

OSTEOPOROSIS AND JOINT REPLACEMENT

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Over the past few decades, the number of implantation of endoprosthetic joint replacements has steadily increased. Many patients who need joint replacements are of older age and have a reduced bone quality due to osteoporosis. In patients with joint replacements and osteoporosis complications are often seen: intraoperative periprosthetic fractures, periprosthetic osteolysis, increased implant migration or postoperative periprosthetic fractures. The evaluation of bone quality therefore seems an essential point in patient management to provide the best possible care and to optimize long term surgical outcomes. If necessary, patients should be educated about a possible calcium and vitamin D supplementation. In addition, it seems reasonable to aim for physiological vitamin D levels perioperatively.

In postmenopausal women, men over 70 years and both women and men with an increased risk of osteoporosis within two years of implantation of a total joint replacement a bone mineral density measurement should be performed.

In patients with reduced bone quality, treatment with bisphosphonates, denosumab or teriparatide should be considered in order to improve the osseous integration of cementless implants, to increase the lifespan of implants as well as to reduce periprosthetic fractures and fractures in general. In individual cases of patients with osteoporosis cementation of prosthetic components (especially in total hip replacements) may be required.

Keywords: osteoporosis, fractures, endoprosthetic joint replacement, bisphosphonates, denosumab, teriparatide.

Introduction

Osteoporosis is a worldwide systemic skeletal disorder characterized by reduced bone quality and increased fracture risk. Basically, osteoporosis can occur at any age, but it increases in older people [1]. Due to the demographic development (especially, the increasing life expectancy in coming decades), this numbers are expected to increase in the future. Many of these patients with osteoporosis require orthopedic-surgical interventions such as endoprosthetic joint replacement or spinal surgery. It can be assumed that the complication rate of such interventions is higher in patients with osteoporosis than in those with healthy bone. Due to the underlying disease, complications such as intraoperative periprosthetic fractures, periprosthetic osteolysis, implant migration or postoperative periprosthetic fractures are more common in osteoporotic patients. The evaluation of bone quality therefore seems to be an essential point in patient management in order to provide patients with the best possible care and to optimize long-term surgical results.

Over the past few decades, the number of implanted endoprostheses has steadily increased [2]. Many patients who require an endoprostheses are older and may have lower bone mass. This is shown for example by a study by Lingard et al. In 199 patients between the ages of 65 and 80 who were scheduled for endoprosthetic joint replacement (hip or knee total endoprostheses), a bone density measurement using dual-energy X-ray absorptiometry (DEXA) was performed. The incidence of osteoporosis (measured by hip or lumbar spine) in the collective studied was 23%. Another 43% of patients had osteopenia [3]. Another study (n = 53) investigated the prevalence of osteoporosis in women who were earmarked for cementless total hip arthroplasty. 28% had osteoporosis and 45% had osteopenia [4]. These data indicate that the prevalence of low bone mineral density is high in this patient population (> 2/3). In this review, therefore, the effects of bone

health on the field of arthroplasty are discussed.

Implant anchoring: cemented versus cementless

An important point of discussion concerning the aforementioned problem arises in the question of prosthesis anchoring, namely cemented versus cementless. The current consensus is to primarily seek cementless anchoring in all patients with normal bone quality, as the bone integrates into the porous structure of the implant [5]. Cemented prostheses were mostly used for elderly patients. This is an approach based on the assumption that elderly patients would have a lower bone quality and a higher risk of implant migration (prior to bony integration), thus benefiting from a cemented prosthesis.

The evaluation of the bone quality with planned implantation of an endoprosthesis has therefore gained in importance. This aspect was examined in a recent study in which the intertrochanteric bone quality of the spongiosa was investigated as a predictor for migration of the prosthetic socket in total hip replacement. Biopsies were taken intertrochanterically in the area of the proximal femur at the site of the future prosthetic socket and examined by means of MicroCT and biomechanical tests. Contrary to the hypothesis, the quality of cancellous bone had only a minor influence on the migration of the prosthetic stem [6].

