Outcomes after multi-modality treatment of musculoskeletal tumours

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Outcomes of treatment of musculoskeletal tumours are evaluated for effectiveness of chemotherapy protocols, function obtained after surgery and survival after treatment. Quality of life achieved after multi-modality treatment is dependent on a combination of all of these factors. Quality of life varies significantly along the treatment pathway, and continuously through the life of a patient. The patient's perception of outcome is based on the total effect of the disease and its treatment, rather than necessarily focussing on separate items of treatment. We have found that visual analogue scales can be used effectively to gauge the patient's perception of their quality of life. Such a method has shown that, overall, perceptions of quality of life seem to be better for those patients who have undergone successful limb salvage surgery when compared with those who have undergone amputation, but the differences are not as great as might be assumed.

Current favoured protocols for the treatment of malignant musculoskeletal tumours have involved surgery, combined with chemotherapy and radiotherapy, alone or in combination. As a result, many variables influence the outcome of the treatment of these tumours. Chemotherapy has ensured improved survival at best, or at least, longevity and improved quality of life, even in late stage disease. Radiotherapy, used either pre or postoperatively, has influenced the extent of surgery necessary to gain local control of soft tissue tumours. The abilities to alter a tumour before operation, and to stage a tumour more accurately by better imaging techniques, have both contributed to making less radical surgery possible. This in turn has lead to the ability, in most cases of musculoskeletal malignancy, to achieve satisfactory limb salvage (Eilber et al. 1984, Carter et al. 1991, Simon 1991, Ruggieri et al. 1993, Rougraff et al. 1994).

We have few problems in accepting limb salvage as an alternative over amputation. In so doing, however, it has become necessary to devise appropriate methods of outcome evaluation to ensure the validity of these various treatment modalities. Such methods should account for quality of life as well as functional performance.

Function

Function then can be influenced by the efficacy of each step of the pathway involved in the management of patients with these tumours. It is decided by the effectiveness of:

1) induction (neo-adjuvant) treatment,
2) surgical resection and reconstruction in limb salvage,
3) amputation,
4.) adjuvant treatment.

Induction treatment

The outcome of induction treatment can be evaluated as to the effect on the patient, the effect on the tumour, and the ability of the induction treatment to influence the extent of surgical resection necessary to gain local control.

The toxicity of chemotherapy agents can be quite profound. Patients lose their hair, their appetite, and their well being. Although these effects are usually temporary, they can influence the patient's perception of value of the treatment. Patients can rightly expect significant returns for putting up with the side effects of this treatment. Marrow suppression, cardiotoxicity, and renal failure all can make chemotherapy a potentially life threatening situation. The local effects of some agents used in regional therapy can be significant and can alter surgical options. Local necrosis caused by streaming of intra-arterial Doxorubicin is a case in point. This can be avoided by careful technique (Marsden et al. 1991). Avoidance of complications of chemotherapy then has to be a major consideration in the use of these agents.

It has become accepted that the value of chemotherapy is primarily in its ability to deal with micrometastatic disease, which must be presumed to be present in all sarcomas at the time of diagnosis. This ability has ensured the improvement in survival following treatment of these tumours. It is also important that the chemotherapy can alter the tumour locally. Shrinkage, perhaps even total disappearance of the extraosseous tumour mass, has been a feature of successful chemotherapy, particularly in osteosarcomas and Ewing's sarcomas. Hardening, with or without encapsulation, makes the tumour more easily defined for the surgeon. Resection of a tumour with an adequate margin is easier after such a response to treatment (Marsden et al. 1989, 1991). This in turn has a significant impact on the level of function achievable for these patients and, consequently, on improved quality of life.

Reconstruction

The functional outcome of limb salvage surgery is governed by the method of reconstruction available to the surgeon following successful tumour resection. Reconstruction using an endoprosthesis should have the advantage of immediate stability, biological compatibility, and freedom from potential intrinsic infection. The design of an endoprosthesis should be such as to maximise the longevity of the implant with freedom from mechanical failure. It may be assumed, however that any mechanical device will eventually fail given a long enough period of use.

