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Advances in orthopaedic oncology

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There are few fields in oncology where such dramatic improvement of treatment results can be observed as in primary bone tumours, especially in osteosarcoma and Ewing's sarcoma. Bone sarcomas are rare; approximately, the overall incidence for osteosarcoma is 1.5–2.5 million per year, for chondrosarcoma 1–1.2 million per year and for Ewing's sarcoma 0.5–1 million per year. Because of the small number of new cases, centres have been developed with participation of orthopaedic surgeons, oncologists, radiologists, pathologists and radiotherapists for the interdisciplinary treatment of bone tumours. Besides the well-known centres and registries in Bologna, Birmingham, Prague, Münster, Paris and London, one of the most respected bone tumour registry and oncological units is at the University of Vienna. Its international activity is underlined in this issue by the paper of Kotz and co-workers who reviewed treatment results of 721 patients with primary malignant bone tumours treated in a single institution during a period of 30 years.

For the establishment of new treatment protocols, however, not even these centres have a sufficient number of patients. International teams have been formed, like the Co-operative Osteosarcoma Study Group (COSS) in the German-speaking area, or the Scandinavian Sarcoma Group (SSG), the European Osteosarcoma Intergroup (EOI), the Children's Oncology Group (COG) in the USA that together cover a population of approximately 400 million people. The advantage of such co-operation is that a sufficient number of patients for a prospective randomised study can be collected in a short time; therefore, results are really evidence based.

The breakthrough in the survival rate of patients with highly malignant osteosarcoma and Ewing's sarcoma was achieved by the introduction of effective chemotherapeutic agents in the early 1970s. Jaffe and Rosen with

their co-workers (1974) were the first to report good results in osteosarcomas that responded well to high-dose methotrexate and adriamycin, drugs that today also constitute the basis of all highly effective chemotherapy protocols. Thus the 5-year survival rate has increased to 60% in Ewing's sarcoma and to 70–75% in non-metastatic osteosarcoma, in contrast to 15% and 20% respectively, observed in the historical control groups. The introduction of pre-operative (neoadjuvant) chemotherapy was also an important step. It is now evidence-based that neoadjuvant chemotherapy is not a risk factor for the patient; it prevents the dissemination and colonisation of tumour cells following the bioptic procedure and pathologic fractures; the primary tumour decreases in size and its surgical stage can usually be down-staged, facilitating limb salvage surgery.

It is also of major interest that the clinical impression of the regression grade of the tumour resulting from chemotherapy can be precisely evaluated histologically at the time of surgery. Tumour response is an important prognostic factor and is decisive for the postoperative chemotherapy protocol.

As we can learn later from the paper by Kotz and co-workers, the application of highly effective chemotherapy has significantly changed the surgical strategy. Limb-sparing surgery is possible in about 65–85% of primary malignant bone tumours. Wide to radical surgical margin at surgery, however, still remains mandatory for survival. A limb-saving procedure can be offered to the patient only when life expectancy is comparable with that of ablative surgery. Treatment results of 925 osteosarcoma patients in a COSS study, and 975 Ewing's sarcoma patients in an EICESS study, justify limb-saving surgery at correct indications; 5-year survival rates are similar or better than at amputation.

Besides effective chemotherapy, the basic conditions for limb-sparing surgery are modern anaesthesiology, progress in imaging techniques and an improvement in surgical reconstruction. The modern tools of anaesthesiology provide the patient with a safe intra- and peri-operative period at limb-saving intervention, which is sig-

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nificantly more time consuming than ablative procedures.

Among the imaging techniques, computed tomography (CT) has an important role in the local and extra-skeletal staging of the tumour in detecting pulmonary metastases. Magnetic resonance imaging (MRI) precisely outlines both the extra- and intra-osseous extension of the tumour and reveals possible skip metastases. Scintigraphy and the recently introduced dynamic contrast-enhanced MR images are useful in objective presurgical prediction of tumour response and regression to preoperative chemotherapy. Early detection of local recurrences and metastases is also an advantage of MRI and the very sensitive but expensive dynamic positron emission tomography (PET).

Reconstructive surgical technique also has presented a rapid progression in the last 3 decades. Following the resection of bone sarcomas, the defect can be replaced either by allograft, tumour endoprosthesis or allograft-prosthetic composites.

Bone banks have been established in specialised bone tumour centres. Among the different preserving techniques, like liophylisation, irradiation, etc., the fresh, deep-frozen procedure is the most widely accepted technique at present. Using this technique, approximately 30% of the cartilage cells of the massive osteochondral allograft remain viable at implantation. Despite this fact, severe osteochondritis usually develops after approximately 6 years following the operation in weight-bearing joints. The complication rate is rather high; it can reach 30–50% of cases. Mankin reported on delayed union of the graft (32%) that can be partly explained by long-lasting chemotherapy, graft fracture (12–20%) and infection (11%). The most important late complications are graft collapse and instability and osteoarthritis of the joint. In his series, the 10-year survival rate for allograft arthrodesis was the lowest (40%), followed by massive osteoarticular (70%) and intercalary graft (85%) and allograft-prosthetic composites (70%). Better results can be achieved using vascularised fibula graft (combined with massive homograft). However, possible locations for its use are limited.

Since the mid-1950s, tumour endoprostheses have been used in reconstructive surgery, first as custom-made

designs then, in the last 3 decades, as cemented or cementless modular constructions. In contrast to the homograft, its advantage is an immediate stability and good function of the limb as early as some months after operation. The complication rate, however, increases more rapidly with time compared with the conventional endoprostheses, which is of great importance considering the young age of most osteo- and Ewing's sarcoma patients. In the large series from Mittermayer, aseptic loosening (27%) infection and fracture (54–54%) of the implant have been the most frequent complications leading to revisions. In general, endoprosthetic failures can be revised without compromising functional results, and more and more follow-up studies report more than 90% long-term limb survival. A special form of these implants is the expandable tumour endoprosthesis, which can be used from the age of 6 or 7 years, and a 6–14 cm leg-length discrepancy can be corrected at least through many "service" operations.

Internal hemipelvectomy, especially periacetabular resection and reconstruction with allograft, autoclaved autograft or computer assisted metallic pelvic endoprosthesis, still seems to present many unsolved problems. Besides the high local recurrence rate, haematoma, infection, loosening of the prosthesis and breakage are the most frequent complications, which also influence the patients' quality of life. Winkelmann reported on promising results with transposition of the femur to the sacrum following resection of tumourous hemi-pelvis.

Parallel to the technical evolution in tumour surgery, limb function and life quality are being analysed intensively. Although amputation remains an indispensable life-saving procedure in 10–30% of cases, a better quality of life can usually be achieved following limb-saving procedures. In addition, patients in Europe and the Middle East demand limb-saving surgery due to traditional social reasons, even in case when the expectable function of the limb and life quality will not exceed the result of rehabilitation following ablative surgery. We possess, however, more and more modern diagnostic tools, highly effective chemotherapeutic agents and better surgical reconstructive techniques for limb-saving procedures, which enable us to achieve a high quality of life for the patient.