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Adipose-Derived Mesenchymal Stem-Cell Therapy Improves Arteriogenesis, Hemodynamics, and Walking Performance in a Porcine Model of Peripheral Artery Disease

Abstract

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Case: A 46-year-old female with history of migraines, obesity and hypertension presented to PCP for left-sided rhinorrhea, headaches and nausea for several months. Patient was seen by multiple providers and conservatively managed with Zofran, nasal decongestants and cold remedies without relief. She denied any recent infections or trauma. Further questioning revealed that headache and rhinorrhea were positional and accompanied by metallic tasting PND, raising suspicion for cerebrospinal fluid rhinorrhea. CT head (**Figure 1**) was ordered showing partial empty sella and thinning/defect of the left sphenoid sinus roof. Nasal discharge tested positive for Beta-2 transferrin confirming cerebrospinal fluid leak. Patient subsequently underwent

nasoseptal flap repair via a transsphenoidal approach. Rhinorrhea resolved after surgery and symptoms improved.

Conclusion: This case highlights the importance of identifying clues in patient history leading to appropriate diagnosis. Beta2-transferrin assay is currently the single best laboratory test for identifying the presence of CSF in sinonasal fluid. Other tests may include MRI, CT, or cisternography. These tests can help to locate the source of the leak and determine the best treatment option. Conservative treatment aims to reduce intracranial pressure, while surgical treatment involves repairing the leak by using a patch, glue, graft, or flap repair.

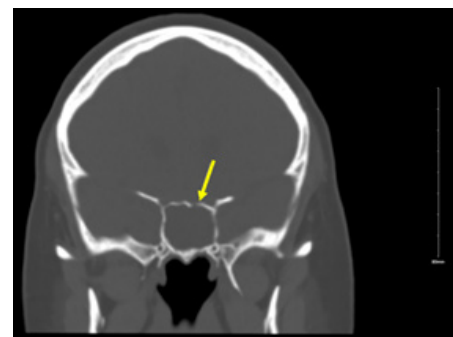


Figure 1. CT Head showing thinning/defect of Left Sphenoid Sinus Roof (arrow).

#22. Diabetes and Claudication: Reduced Pain Perception; Worse Walking Impairment and Quality of Life

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Mentor: Pooneh Bagher

Program: General Surgery

Type: Original Research

Background: The effects of diabetes in patients with peripheral artery disease (PAD) who present with claudication is poorly defined. We hypothesized that claudicating patients with diabetes would display worse characteristics including angiographic disease distribution, physiology of oxygen delivery, walking ability, at home physical activity (HPA), and quality of life (QoL) than patients without diabetes.

Methods: We recruited claudicating PAD patients and compared diabetics (N=15, HbA1c>6.5%) to non-diabetics (N=61). We

reviewed baseline Ankle Brachial Indices (ABI), CT angiography (CTA), 6 minutes walking distance (6MWD), treadmill initial (ICD) and maximal (MCD) claudication walking distance with concurrent calf muscle oxygenation (STO2) measurements with near infrared spectroscopy, QoL questionnaires and HPA measured using pedometers.

Results: The diabetic group had higher BMI (31.1 ± 6.8 vs 26.4 ± 4.4 , $p < 0.01$), and hyperlipidemia (93% vs 72% , $p < 0.01$). There were no differences in ABI, CTA, MCD and parameters of (STO2). Diabetic patients had longer initial claudication distances (ICD) (208.2 ± 133.7 meters vs 124.0 ± 94.5 , $p < 0.02$) and shorter pain recovery times (RT) (287.4 ± 234.8 seconds vs 133.9 ± 126 , $p < 0.005$). Diabetics had shorter 6MWD

(252.3 ± 62.3 meters vs 298.4 ± 60.2 , $p < 0.02$), 50% ($p < 0.005$) lower HPA, and worse measures of social functioning, emotional well-being, energy, and fatigue.

Conclusion: Diabetic PAD patients had unexpected longer ICDs, and shorter RTs suggesting significant alterations in the pain perception and pain pathways of the leg. They also had decreased performance on HPA and 6MWD with worse QoL measures suggesting that diabetes predisposes to worse walking outcomes and QoL in PAD. Identification and aggressive management of PAD should be given priority in diabetics as presenting symptoms may be milder despite worse outcomes and QoL.

#23. Length and Proximal Extent of Occlusion Dictates Severity of Disease in a Mini-Swine Model of Peripheral Artery Disease

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Mentor: Mark Carlson

Program: General Surgery

Type: Original Research

Background: There is ongoing need for large animal models of peripheral artery disease (PAD) mimicking human disease. We present mild, moderate and severe phenotypes of PAD in an Ossabaw swine model.

