Comparative Analysis On The Effects, Costs, And Clinical Indications For Autograft, Allograft, And Bone Graft Substitutes In The Setting Of Orthopedic Trauma Surgery

Ariel Kidron, OMS-II, Hiep Nguyen, OMS-II, Tianyi Liu, OMS-II, Jack Bayer, MS-II, Tim Niedzielak, D.O., PGY-III, Brian Cross, D.O., Edward Perez, M.D.

Nova Southeastern University Dr. Kiran C. Patel College of Osteopathic Medicine

Background and Introduction

Utilizing bone grafts has been well known to benefit the orthopedic community for decades by enhancing bone repair when considering cases such as reconstructions of bone loss and voids in trauma settings. These bone defects have been classically treated using autograft material sourced from the iliac crest; however, this practice has also been associated with harvest site morbidity. Developments in sterilization techniques and technology have provided surgeons with further bone allograft materials. Subsequently, synthetic materials have been introduced as a promising new source of graft materials, largely due to avoiding morbidity issues experienced with autografts and potential infection transmission associated with allografts.

Graft materials should also be assessed on their potential for bone repair, an aspect dominated by:

- *Osteoconductivity,* relating to the materials ability for cells to grow on a three dimensional surface which can include materials such as cancellous bone grafts or demineralized bone matrix (DBM),
- *Osteoinductivity*, relating to the material's potential recruitment and induction of progenitor cells into active osteoblasts and osteocytes, largely dominated by the presence of bone morphogenic protein (BMP) in the material, or,
- *Osteogenicity*, relating to the material's propensity for deposition of new bone matrix, a property reserved for materials such as autologous grafts and bone marrow aspirate.

Ideal bone grafts would contain all three properties, yet most materials utilized employ only one or are used in conjunction with other biologics to attain ideal bone repair. In addition, risk assessment strategies must be considered when selecting materials for grafting, as complications from donor site morbidity associated with autografts or infection prevention with allografts should be examined. Furthermore, cost variances have a large role in determining appropriate graft materials since factors associated with material development, graft harvesting, and surgery itself may lead to large differences in procedural costs. A combination of all of these factors, ranging from graft properties, potential for complications and morbidity, and cost should be employed for effective biologic usage in orthopedic trauma.

Methods

A systematic literature review of PubMed and UpToDate databases was conducted. Articles published between 2010 and 2020 were retrieved, and the search was expanded by reviewing articles from reference sections of selected papers. A total of seventy-five articles were selected for the initial review. After examining each article, a total of thirty studies met inclusion criteria.

Functions, Properties, and Cost of Graft

		Osteoconductive	Osteoinductive	Osteogenic	Cost [1]	Complications
Autograft	***Cancellous Bone***	XXX	XXX	XXX	----------	- Donor site morbidity - Increased operative time - Increased blood loss
	Cortical Bone	XX	X	X	----------	*Same as above*
	Bone Marrow Aspirate	X/-	XX	XXX	----------	*Same as above*
	Vascularized Bone	XX	X	XX	----------	*Same as above*
Allograft	***Cancellous***	X	X/-[2]	----------	$380/30 cc[3]	- No osteogenic potential - Infection Potential - Host Rejection
	Cortical	X	X/-[2]	----------	$530/3 cm[4]	*Same as above*
	DBM	X	XX	----------	$730– 1300/10 mL	- Host Rejection - No structural properties
Synthetic	***Calcium Phosphate***	X	----------	----------	$1520/10 mL[5]	- Osteoconduction only
	Calcium Sulfate	X	----------	----------	$655/10 mL[5]	- Osteoconduction only - Rapid Resorption
	BMP	X[6]/-	X	----------	$3500-5000/vial[7]	- Increased neurovascular complications - Expensive - Limited FDA approval

[1] subject to market availability price fluctuations; [2]X, typically associated with fresh allograft, - associated with frozen-preserved allograft; [3] freeze dried cancellous chips; [4] typically femoral shaft allografts, sold by cm; [5] prices based on average sale price from market leaders of pure products; [6] X when delivered by collagen-based carriers; [7] price change between various market leaders; Medtronic-Sofamor Danek $3500, Stryker $5000

Results

Of the three main categories of biologics (auto-, allo-, and synthetic grafts), autografts display the highest compatibility and highest array of desired properties within orthopedics, including optimal osteoconductivity, osteoinductivity, and osteogenicity. Autografts also include the least cost burden, but at a greater risk of morbidity to the patient.

Allografts demonstrate slightly less osteoconductive properties, less potential osteoinductive properties, and no osteogenic potential. However, allografts spare the patient of donor site morbidity associated with autograft harvesting. Nevertheless, there is a large propensity for infection transmission and host rejection due to a lack of histocompatibility. Allograft costs vary widely, yet stay relatively comparable to structural synthetics. These costs exclude surgical preparation costs.

Structural synthetics only provide osteoconductive properties and pose greater risk of resorption. Synthetic biologics such as bone matrix proteins (BMP) exhibit osteoinductive potential due to their TGF-beta factors involved with osteogenic commitment for mesenchymal stem cells in surgical regions.

