Surgical and Molecular Advances in Osteonecrosis

Editorial Comment

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Osteonecrosis (ON) continues to be a considerable challenge to orthopaedic surgeons and researchers. There has been no major breakthrough in research of this devastating disease at the basic science and clinical level. However, the recent explosion of molecular technology, advancement of biomaterials, state-of-the-art computing and diagnostic tools, and better defined surgical techniques has increased our contemporary knowledge base. This symposium contains peer reviewed scientific manuscripts selected from the work of international experts across the globe, representing current developments in etiology, pathogenesis, diagnosis and treatment of ON.

The pathogenesis of ON still is unknown. To some extent, this is because there is no ideal animal model that can reproduce the human form of ON. Chemically induced and traumatic bipedal animal models have shown promise but need further study and validation. Quadruped animal models only showed marrow and bone cell death but no collapse consistent with early stage ON of the human. Many hypotheses regarding pathogenesis of ON have been proposed, including intravascular coagulation, fat emboli, fat cell hypertrophy, intraosseous hypertension, microfractures, and vasculitis, however none of these are conclusive. Due to the lack of understanding of pathogenesis of the disease, many therapeutic options including electromagnetic field are developed and evaluated. Further studies are needed for their effectiveness and validation.

Genetic factors may play an important role in the development of ON. A large body of work on inherited

thrombophilia and hypofibrinolysis by Dr. Glueck and his colleagues has indicated that patients' genetic characteristics do associate with ON. Similar findings were also reported in the Korean population, although the genetic risk profile of ON may differ among ethnic groups.

Adipogenesis by bone marrow stem cells also may be critical for the development of ON. As reported by Wang et al. and Yeh et al., both glucocorticoid steroids and alcohol can enhance adipogenesis while inhibiting osteogenesis. In addition to changes in transcription factors, Wnt/ β -catenin signaling pathway was also involved in this process. Previous studies and reports by Wang et al. and Nishida et al. in this symposium have demonstrated that lipid lowering agents have therapeutic effects in the treatment of ON in human and animal models.

Although many treatment options for ON are available, total hip replacement (THA) is the most common for postcollapse stages of the disease. Historically, THA had poor outcomes in patients with ON when compared to those with osteoarthritis (OA). However, recent studies have demonstrated improved outcomes using the latest surgical techniques and implant designs. Nevertheless, there is still a subset of patients that have less than favorable results when compared to OA.

Dorr and colleagues reported their midterm outcome study using a metal-on-metal bearing surface and found that patients with ON (27 patients, 30 hips) or OA (80 patients, 82 hips) were similar in clinical and radiographic performance at a mean followup of 5.5 years (range 2.2–11.7 years). In another study by Koo et al., survivorship analysis has revealed a survival rate of 93.3% in 36 patients (46 hips) with a minimum followup of 10 years. However, long term outcome studies in patients with ON regarding prosthetic hip surgery, including hemi- and total hip resurfacing arthroplasty, are still needed.

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Treatment of patients with early stage ON continues to be controversial. Core decompression is the most commonly applied form of precollapse treatment, but the results are not variable. Free fibular graft, rotational osteotomies, and nonsurgical managements are less commonly used. Osteotomies are primarily used in Asian countries and continue to produce favorable results. Dr. Sugioka and his associate reported their long term results of transtrochanteric posterior rotational osteotomy for ARCO (Association Research Circulation Osseous) stage III and IV ON; Dr. Yoon and colleagues of Korea used a modified transtrochanteric rotational osteotomy for ARCO stage II and III disease with a short term followup. Their results indicate osteotomy is effective not only for early stage but also for advanced stages of ON. Free fibular transfer also has generated relatively good outcomes in a skillful surgeon's hands, but its indications are limited due to technical difficulties. In a study by Yoo et al., 110 patients (124 hips) had received free vascularized fibular graft and were followed for a minimum 10 years (range 10 to 23.7 years). Thirteen hips (10.5%) failed and converted to total hip arthroplasty. The remaining patients had a mean Harris Hip Score of 88 at final followup. Aldridge and Urbaniak reviewed 154 patients of various subgroups treated with free vascularized fibular graft with a minimum followup one year (range 1 to 19 years) and found it highly successful in treating athletic or pregnant patients and patients with pyarthrititis or slipped capital femoral epiphysis. A high failure rate was noted in patients with organ transplant. It is generally accepted patient selection is the key for a successful joint preserving procedure. The size of the lesion, extent of femoral head depression, and involvement of the acetabulum are important parameters dictating outcomes of the treatments.

Modern core decompression techniques, including multiple small diameter drilling, in conjunction with use of bone marrow stem cells, growth factors such as bone morphogenetic proteins, and nonvascularized bone grafts have produced improved outcomes in limited studies with short to midterm followups. The major limitations of the procedure include incomplete removal of necrotic bone and lack of a mechanism to prevent subchondral collapse. Endoscope-aided core decompressions and sophisticated grafting techniques may surmount these shortcomings. However, data from randomized, double-blinded, prospective clinical trials evaluating modern core decompression techniques, different bone grafts, and graft substitutes are needed.

Many classifications for ON of the femoral head have been used in the past. Ficat and Arlet, Steinberg (the University of Pennsylvania), ARCO and Japanese Orthopaedic Association classifications are the most commonly

used systems. Although there is no consensus supporting the use of any one classification system, the Steinberg and ARCO classification systems are comprehensive and incorporate the most sensitive diagnostic techniques such as magnetic resonance imaging and other important parameters that allow for a uniform data collection and cross-study comparison. We encourage use of these two classification systems in reporting studies on ON of the femoral head. Otherwise, the key parameters including size of the lesion, presence or absence of collapse, amount of depression of the femoral head, acetabular involvement, and the location of the lesion should be collected and reported. As further information becomes available, the classification system will be further defined and one universal classification system should be used.

Magnetic resonance imaging (MRI) continues to be the most sensitive and accurate diagnostic tool for ON of the femoral head. Size and extent of the necrotic lesion, an important prognostic parameter, can be better defined on MRI than on radiographs. Measurement should be performed on both coronal and sagittal planes. Min et al. prospectively monitored 81 patients (81 hips) with asymptomatic ON of the femoral head. The diagnosis was established by MRI. Patients were followed for 8.3 years (range 5 to 16 years). Twenty-six hips (32%) progressed to collapse. They found no correlation between the collapse and patients' age, gender, weight, causes of the disease, and the length of followup. However, the size and location of the lesion were the factors that predicted collapse. The concept also can be applied to shoulder ON. Sakai and colleagues have found the extent of the lesion measured as necrotic angle on mid-oblique coronal and sagittal planes of the humeral head can predict collapse of the humeral head. Newer technologies are evolving. As reported by Dasa et al., F-18 positron emission tomography (PET) seemed more sensitive detecting early changes in the acetabulum than traditional imaging systems but it is uncertain whether and how these changes relate to the pathophysiology of ON. But further studies are needed to validate the use of newer diagnostic tools.

Challenges still lie ahead. We hope in the next few years there will be more studies on the development of animal models that can be used to evaluate various etiologies and treatment options. Knowing the predisposition factors, capability for early detection of the disease and available effective therapeutic agents may prevent the disease process in the future. With further defined surgical techniques and availability of osteogenic and angiogenic growth factors, early stage ON will hopefully become treatable. This approach can optimally decrease or eliminate the need for total joint replacement for this young, productive patient population.

We conclude by thanking all the authors for taking time to contribute to this special symposium on Surgical and Molecular Advances in ON. We also would like to express

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