Methods: After 8 weeks of a western diet, we induced right hindlimb Ischemia induction (T0) with open ligation and resection of Right Superficial Femoral Artery for mild (N=4), endovascular coil occlusion of Right External Iliac Artery, Right Superficial Femoral Artery for moderate (N=9) and coil occlusion of Right External Iliac Artery, Right Superficial Femoral Artery, and right internal iliac artery for severe (N=4). At 4 weeks (T4)

and 8 (T8), all swine underwent angiography and bilateral gastrocnemius biopsy. All swine underwent bilateral ankle brachial indices (ABI), and calf muscle tissue oximetry (STO2) measurements at T0, T4, and T8, and weekly measurement of their treadmill walking distance.

Results: At T4 and T8, there was worsening of Right ABI, Right calf STO2, and treadmill

function with severity of phenotype (**Table 1**). Angiographically, at T4 and T8, the arteries that had the largest growth were the Right Profunda Artery in mild, the Right Internal Iliac Artery in moderate, and the Left Internal Iliac Artery in severe. T4, moderate and severe had similar delays of Right Profunda Artery reconstitution, however this improved at T8 in moderate unlike in severe. Histologically, mild had no obvious myopathy. There was moderate myopathy in moderate and severe end stage myopathy in severe. All severe subjects developed ischemic ulcers and tissue loss.

Conclusion: The length and proximity of occlusive disease dictates the characteristics and severity of phenotypes in an Ossabaw swine model of PAD.

Table 1. Data Overview.

	Mild (N=4)		Moderate (N=9)		Severe (N=4)		P value
	T4	T8	T4	T8	T4	T8	
R ABI/L ABI	0.79±0.09	0.84±0.14	0.53±0.07	0.56±0.13	0.38±0.18	0.4 ±0.11	T8 v T8 MI v MD <0.01 MD v S <0.05
STO2 Difference R-L Calf	0.75±3.3	1±2.45	20±6.56	14.3±3.68	19.3±2.1	28±9.6	T8 v T8 MI v MD <0.05 MD v S <0.05
TM * T4 or T8/T0	0.92±0.17	0.78±0.22	0.53±0.28	0.46±0.26	0.16±0.21	0.06±0.05	T8 v T8 MI v MD <0.03 MD v S <0.01
Angiographic growth -R/L	1.58±0.2 1.22±0.3	1.55±0.4 1.08±0.1	N/A N/A	N/A N/A	N/A N/A	N/A N/A	
R PFA R EIA R IIA	0.99±0.1	1.31±0.2	1.56±0.3	1.8±0.5	N/A	N/A	
Angiographic growth T4 or T8/T0	N/A N/A N/A	N/A N/A N/A	2.04±0.63 1.24±0.4 1.32±0.28	2.2±0.56 1.21±0.3 1.36±0.49	N/A 1.96±0.9 1.44±0.9	N/A 2.18±0.28 1.38±0.22	MD T8 v T8 RIIA v LIIA <0.01 RIIA v LEIA <0.01 S T8 v T8 LIIA v LEIA <0.05
R PFA/L PFA Appearance time	0.65±0.05	0.65±0.12	3.28±0.59	2.41±0.39	3.2±0.71	3.2±0.72	T4 v T8 MI >0.45 MD <0.01 S>0.49

R: Right, L: Left, ABI: Ankle Brachial Index, STO2: Muscle Tissue Oximetry, EIA: External Iliac Artery, IIA: Internal Iliac Artery, PFA: Profunda Femoris Artery, Bold: P value R v L <0.05, *: no R v L possible.

#24. Resident Perceptions of a Residents as Teachers Curriculum: A Qualitative Assessment

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Mentor: Abbey L. Fingeret

Program: General Surgery

Type: Original Research

Background: General surgery residents educate medical students, although may lack formal training with a “Residents as Teachers” curriculum (RaTC). This study’s aim was to understand the resident perspective on what makes an excellent surgical educator, strengths of single institution-developed RaTC, and identify teaching scenarios residents find challenging.

Methods: A longitudinal eight-hour RaTC was developed and administered in one-hour sessions over two years. Content included interactive clinical and technical skills teaching, feedback, evaluation and assessment, and interpersonal skills. Residents who had completed the RaTC were invited to participate in interviews exploring their perceptions of the RaTC and their own clinical teaching experiences. Interview comments were coded and analyzed for thematic content.

Table 1. Resident-identified facilitators and barriers to providing excellent medical student education.