Allograft reconstruction has the obvious advantage of better anatomic match with the ability to achieve soft tissue attachment (Gebhardt et al. 1991, Johnson and Mankin 1991). This has to be weighed against the increased potential for infection and problems of late fracture.

Function is determined particularly by the ability to restore soft tissue anatomy which is more likely to ensure stability of the limb. In this, the ability of induction therapy to reduce the extent of the surgical resection has significant influence on the outcome. The life of the implant is decided by materials, design, and appropriate surgical skill at the time of the initial reconstruction. Finally, any reconstructive method has to be evaluated as to potential, or actual long-term complications.

Amputation

The level of amputation has to be compatible with local tumour control. Within those limits, the level of amputation able to be achieved affects the functional outcome. Standard amputation techniques may need to be modified. For example, there is a significant difference in the life of an amputee at hindquarter level compared with a hip disarticulation. Preservation of pelvic continuity, and in particular preservation of the ischium, are often possible and indeed preferable to conventional hindquarter amputation for tumours involving the pelvic ring.

Adequate stump length and the use of myodesis and myoplastic techniques can transform an amputation from a destructive to a reconstructive procedure with functional gain for the patient (Marsden 1977). Developments in modern prosthetics have ensured significant improvements in the lot of the amputee. The age of the patient will influence the outcome following amputation, prosthetic fitting and appropriate rehabilitation. Young patients do adapt well and achieve high levels of physical performance, particularly with good prosthetic services. Flexible sockets and dynamic feet have had a significant impact on the physical performance of these young people. As a result, performance of the athletic amputee is approaching that of the normal "whole" athlete.

Adjuvant treatment

This modality must be evaluated as to the effect on the patient with its likely complications. Evaluation of the effect on the disease and, in particular, the influence on survival rates, is especially important, particularly when prolonged periods of adjuvant chemotherapy are given after a gruelling period of pre- and then perioperative treatment.

Multicentre studies have established the efficacy of chemotherapy protocols (Tomita et al. 1989, Ruggieri et al. 1993). Functional evaluation scales (Enneking et al. 1993) have allowed us to evaluate surgical methods and reconstruction on a consistent and comparative basis. Many factors, however, influence these outcomes. These also influence the total quality of life available to these patients as the result of their disease and its treatment.

Quality of life

All of these factors influencing outcomes of the various treatment modalities can have a impact on the quality of life of these patients. Efforts to evaluate quality of life must recognize that this will vary at different times in the progress down the treatment pathway. There may be significant variability in the effectiveness of each treatment modality so that quality of life may be different at various times and phases. Thus, there may be differences within any cohort of patients if the evaluation occurs during treatment, during convalescence and rehabilitation, and after the conclusion of treatment.

The future is of profound significance for these patients. Effectiveness of treatment influences quality of the whole of the lives of these patients irrespective of whether they achieve a disease free state for the remainder of their life or for a relatively limited time. Thus, surgery that may be appropriate for disease-free patients may not be particularly welcome for patients living with late stage disease or even controlled disease. Similarly, a degree of instability of a prosthetic reconstruction may be quite tolerable for a patient in a well stage, but quite unacceptable for a patient with late stage disease. Most evaluations of quality of life are problem-oriented and tend to focus on the immediate period from diagnosis to treatment conclusion, assuming a steady disease free state as a continuum. Evaluation of function and quality of life, to be truly effective, must address the temporal variability that will occur in the outcome of any form of treatment of patients with musculoskeletal malignancy (Weddington et al. 1985).

To show this, comparison is made between two separate studies on the same cohort of patients with musculoskeletal tumours. The first study is of functional outcomes in a group of patients who had a resection and endoprosthetic reconstruction for malignant tumours about the knee (Witt and Marsden 1994). These patients were evaluated according to the method recommended by the International Society of Limb Salvage, and the Musculoskeletal Tumour Society (Enneking et al. 1993).