This aspect is particularly important in the treatment of osteoporotic femoral neck fractures. A recent meta-analysis investigated the results of cemented versus cementless endoprostheses (CEP) in osteoporotic femoral neck fractures. Five prospective randomized trials involving a total of 950 patients were included. Cementless CEPs had a significantly higher implant-associated complication rate (postoperative periprosthetic fractures) compared to cemented KEPs. The duration of surgery was significantly shorter for cementless CEPs. There were no differences in cardiovascular events, mortality and functional outcome. Because

of the lower complication rate, study authors favor cemented head endoprostheses in patients with osteoporotic femoral neck fractures [7].

These data were confirmed in a recent randomized prospective study. In 69 patients of the 140 planned patients to be included, the study was discontinued due to significant differences in the complication rate. In the cementless prosthesis anchorage group ($n = 34$), 9 complications occurred (three dislocations, three intraoperative periprosthetic fractures, one postoperative periprosthetic fracture) [8].

Periprosthetic fractures

Periprosthetic fractures often lead to serious consequences, since they may be difficult to reconstruct and the recovery process of the affected patients tedious. In addition, many of these patients no longer reach their previous level of activity. A relatively large study from the UK examined the risk of periprosthetic fractures five years after implantation of hip or knee total endoprostheses. The incidence of fractures after primary total hip arthroplasty was 0.9%, after revision of total hip arthroplasty 4.2%, after primary total knee arthroplasty 0.6%, and after revision of total knee arthroplasty 1.7%. The incidence of fractures was higher in female patients over the age of 70 years [9].

Periprosthetic fractures in the area of the femur in lying total hip endoprostheses are frequently seen in everyday clinical practice and generally difficult to treat. The typical patient suffering from such a fracture is older, generally frail and has osteoporosis. There is no clear consensus on the supply of these fractures as there is a lack of high quality studies. In addition, there are recent case reports of bisphosphonate-induced periprosthetic fracture [10]. Such fractures have a significantly increased risk of pseudarthrosis and are particularly difficult to treat due to the pathologically altered bone quality.

Low bone quality increases the risk of periprosthetic fracture. The clinical significance of a generalized reduced bone quality is also shown by a locally reduced bone mass in the area of the bone-implant interface or bone-cement interface. For this reason, one group studied periprosthetic bone density in patients with cemented total knee arthroplasty and cementless total knee arthroplasty. In both groups, a median reduction of periprosthetic bone density independent of the anchoring method was seen four years after implantation. The conclusion was that a low load or mobility was responsible for bone resorption [11].

Periprosthetic osteolysis

Osteolysis is a local reaction that can lead to reduction of bone at the interface between bone and implant when the implant is lying. The clinical consequence of this local bone loss is aseptic implant loosening, a primary cause of revision [12].

Various studies have shown that bisphosphonate therapy can reduce osteolytic processes and / or be useful in their treatment. In addition, several case reports have been published that have demonstrated the positive effect of teriparatide on periprosthetic

osteolysis. In general, however, the data in this area is rather low. In particular, there is a lack of high quality studies in the literature [12].

Vitamin D and arthroplasty

Vitamin D is essential for bone development, bone remodeling, physiological fracture healing and possibly muscle strength as well [13].

There are many questions regarding the optimal vitamin D level in orthopedic surgery, including endoprosthetics. This not only relates to the bone metabolism-associated effects of vitamin D, but also its general effect on postoperative function in the aforementioned procedures. A positive influence of vitamin D on remobilization and fall prevention is suspected. The presumed positive effect of vitamin D is due to the high prevalence of vitamin D deficiency in various observational studies.

A retrospective study of 723 patients undergoing various orthopedic surgical procedures showed that 40% of these patients had vitamin D deficiency (according to the Institute of Medicine Standards – 25-OH Vitamin D level $\leq 20 \text{ ng ml}^{-1}$) [14].

A study involving a smaller group of patients undergoing hip or knee total replacement surgery examined the relationship between bone mineral density, vitamin D, and osteoarthritis. 84.7% of patients had a vitamin D level $\leq 30 \text{ ng ml}^{-1}$, 20% of men and 23.2% of women had a T-score below -2.5 as an indication of osteoporosis [15].

