Bone Graft Options for Spine Fusion in Adolescent Patients with Idiopathic Scoliosis

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Introduction

Adolescent idiopathic scoliosis (AIS) is one of the most prevalent diseases among teenagers, with an incidence rate of 1–3% worldwide, and at least 0.02% of patients require surgical treatment.[1] The "gold standard" procedure is instrumentation and fusion of 10 or more vertebrae with forceful correction of the deformity.[2] Although autogenous bone grafts are the "gold standard" for spine fusion,[3] significant progress has been made in discovering bone graft alternatives, including freeze-dried allograft, demineralized bone matrix (DBM), triosite ceramics, and bone marrow aspirate (BMA), which have been used as substitutes for iliac crest in AIS surgery.[4-7] Results show that these substitutes could gain similar benefits for spine fusion, while other evidences fail to be replicated. Orthopedic surgeons are put into a dilemma of which substitute is the best for AIS surgery with less complications while achieving higher fusion rate. In this article, we presented our viewpoint on this issue.

Allograft

Allograft bone is osteoconductive and weakly osteoinductive depending on the preservation of growth factors. Allograft is harvested from cadaveric tissue donors and can be stored in bone banks. There are many forms comprising of freeze-dried, fresh-frozen, and DBM grafts. The advantages of allograft include structural strength (not DBM), easy to access and low price compared with bone morphogenetic protein (BMP), and other graft substitutes. Yet, it may take a longer time to achieve complete fusion compared with iliac crest bone graft (ICBG).[8] Besides, risks of disease transmission have been raised, including human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and bacterial infections.[9] However, it is quite rare to get infected by allograft transmission. Studies also reported that delayed infection following spine fusion were related to blood transfusion rather than allograft.[10]

Dodd *et al*.[11] did a prospective cohort study, comparing the fusion performances between allograft and ICBG with 20 patients included in each group. No statistical differences were found between groups through a blind, radiographic assessment at 6 months, nor did the correction loss. However, a marked reduction of surgery time and blood loss were noticed in the allograft group. Blanco *et al*.[12] and Grogan *et al*.[13] retrospectively reviewed patients undergoing posterior spine fusion with allograft and found that the complication rates and an average loss of correction were favorably less compared with ICBG. Knapp *et al*.[14] retrospectively reviewed 111 patients and found that a combination of freeze-dried allograft chips and local autograft could achieve a 97% postoperative fusion rate at 5 years. To be noticed, loss of correction has been discovered to be correlated with types of construction. Less loss of correction was described in patients undergoing

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pedicle screw system compared with those undergoing Cotrel-Dubousset or Harrington instrumentation (1.1 vs. 5.9 or 6.5°, respectively).[15]

Demineralized Bone Matrix

DBM has emerged as supplant to allograft in fusion with the both osteoinductive and osteoconductive properties. Generally, DBM products are decalcified cortical bones, retaining the organic phase including collagen, noncollagenous proteins and osteoinductive growths factors such as different fractions of BMPs. There are many products available in the USA. It could be manufactured in gel, powder, fiber, pellet, sheet, etc. DBM has many practical advantages over allograft, such as flexible shape and being easy to insert, expansion with blood while being difficult to dislodge. Moreover, DBM is inexpensive with no donor-site morbidities. The main disadvantage is the variability of osteoinductive abilities due to different preservations of growth factors resulting from different processing techniques.

Price *et al*.[4] performed a retrospective analysis of 88 participants assessing the contribution of DBM in fusion with a minimum of 2 year's follow-up. Patients were allocated to three groups: ICBG, freeze-dried corticocancellous allograft, and autologous bone marrow with DBM. Pseudarthroses (including loss of 10° or more of correction) was assessed by radiographs. The fusion failure rate was 12.5% in Group A (ICBG), 28% in Group B (freeze-dried corticocancellous allograft), and 11.1% in Group C (composite graft of autologous bone marrow and DBM). Intraoperatively, autogenous bone marrow was supplied by autogenous bone graft, including lamina, spinous processes, facets, or ribs. DBM combined with autogenous bone marrow was found to have similar performance with ICBG in promoting spine fusion, though the follow-up period was relatively short. Weinzapfel *et al*.[16] investigated the performance of DBM in anterior fusion. They applied video-assisted thoracoscopic surgery for anterior release and fusion in large thoracic curve scoliosis patients. Forty patients were included and followed up for at least 1 year, 12 patients with allograft and 28 patients with DBM. Interbody fusion was assessed using radiographs. The fusion rates were not statistically different between groups (68% vs. 92%, $P = 0.088$). Crankshaft, pseudoarthrosis, or hardware failure were not found in any participants. Cammisa *et al*.[17] prospectively reviewed the use of DBM in 120 patients undergoing posterolateral fusion. Results showed equivalent benefits between patients receiving both DBM and ICBG and patients with ICBG alone (52% vs. 54%). DBM could favorably help to reduce the amount of ICBG needed for fusion.