Between 1985 and 1992, of 39 patients presenting with primary malignant neoplasms about the knee, 28 were considered suitable for limb salvage surgery. They underwent reconstruction using a modular endoprosthetic replacement. 20 of these patients were available for assessment. 18 patients had resection of the distal femur and two had resection of the proximal tibia. The average follow-up was 37 (6–93) months. Functional result was rated as excellent in 2, good in 16, fair in 2and there were no ratings as poor. Seven criteria are used in this rating system to arrive at an overall result. These criteria are: motion, pain, stability, deformity, strength, functional activity, and emotional acceptance. In this group functional activity was rated as excellent in 3, good in 15 and fair in 2. Emotional acceptance was rated as excellent in 11, good in 8 and fair in 1 patient. There were no ratings as poor (Witt and Marsden 1994).

Two years after completion of this study, a study of issues in quality of life was conducted in patients who had undergone surgery for aggressive or malignant musculoskeletal tumours (Swanson et al. 1995). In this group the treatment choice had been between local resection, with or without appropriate reconstruction, and amputation, and included those patients from the functional study who could be contacted and who agreed to participate. Participants were asked to complete a mail-out questionnaire comprising visual analogue scales for various aspects of quality of life (physical, psychological, social, occupational and, financial), as well as questionnaires about social support and life events. This proved to be a successful and acceptable method of survey, with 43 of 54 patients identified as eligible returning completed questionnaires. The patients who participated in this study (23 women, 20 men, median age 32 years) represent the range of ages and histological and surgical types found in a large musculoskeletal tumour service (Table).

Respondent characteristics—diagnosis and treatment details

Characteristic	Women (n=23)	Men (n=20)
Anatomical Site:		
Axilla	1	–
Humerus	1	5
Ulna	–	1
Pelvis	4	2
Sacrum	1	–
Femur	9	9
Tibia	5	3
Calcaneum	1	–
Forefoot	1	–
Histology:		
Aneurysmal bone cyst	1	1
Giant cell tumour	3	1
Adamantinoma	–	1
Chondrosarcoma	3	5
Fibrosarcoma	–	2
Haemangiopericytoma	–	1
Leiomyosarcoma	–	1
Malignant fibrous histiocytoma	3	2
Osteosarcoma	8	6
Ewing sarcoma	1	–
Clear cell sarcoma	1	–
Synovial sarcoma	1	–
Undifferentiated sarcoma	1	–
Surgery:		
No reconstruction	3	1
Cementation	1	1
Allograft	1	–
Autograft	4	–
Upper limb endoprosthesis	1	3
Lower limb endoprosthesis	7	8
Resection/arthrodesis	1	2
Amputation	5	5
Induction chemotherapy:		
Intra-arterial	11	9
Intravenous	1	2
Adjuvant chemotherapy:	6	10
Radiotherapy:	2	2

While differences in ratings for the items did not reach statistical significance between patients classed

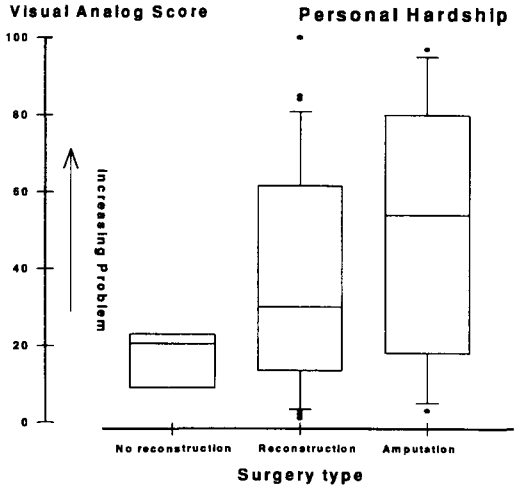

Figure 1. Box plot of visual analog scores for personal hardship experience by surgery type.