In a large prospective study on the influence of vitamin D status and bone mineral density on the development of a nonspecific radiologic gonarthrosis, those with the lowest vitamin D levels at the beginning of the study also showed the fastest progression of the gonarthroses [16]. However, a study analyzing the effect of the vitamin D level on various functional parameters after implantation of total hip arthroplasty revealed that low vitamin D levels ($\leq 20 \text{ ng ml}^{-1}$) did not affect short-term functionality [17]. The authors concluded that surgery should not be postponed due to low preoperative vitamin D levels, but that vitamin D should be corrected postoperatively.

Bisphosphonates and arthroplasty

Bisphosphonates are approved for the prevention and treatment of osteoporosis. Bisphosphonates inhibit the activation of osteoclasts and thereby reduce bone resorption. Various studies have shown the reduction of fracture risk in patients with low bone density under bisphosphonate therapy.

Animal studies in which allografts or implants were inserted into bisphosphonate solutions prior to implantation have been shown to enhance bony integration and mechanical stability of the implant or allograft. However, this effect has been refuted by several other studies [18].

The use of ibandronate, alendronate, risedronate, pamidronate and zolendronic acid has been shown to reduce periprosthetic bone loss in cementless total hip arthroplasty. Most studies had a follow-up up to five years after implantation. Data with a longer follow-up interval is missing [19].

A randomized, prospective study on the effect of a single zolendronic acid infusion on Pan and

stem migration after implantation of a cementless hip total endoprosthesis. The infusion or placebo was administered to the patients on the first postoperative day. After two years, a significantly lower pan migration was seen in the zolendronic acid group compared to placebo control, whereas stem migration was only one trend.

A study group from Scandinavia investigated the migration of the acetabular component after implantation of total hip endoprostheses. In this study, after the acetabulum was milled, a swab previously placed in an ibandronate solution was placed before implantation of the definitive implant. With this method, pan migration was significantly reduced compared to the comparison group. In addition, the rate of peri-radical loosening ("radiolucent lines") was also significantly reduced [20].

A registry study from Denmark investigated the effect of bisphosphonates on the incidence of revisions after implantation of a total hip endoprosthesis. Long-term use of bisphosphonates reduced the risk of over-revision (all causes included), but the risk of revision due to periprosthetic infection was increased [21]. Other studies showed no increased infectivity under bisphosphonate therapy.

Total hip arthroplasty patients on bisphosphonate therapy show a lower fracture risk compared to those without treatment [22]. Even in patients with total knee replacement, it was shown that taking alendronate 6 months postoperatively resulted in less periprosthetic bone loss one year after surgery. However, this difference could no longer be proven after three years [23]. Patients taking bisphosphonates have a longer lifetime of implanted total knee arthroplasty compared to patients without therapy [24], although this effect has not been demonstrated in all studies [25]. Patients on bisphosphonate therapy also have a lower fracture risk than those without therapy [26].

The majority of available studies indicate that bisphosphonate therapy improves bony integration of implants, results in longer lifespan, and fewer fractures postoperatively. Therefore, continuation of bisphosphonate therapy may be recommended in the case of planned arthroplasty.

Teriparatide and arthroplasty

Teriparatide is a recombinant human parathyroid hormone derivative and has an osteo-anabolic effect. It is approved for the treatment of postmenopausal osteoporosis, steroid-induced osteoporosis and male hypogonadal osteoporosis. Teriparatide is administered daily as a subcutaneous injection [27]. Teriparatide is also used off-label to support bone healing.

In an experimental study on dogs, the use of teriparatide improved the integration of the implant in press-fit technique and the healing of the implant into the surrounding bone [28].

Two case reports describe an improvement in the radiographic outcome of aseptic loosening of total hip endoprostheses, and another in aseptic loosening of a total knee endoprosthesis [29, 30, 31].

A study from Taiwan investigated the effect

of teriparatide therapy in osteoporotic femoral neck fractures treated with cementless head endoprostheses. In the intervention group there was a significantly lower stem migration 6 and 12 weeks after implantation compared to the control group [32].