	Facilitator	Barrier
Educator behaviors/teaching methodologies	Educator possesses strong ability to verbally articulate steps of procedural tasks	Personal mastery of the skill is not sufficient to teach details of complex tasks at the learner’s level
Learner attitudes and behaviors	Learner appreciates specific constructive criticism from educators to improve performance	Concern that constructive criticism given to students will be negatively perceived
Structural/Environmental factors	Presence of a “Residents as Teachers” Curriculum during training	Time constraints during a busy clinical day

Results: Seven subjects participated in interviews. Subjects reported that the RaTC was helpful in enhancing their skills as surgical educators and emphasized that teaching is an important part of their job. Thematic analysis identified three areas in which subjects commented on both facilitators and barriers to educating in the clinical environment: educator behaviors and teaching methodologies, learner attitudes and behaviors, and structural or environmental factors (**Table 1**).

Conclusion: The RaTC was well received by our participants, who reported that it helped improve their ability to teach medical students. However, they often felt uncomfortable implementing these skills, particularly when teaching procedural tasks, giving

constructive criticism, and finding time to teach throughout the day. Future curricula could be designed to provide more time to practice these skills in a low-stakes setting, which may help residents feel more confident utilizing them while teaching.

#25. Adipose-Derived Mesenchymal Stem-Cell Therapy Improves Arteriogenesis, Hemodynamics, and Walking Performance in a Porcine Model of Peripheral Artery Disease

Ali H. Hakim^{1,2}, Yuqian Tian^{1,2}, Al-Murtadha Al-Gahmi^{1,2}, Katya Brunette¹, Julian Kim^{1,2}, Zhen Zhu¹, George P. Casale¹, Mark A. Carlson¹, Iraklis I. Pipinos^{1,2}

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Mentor: Iraklis Pipinos

Table 1. Data Summary.

Program: General Surgery

Type: Original Research

Background: In our porcine model of Peripheral Artery Disease(PAD), we test adipose-derived stem cells(ADSC) injected transvenously around the retroperitoneal aortic trifurcation as an alternative to revascularization.

Methods: In Ossabaw mini-swine (N=13; age=6mo) right (R) hindlimb ischemia was induced with R Superficial Femoral and R External Iliac Artery coil occlusion using carotid access. Swine underwent weekly treadmill performance testing (TP). At weeks 0(T0), 4(T4), and 8(T8), ankle brachial indices (ABI) and resting muscle tissue Oximetry(STO2) were measured in calves and thighs. At T4 and T8 all swine had angiography. At T4, in treatment (Tx) swine (N=4) ADSC was isolated using stromal vascular

fractionation. Transvenously, a catheter with a retractable side-deploying needle is inserted in the R iliac vein and the needle is deployed to access the retroperitoneum and infuse ADSC around the iliac arteries.

Results: Ischemic controls (IC) had no differences between T4 and T8 in ABI, and mean STO2 differences between R and L in calves and thighs. Tx improved ABI and mean STO2 measurements (**Table 1**). IC had no changes in TP between T4 and T8. Tx showed

improvements (Table 1). On angiography, IC had growth of R Internal iliac artery (RIIA) and shorter appearance time (AT) of RIIA compared to L with no difference between T4 and T8. Tx showed increased growth of RIIA and shorter AT at T8 compared to T4 (Table 1).

Conclusion: In a swine model of PAD, ADSC injected around the aortic trifurcation showed improvement of multiple hemodynamic and performance endpoints.

	Ischemic Control Group			ADSC Group		
	T4	T8	P Value	T4	T8	P Value
ABI reduction (%) R v L	47±7	43±13	>0.35	48±8	22±6	<0.01
STO2 Difference L-R Calf	20 ±6.6	14.3±3.7	<0.03	19.3±8.7	2±2.1	<0.02
STO2 Difference L-R Thigh	11.4±5.7	10.7±8.3	>0.4	12.8±2.6	2.5±1.7	<0.01
TP reduction (%) T4 or T8/T0	47±28	53±26	>0.3	85±9	71±16	<0.04
Angiographic Growth of Artery (%) R IIA -T4 or T8/T0	104.3±62.7	119.1±56	> 0.3	58.9±25.9	161.5±60.1	<0.04
R IIA/L IIA appearance time	0.75± 0.13	0.80±0.10	<0.17	0.65±0.04	0.46 ± 0.05	<0.01

T0: Ischemic Induction Procedure, T4: 4 Weeks Procedure, T8: 8 weeks procedure, R: Right, L: Left, ABI: Ankle Brachial Index, STO2: Muscle Tissue Oximetry, IIA: Internal Iliac Artery.

