatment requires special training and expertise and will not be available in all centres. Chemotherapy administered intra-arterially or systemically with or without irradiation has been tried. The overall impression is that currently chemotherapy has limited value in improving local control. Other modalities are even more experimental, and include hyperthermia and different biological agents such as tumour necrosis factor α , and interferon γ . These treatments cannot be reliably evaluated as yet. One of the main problems in comparing different treatments are differences in patient population and size of series, inclusion criteria, tumour characteristics, follow-up time, etc. Thus, the figures from the purely surgical series with an observed long follow-up appear to be the most reliable. One may conclude that amputation with adequate surgical margins is more likely to bring about local control than combined modality treatment.

WHAT IS THE AMPUTATION RATE IN 'LIMB SALVAGE CENTRES'?

Does multimodality treatment really allow for narrower surgical margins and thus reduce the need for amputations? Several reports maintain this, but recent reports by Levine and associates [31] and Keus and associates [32] showed that even with multimodality treatment the ultimate amputation rate was 19% and 17%, respectively. These figures equal the amputation rates in the Scandinavian series where surgery was the only treatment unless margins proved to be unsafe [13, 15, 33].

COMPLICATIONS AFTER AMPUTATION VERSUS LIMB SALVAGE?

No report focuses on the complication rate after amputation for soft tissue sarcoma. In our centre, complications after amputation with a curative intent occur in approximately 5%. The problems after limb salvage surgery are more frequently reported. Limb salvage surgery without adjuvant therapy is followed by 14–40% wound complications [29, 34–36]. Limb salvage followed by radiotherapy results in complications in

10–35% of the patients [8, 20, 23, 37] and these complications appear to be more severe, persistent and sometimes even progressive. In addition to infection, necrosis, haematoma and seroma, the complications include ulcers, oedema, fibrosis, contracture, fracture, neurological and vascular problems and intolerable pain. The complications lead to a number of unplanned amputations. Pre-operative radiotherapy, brachytherapy or intra-arterial chemotherapy are equally or even more tainted with complications [25, 28, 29, 34, 37–41]. Thus, major complications after limb-sparing surgery for soft tissue sarcoma remain a severe problem which cannot be overlooked. In terms of complications, amputation compares very favourably.

IS FUNCTION BETTER AFTER LIMB SALVAGE THAN AMPUTATION?

Much of the development of limb salvage techniques was based on the assumption that limb salvage would provide better function and quality of life than amputation. It is still more or less an assumption. Few investigators have studied these aspects. In bone sarcoma surgery, a study has indicated that there is no significant difference between amputees and those with reconstructed limbs as regards function and quality of life [42]. This also seems to be true in soft tissue sarcoma surgery. Sugarbaker and associates [43] in a randomised study compared amputees and patients who had limb salvage and irradiation. They found no difference in quality of life parameters. Their study included a number of different assessment scales and clinical evaluations. Weddington and associates [44] also failed to demonstrate a significant difference in quality of life after amputation versus limb salvage. Chang and associates [45] noted considerable negative functional and psychosocial effects of multimodality limb-sparing therapy in patients with soft tissue sarcoma. Thus, the hypothesis that limb-sparing surgery would provide better quality of life and function when compared with amputation has not been substantiated.

Rehabilitation after amputation can be expected to improve in the future with new developments and techniques. Thus, adequate stump lengths may be maintained with the step-cut technique where involved soft tissues are severed at a much higher level than the bone. Also bone lengthening can be done in amputees. The most interesting development is the concept of osseointegrated amputation prosthesis which means direct skeletal anchorage of the prosthesis. This technique has been tested in patients since 1990 in Gothenburg, Sweden. The results are very promising.

DISCUSSION AND CONCLUSIONS

One of the main problems in trying to judge what is really the best treatment lies in the difficulties of interpreting the literature. Almost all studies include retrospective series of very varying sizes, with differences in patient selection, tumour characteristics, treatment protocols, and follow-up is often inadequate, actuarial figures may not stand the test of observed long-term results, etc. To amputate or not to amputate? The expectations and demands of the patient must be considered as well as age and general condition. In my opinion, the recommendation should be mainly based on the anticipated quality of the surgical margin. In advanced soft tissue sarcoma, amputation appears to be superior to other treatments for accomplishing local control. Complications, severe or moderate, are much more common following

limb-salvage than amputation. Function and global quality of life parameters do not differ between the two patient groups with amputation and limb salvage.

Adequate surgical procedures preceded by adequately placed and performed biopsies or cytological aspirations in a centralised setting will locally control 90% or more of soft tissue sarcomas. 15–20% of these patients need an amputation. These candidates for amputation would not be better off oncologically or functionally, some more likely worse, with limb-sparing surgery and the adjuvant treatment that is available today.

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