Another study examined the effect of teriparatide on periprosthetic bone density in total hip arthroplasty compared to alendronate and placebo. In the teriparatide group there was a significantly increased bone density compared to placebo, but the values were comparable to alendronate [33].

This effect was confirmed in a recent study in patients with total knee replacement. One year after implantation, the intervention group showed a significantly higher bone density in the examined periprosthetic areas both femoral and tibial compared to the control group [34].

The effect of teriparatide on tibial implant migration in total knee arthroplasty was investigated in a randomized study in 50 patients. Patients in the intervention group received a subcutaneous injection of 20 µg teriparatide once daily for 2 months postoperatively from the first postoperative day. The primary endpoint was migration 1 or 2 years postoperatively. However, no significant difference was found in the two study groups [35].

The data suggest that teriparatide can be used as an adjuvant to support osseous integration in cementless implants and maintain periprosthetic bone density. This is especially true for patients with osteoporosis and poor bone quality.

Denosumab and arthroplasty

Denosumab is an IgG2 anti-RANKL antibody that mimics the effects of osteoprotegerin (OPG) in bone metabolism and binds Kappa B ligand (RANKL) with high affinity to the Receptor Activator of Nuclear Factor, thus interacting with the Receptor Activator of Nuclear Factor Kappa B (RANK) inhibits. Thus, osteoclast differentiation and subsequently bone resorption is reduced. The data on the effect of Densomab on hip or knee total endoprostheses is low.

A recent study from Scandinavia investigated the effect of denosumab on tibial implant migration in total knee replacement in a randomized study in 50 patients. Patients received an injection of denosumab on the first postoperative day and again 6 months postoperatively. The primary endpoint was migration 1 or 2 years postoperatively. In the group with denosumab therapy, there was a significantly lower migration compared to placebo after one and two years. As the study authors also performed the study described above regarding prosthesis migration and teriparatide, they concluded that inhibition of bone resorption is probably more important than postoperative osteoanabolic stimulation in total knee replacement [36].

Due to the lack of data, there are no recommendations regarding endoprostheses regarding denosumab at the current time.

Heterotopic ossifications

Heterotopic ossifications, ie the formation of periarticular bone, are common complications

after trauma, but also as a result of implantation of endoprostheses. As a rule, the formation of a heterotopic ossification is not clinically relevant, but it can cause pain and functional limitations in individual cases. Frequently one sees heterotopic ossification in men and in patients with certain rheumatic diseases such as ankylosing spondylitis.

A clinical study investigated the occurrence of heterotopic ossification 6 months after total hip arthroplasty and the effect of etidronate versus indomethacin on the formation. No difference could be detected between the two preparations [37].

Another smaller study showed that pamidronate can reduce heterotopic ossification after total hip arthroplasty implantation [38].

Recommendations

As this overview shows, the proportion of patients with reduced bone quality is high among endoprosthetic patients. Therefore it seems sensible to evaluate the bone quality of patients in the case of planned endoprostheses implantation preoperatively. If necessary, patients should be educated about a necessary calcium and vitamin D supplementation. In addition, it seems reasonable to aim for physiological

vitamin D levels perioperatively. Drugs that have known negative effects on bone quality, such as proton pump inhibitors or glucocorticoids, should be paused or at least administered at the lowest possible therapeutic level. In postmenopausal women, men over 70 years of age, and women and men at increased risk of osteoporosis, a bone density measurement should be performed within two years after implantation of a hip or knee total endoprosthesis. Another instrument that can be used for individual fracture risk assessment is the Fracture Risk Assessment Tool (FRAX). FRAX uses various patient-related factors to determine the probability of the 10-year fracture risk. FRAX can be combined with the bone density measurement to make it more precise. In patients with reduced bone quality, treatment with bisphosphonates or teriparatide should be considered as it may increase the bone integration of cementless implants, increase the life of the implants, and generally reduce periprosthetic fractures and fractures. In patients with established osteoporosis, cementation of prosthetic components (especially hip total endoprostheses) may be required in individual cases. This decision is up to current knowledge of the surgeon.