Conclusion

Effective bone healing rests upon the judicious usage of bone grafts, bone substitutes, and synthetic factors. The determination is based on the ability to foster osteogenesis, osteoconduction, and osteoinduction while considering the associated costs and complications. Autograft remains the "gold standard" in regards to histocompatibility and osteointegration properties albeit posing donor site morbidity.

To mediate these health risks, allografts and structural synthetics have been utilized. However, the reduced osteogenic and osteoinductive potentials in combination with the relative higher costs and risk of infectious transmissions and resorption has rendered them a case by case modality. The use of BMP successfully increased osteoinductive effects through signaling pathways in osteoblastic differentiation and osteogenesis involving TGF-beta.

The development of different bone graft modalities have nuanced the management possibilities available to surgeons and may spearhead rapid bone healing with increasing clinical effectiveness, safety, and narrower indications for maximized treatment success.

References

Baldwin P, Li DJ, Auston DA, Mir HS, Yoon RS, Koval KJ. Autograft, Allograft, and Bone Graft Substitutes. *J Orthop Trauma*. 2019;33(4):203-213. doi:10.1097/BOT.0000000000001420

Bostrom MPG, Seigerman DA. The Clinical Use of Allografts, Demineralized Bone Matrices, Synthetic Bone Graft Substitutes and Osteoinductive Growth Factors: A Survey Study. *HSS J*. 2005;1(1):9-18. doi:10.1007/s11420-005-0111-5

Chahla J, Mannava S, Cinque ME, Geeslin AG, Codina D, LaPrade RF. Bone Marrow Aspirate Concentrate Harvesting and Processing Technique. *Arthrosc Tech*. 2017;6(2):e441-e445. doi:10.1016/j.eats.2016.10.024

Effect of Single Injection of Recombinant Human Bone Morphogenetic Protein-2-Loaded Artificial Collagen-Like Peptide in a Mouse Segmental Bone Transport Model. https://www.hindawi.com/journals/bmri/2019/1014594/. Accessed June 17, 2020.

Gangji V, De Maertelaer V, Hauzeur JP. Autologous bone marrow cell implantation in the treatment of non-traumatic osteonecrosis of the femoral head: Five year follow-up of a prospective controlled study. *Bone*. 2011;49(5):1005-1009. doi:10.1016/j.bone.2011.07.032

Goff T, Kanakaris NK, Giannoudis P V. Use of bone graft substitutes in the management of tibial plateau fractures. *Injury*. 2013;44(SUPPL.1):S86-S94. doi:10.1016/S0020-1383(13)70019-6

Gruskin E, Doll BA, Futrell FW, Schmitz JP, Hollinger JO. Demineralized bone matrix in bone repair: History and use. *Adv Drug Deliv Rev*. 2012;64(12):1063-1077. doi:10.1016/j.addr.2012.06.008

Khan WS, Rayan F, Dhinsa BS, Marsh D. An Osteoconductive, Osteoinductive, and Osteogenic Tissue-Engineered Product for Trauma and Orthopaedic Surgery: How Far Are We? *Stem Cells Int*. 2012;2012. doi:10.1155/2012/236231

Moon JK, Yoon JY, Kim CH, et al. Multiple drilling and multiple matchstick-like bone allografts for large osteonecrotic lesions in the femoral head: an average 3-year follow-up study. *Arch Orthop Trauma Surg*. February 2020:1-9. doi:10.1007/s00402-020-03364-z

Rajadurai J, Lovric V, Mobbs RJ, Choy WJ, Walsh WR. The use of demineralised bone fibres (DBF) in conjunction with supercritical carbon dioxide (SCCO2) treated allograft in anterior lumbar interbody fusion (ALIF). *J Spine Surg*. 2019;5(4):589-595. doi:10.21037/jss.2019.10.04

Roberts TT, Rosenbaum AJ. Bone grafts, bone substitutes and orthobiologics the bridge between basic science and clinical advancements in fracture healing. *Organogenesis*. 2012;8(4):114-124. doi:10.4161/org.23306

Seagrave RA, Sojka J, Goodyear A, Munns SW. Utilizing reamer irrigator aspirator (RIA) autograft for opening wedge high tibial osteotomy: A new surgical technique and report of three cases. *Int J Surg Case Rep*. 2014;5(1):37-42. doi:10.1016/j.ijscr.2013.11.004

The Holy Grail of Orthopedic Surgery: Mesenchymal Stem Cells-Their Current Uses and Potential Applications - PubMed. https://pubmed.ncbi.nlm.nih.gov/28698718/. Accessed June 17, 2020.

Xie H, Wang B, Tian S, Liu B, Qin K, Zhao D. Retrospective Long-Term Follow-Up Survival Analysis of the Management of Osteonecrosis of the Femoral Head With Pedicled Vascularized Iliac Bone Graft Transfer. *J Arthroplasty*. 2019;34(8):1585-1592. doi:10.1016/j.arth.2019.03.069