Ceramics

Ceramics is a kind of specific material structure, which is composed of pure β-tricalcium phosphate, or a compound of β-tricalcium phosphate and hydroxyapatite. β-tricalcium serves as quick action material recruiting cells promoting bone formation, while hydroxyapatite has a stable structure and prolongs the effect of β-tricalcium.[18,19] Compared with ICBG, ceramics are easy to access. Noticeably, satisfactory biocompatibility has been obtained without any reports of immune-rejection or virus contamination, which are the risks of the allograft.[20] The disadvantage of ceramics is a lack of osteoinductive properties due to the absence of growth factors. Thus, it requires a longer time to achieve clinical fusion.

Ransford *et al.* and other investigators performed four randomized controlled trials (RCTs)[5,6,19,21] involving 467 participants, of which 227 participants used ceramics in combination with local grafts for spine fusion with mean follow-up time ranging between 13 and 48 months. Participants in both ceramics and autograft obtained comparable excellent clinical results in adolescent patients. When excluding complications related to donor-site, patients from both groups shared the same rate of back complications, such as back pain, hardware problems, and wound healing delays. Ransford *et al*.[21] found more correction loss in the ceramics group (8% vs. 4%). However, Lerner *et al*.[5] found less correction loss in the ceramics group (2.6% vs. 4.2%). To be noticed, half of the participants in the Ransford *et al.* study underwent a Harrington-Luque instrumentation, which provided less fixation compared with Cotrel-Dubousset system. Ransford *et al.* found the correction loss in ceramics and autograft were 4.2% and 2.4%, respectively. This result was in consistent with the literature which reported a 2–10° correction loss in patients undergoing modern segmental spinal instrumentation.[6] Compared with the spine instrumentation, grafts seem to play a minor role in leading to correction loss. Lerner *et al*.[5] and Delécrin *et al*.[6] particularly described the pain intensity (visual analog scale) before surgery, postsurgery, and at final follow-up. No differences were noted regarding back pain after surgery, while some patients in the ICBG group experienced moderate chronic pain at donor-site. Wang *et al*.[22] found surgery time was longer by 1 h in patients fused with ICBG compared in patients with allograft or ceramics. Moreover, patients fused with ICBG suffered more blood loss. Our own clinical experiences also indicate that ICBG is associated with longer surgery time and more blood loss.

Perspective

Donor-site morbidities are of great concerns when ICBG is under consideration. In a meta-analysis with 6449 patients included, 9.71% patients suffered from chronic donor-site pain, which was ranked as the number one complication among infections, hematoma, fractures, nerve and vascular injuries, as well as wound healing problems.[23] Compared with ICBG, allograft, DBM and ceramics are easy to access. Furthermore, they are much cheaper than grafts loaded with BMP. Adolescent patients have been endowed with a strong ability to regenerate and healing. Thus, allograft, DBM, and ceramics exhibit favorably similar benefits in achieving spine fusion while do not increase pseudoarthrosis

rate and surgical morbidities. Specifically, these bone graft alternatives can obviously avoid donor-site complications. BMP is not recommended for use in adolescent patients due to infections, osteolysis, heterotopic bone formation, and even tumor risks, while the adolescent patients are less likely to get nonfusion.[24-26] Recently, BMA has been recognized for its remarkable ability to promote bone fusion.[27] Yamada *et al.*[28] performed an RCT and found ceramics loaded with BMA had a higher fusion rate at 6 months after surgery (68.9% vs. 49.2%) without donor-site complications. Future studies may include the application of BMA for spine fusion in AIS patients. In summary, allograft and ceramics are recommended bone graft extenders for spinal fusion in adolescent scoliosis patients in mainland China. Newly-developed grafts as BMA still need further investigation.

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Conflicts of interest

There are no conflicts of interest.

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