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ОСТЕОПОРОЗ И ЭНДОПРОТЕЗИРОВАНИЕ

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В последние десятилетия количество имплантаций эндопротезных суставов постоянно увеличивается. Многие пациенты пожилого возраста, нуждающиеся в замене суставов, имеют пониженное качество кости из-за остеопороза. У пациентов с эндопротезами и остеопорозом часто наблюдаются следующие осложнения: интраоперационные перипротезные переломы, перипротезный остеолиз, увеличение миграции имплантатов или послеоперационные перипротезные переломы. Таким образом, оценка качества костной ткани является важным этапом в лечении пациентов для обеспечения наилучшего ухода и оптимизации долгосрочных хирургических результатов. При необходимости, пациенты должны получить информацию о возможном дополнительном приеме кальция и витамина D. Кроме того, представляется целесообразным ориентироваться на физиологические уровни витамина D в периоперационном периоде.

Обзоры

У женщин в постменопаузе, мужчин старше 70 лет, а также женщин и мужчин с повышенным риском развития остеопороза в течение двух лет после имплантации эндопротеза должны быть выполнены измерения минеральной плотности кости.

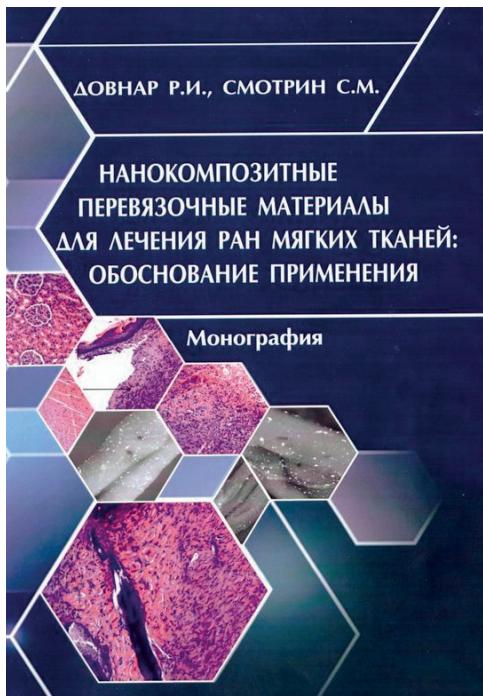
У пациентов со сниженным качеством кости следует рассматривать лечение бисфосфонатами, Деносумабом или Терипартидом для улучшения костной интеграции цементных имплантатов, увеличения срока службы имплантатов, а также для уменьшения перипротезных переломов и переломов в целом. В отдельных случаях у пациентов с остеопорозом может потребоваться имплантация с цементной фиксацией протезных компонентов (особенно при замене тазобедренного сустава).

Ключевые слова: остеопороз, переломы, эндопротезирование суставов, бисфосфонаты, Деносумаб, Терипартид.

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НОВЫЕ ИЗДАНИЯ



Довнар, Р. И. Нанокомпозитные перевязочные материалы для лечения ран мягких тканей : обоснование применения : монография / Р. И. Довнар, С. М. Смотрин ; Министерство здравоохранения Республики Беларусь, УО "Гродненский государственный медицинский университет". – Гродно : ГрГМУ, 2018. – 160 с. : табл., рис. – Библиогр.: С. 127-159.

В монографии отражены результаты экспериментального изучения антибактериального, противогрибкового эффекта нанокомпозитных перевязочных материалов, содержащих наночастицы серебра или золота. Показано усиление этого эффекта при воздействии низкоинтенсивным лазерным излучением соответствующей длины волны и времени воздействия. Продемонстрировано ускорение заживления экспериментальных асептических и контаминированных ран при использовании для их лечения предлагаемых перевязочных материалов. Авторы экспериментально доказали возможность применения вакуумного автоклавирования для стерилизации перевязочных материалов, содержащих наночастицы серебра или золота, а также продемонстрировали отсутствие токсического влияния данных материалов.

Монография предназначена для врачей-хирургов, интернов, клинических ординаторов, аспирантов, студентов всех факультетов учреждений, обеспечивающих получение высшего медицинского образования.