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OBJECTIVE: The purpose of this study is to elucidate genetic variants contributing to nonsyndromic craniosynostosis by comparing samples from abnormally fused bones, unaffected bones, and parent saliva, to those from patient peripheral whole blood (PWB).

METHODS: We applied whole genome sequencing, then performed best practice genomic alignment and variant calling, trio joint genotyping for germline genomic variants, consensus somatic variant calling for PWB-bone comparisons, and variant annotation. Alternative allele frequencies, variant damaging predictions, and inheritance models were used to filter variants.

RESULTS: The study included 109 DNA samples from 26 trios, in which 17 families have affected bone tissue DNA. Patients’ affected bone samples were sequenced to an average depth of 112.7X with the rest biospecimens to 35.7X. On average, 2629 somatic variants were identified in the affected bones. After filtering, we identified 40 genes with somatic pathogenic/likely pathogenic (P/LP) variants. We also detected germline P/LP variants, mostly from de novo events. We confirmed known craniosynostosis genes FGFR3 and IHH (both with germline de novo variants), and FREM1 (with a somatic variant in affected bone). From a single patient, we also discovered a germline de novo CHPF variant and a somatic CHPF variant in affected bone.

CONCLUSION: We identified a novel candidate craniosynostosis gene CHPF in the same pathway as those required for bone development and digit patterning, which shows promise for further investigation.

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INTRODUCTION: The “core surgical principles” section was added to the Plastic Surgery In-Service Training Exam (PSITE) in 2016. To our knowledge, assessment of the “core surgical principles” references has not been performed previously. The main objective is to characterize the references provided as supporting evidence of the PSITE syllabi, including those on the novel “core surgical principles” section. In addition to analyzing the newly instituted “core principle section,” the secondary aims of this study are to determine (1) the most frequently referenced journal and textbooks, (2) the publication lag of journal and textbook references, and (3) the impact factors for referenced journal articles in five consecutive PSITE syllabi. It is our hope that such an analysis will allow for better preparation for the examination and more relevant focus of educational efforts on the part of residents, fellows, and program directors.

METHODS: We analyzed the references from five consecutive PSITE syllabi (2016–2020). We collected the following information from each question: year of the examination, question section, the total number of references per question, source of publication of each reference, and year of publication of each reference. We assessed the top journals and textbooks that provided supporting references for the questions. Mean and median were used to summarize continuous variables, while percentages and proportions were used to present categorical data. To compare the JIF and publication lag among the sections and examination years, we used the Kruskal–Wallis one-way analysis of variance test. A P value of <0.05 was considered statistically significant.

RESULTS: We analyzed 1250 questions and 3436 references. Plastic and Reconstruction Surgery (PRS) was overall the most frequently referenced journal followed by Journal of Hand Surgery (American Volume) and Annals of Plastic Surgery. The most commonly referenced textbooks were Plastic Surgery (by Neligan), Green’s Operative Hand Surgery, and Grabb and Smith’s Plastic Surgery. Regarding the “core surgical principles” section, PRS remained the most frequently cited journal, followed by Journal of the American Medical Association (JAMA), New England Journal of Medicine (NEJM), Annals, and Aesthetic Surgery Journal. “Core surgical principles” contained the largest number of unique journals (n = 209) among all test sections. Within the “core” section, Statistics in Medicine was the most frequently referenced textbook followed by...
Grabb and Smith’s Plastic Surgery, Guyton and Hall Textbook of Medical Physiology, Plastic Surgery (by Neligan), Principles and Practice of Pediatric Plastic Surgery, and Essential Medical Statistics. There were significant differences in JIF between the sections ($P < 0.0001$) with references in “core surgical principles” having the highest mean JIF ($9.6 \pm 19.5$). The median journal publication lag for the all references was 6 years (IQR, 3–10).

CONCLUSIONS: The main plastic surgery texts and literature were used to support approximately half of the answers within the “core surgical principles” section. The references within this section originated from the largest number of different journals, thus highlighting the breadth and variety of this content and the challenges in preparing for this section.

A Solution to Poorly Tolerated Lower Limb Amputations: Osseointegrated Prostheses Prove Cost-effective in the United States

Presenter: Grant G. Black, BA

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PURPOSE: This study is the first cost–benefit analysis of osseointegrated implant (OI) prostheses compared with socket-suspended (SS) prostheses for lower limb amputees in the United States. The use of traditional SS prostheses for patients with transfemoral and transtibial amputations can be complicated by issues like poor fit, tissue damage, and pain at the socket-limb interface. These complications often require management by plastic surgeons. Osseointegration provides an alternative solution by anchoring the prosthesis directly to an implant in the user’s residual limb; this procedure involves both orthopedic and plastic surgery teams. The operation, materials, and maintenance associated with osseointegration can be expensive, but patient-reported data suggest that OI leads to better quality of life in patients who are dissatisfied with their SS prosthesis.

METHODS: We used a Monte Carlo model to project costs and lifetime quality-adjusted life years (QALYs) for patients with OI and SS prostheses. Simulation parameters for the base-case scenario were derived from a cohort of 25 patients who underwent osseointegrated implantation following unilateral lower limb amputations at our institution between October 2017 and February 2020. An IRB-approved retrospective chart review was performed on each patient. CPT codes, material costs, length of surgery, and length of inpatient stay were collected for all encounters related to the amputation site. Utilities and SS prosthesis costs were derived from the literature. We calculated and compared incremental cost-effectiveness ratios (ICERs) for OI and SS prostheses. Parameters were varied individually in one-way sensitivity analyses to evaluate the sensitivity of the results to plausible variations in model inputs.

RESULTS: Our patients had an average age of 49.6 years at implantation and were followed for 17 months on average. In total, 84% of patients had traumatic amputations. We found the average cost of osseointegration surgery to be $54,503. An estimated 20% of patients required a pre-implantation residual limb revision surgery, averaging $49,191. Maintenance of a healthy OI prosthesis cost on average $2626 per year. Complication rates per year and average costs were as follows: soft tissue infection (29%, $435), bone/implant infection (11%, $11,721), painful neuroma (14%, $14,659), and mechanical failure (17%, $46,513). In the base-case scenario, the ICER of OI prostheses compared with SS prostheses was $44,660. A cost effectiveness acceptability curve showed that OI was favored over SS in 71% of cases at a willingness-to-pay of $50,000 per QALY. In one-way sensitivity analyses, the ICER was most sensitive to the mechanical failure rate, mechanical failure cost, and alternative yearly SS prosthesis cost.

CONCLUSIONS: Our model suggests that osseointegrated implantation can provide a higher quality of life at affordable costs when compared with poorly tolerated SS prostheses in patients with lower limb amputations in the United States. Intraoperative reconstruction and postoperative management by a plastic surgeon is essential to minimize complications and thus improve cost-effectiveness and patient satisfaction. More follow-up must be done to understand the long-term benefits and risks of OI-based prostheses.

Cytokines Released from Human Adipose-tissue–Derived Stem Cells By b-FGF Stimulation: Effects on Angiogenesis and Lymphatic Vessels Formation By IL-8 and CXCL1

Presenter: Chihiro Matsui, MD