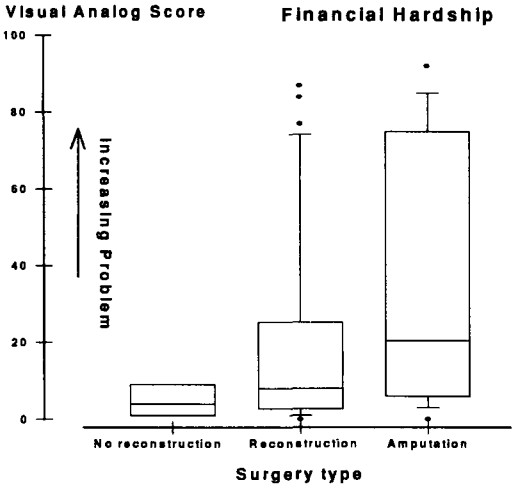

Figure 2. Box plot of visual analog scores for financial hardship experience by surgery type.

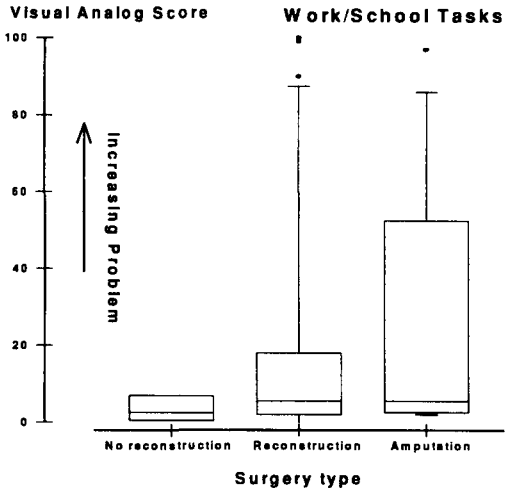

Figure 3. Box plot of visual analog scores for performance of work/school tasks by surgery type.

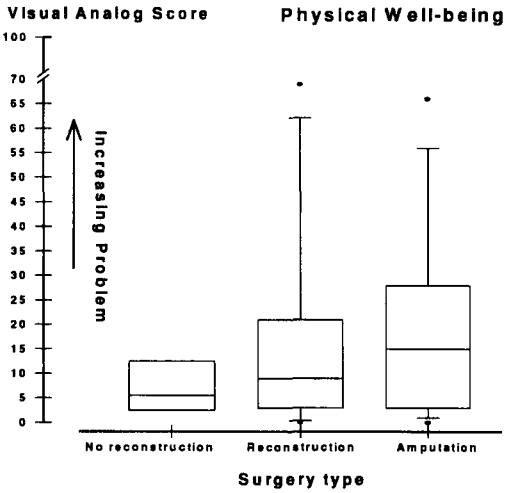

Figure 4. Box plot of visual analog scores for personal well-being by surgery type.

by type of surgery, a trend was present towards scores representing better outcomes. Fewer problems were reported by patients for whom limb salvage was possible compared with patients who had undergone amputation, examples of which are shown in Figures 1 to 4. Interesting associations between concerns about appearance and economic hardship and type of surgery were found through exploratory factor analysis, suggesting that social and economic costs may be relatively high for amputee patients.

As a final note in the questionnaire, participants were invited to write down their comments on any aspects of the questionnaire itself, of quality of life or any problems that they wished to offer. A number of patients reported a lack of support or counseling or preparation for the problems they faced after surgery. Each of these patients had, in fact, been treated as standard protocol in an intense hive of activity from physical therapists, social workers and other counsellors that normally gathers around patients in a hospital amputee service. These perceptions may be a consequence of the timing of these interventions following the surgery itself when some patients may not have been able to take in all the information and advice being offered at that time. Such patients may benefit from an additional 'refresher' session a few months later.

Conclusion

Comparison of these two studies highlights the great variability, not only in terms of factors involved in outcomes and total quality of life achieved, but also in our own perceptions of success. Similarly it is very difficult to devise any evaluation system that accounts for the impact of the disease on the patient and the true role of limb salvage surgery in the whole life of the patient rather than in the early days of survival.

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