#26. Student, Resident, and Faculty Perceptions on Providing Excellent Surgical Education: A Qualitative Analysis

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Mentor: Abbey L. Fingeret

Program: General Surgery

Type: Original Research

Background: Surgical residents provide clinical education for medical students. However, most have no formal training in teaching before beginning residency. This study aimed to determine, from the perspective of students, surgical residents, and faculty, how to provide excellent surgical education to medical trainees.

Methods: Fourth-year medical students, surgical residents, and faculty were recruited to participate in a semi-structured interview. The interview guide included questions about what qualities make good surgical educators, teaching scenarios in which they struggle to teach effectively, and strategies they have found to improve their teaching. All interviews were recorded, transcribed, coded, and analyzed for thematic content.

Results: Two students, two residents, and two

faculty from four institutions participated. Subjects felt formal curricula on teaching are lacking in surgical training. Participants commented on the importance of departmental culture and interpersonal skills, including enthusiasm for teaching, inclusivity for learners, and creating a safe space for building learner confidence. Teaching to each learner's level and interest, patience with learners, and finding time to create learning opportunities during a busy day were important, although educators commented that time was a frequent barrier to teaching effectively. Participants felt that it was the educator's responsibility to take ownership of their teaching ability and to personally reflect and adapt their strategies when a learner is struggling.

Conclusion: Formal training in education is lacking in surgical residency programs. Developing curricula focusing on honing interpersonal skills, strategies to maximize teaching efficiency, and self-reflection of each educator's teaching skills may help improve residents' confidence and effectiveness in teaching medical trainees.

#27. Impact of Speed of Seizure Spread on IQ and Post-operative Seizure Freedom in Refractory Epilepsy

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Mentor: Olga Taraschenko

Program: Neurological Sciences

Type: Original Research

Background: Resection zone extension in medically refractory epilepsy patients to include the area of seizure spread may result in better postoperative seizure control, resulting in intact cognition and seizure freedom. We explore the relationship between seizure propagation speed and seizure control after resection focusing on presurgical IQ test performances.

Methods: Epilepsy surgery records between 2008 and 2016 were reviewed. Demographics, presurgical scores on the Wechsler Adult Intelligence Scale (WAIS-IV) and Wechsler Abbreviated Scale of Intelligence (WASI-II), including General Adult Intelligence Standard

Score (GAI), Full-Scale Intelligence Quotient (FSIQ), Verbal Comprehension Index (VCI), and Perceptual Reasoning Index (PRI), were recorded and Engel scores at 2-year post-surgical visit were noted. Two epileptologists reviewed the presurgical intracranial EEG tracings to denote seizure onset as well as spread. Early spread was defined as propagation within ≥ 2 surrounding grid contacts within the first 10s of seizure onset. After identification of the primary channel by visual review, a frequency range of interest and then the power of all channels at ± 1 Hz were identified. Channels within 10sec from seizure onset with power $> \text{mean} + 2\text{SD}$ of identified channel for ≥ 2 consecutive epochs (epochs=1 sec with 0.5sec overlap) were noted.

Results: Among 45 patients, 71% were female, and the mean age at surgery was 38 ± 13 years. During visual analysis, 20(44%)

had early spread, 16(35.5%) had late spread, and 9(20%) had absent spread. There were no statistically significant differences between early and late spread groups regarding their performance on GAI/FSIQ, VCI, and PRI tests, and no association was observed between early/late spread and Engel score distribution. The signal processing algorithm has agreed with the clinical categorization of early vs. late ictal spread in 78.5% of seizures.

Conclusion: Early seizure spread in focal medically refractory epilepsy may not affect patients' general intellectual function nor determine their postoperative seizure freedom. A signal processing algorithm for the analysis of seizure spread on intracranial EEGs can be applied to supplement the visual analysis of seizure data.

#28. Pregnancy and Motherhood in Neurosurgery Residency Training and Beyond

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Mentor: Aviva Abosch

Program: Neurosurgery

Type: Original Research

Background: With the increasing number of women pursuing careers in neurosurgery, it is important to assess perceptions, attitudes, and experiences around surgeon pregnancy to identify barriers to attracting women into the neurosurgical workforce.

Methods: A voluntary anonymous 85-question survey was electronically distributed in July 2023 targeted towards women in neurosurgery who were pregnant during their residency training, fellowship, and/or attending years. The survey was sent to 362 women at all stages of professional development in neurosurgery.

Results: Eighty-five eligible female residents, fellows, and attendings responded to the survey (response rate 23.5%). Most respondents (72%) were concerned that their work schedule adversely affected their health or the health of their unborn child, and 46% experienced adverse events during pregnancy.

Nearly a third of women experienced at least one miscarriage – half of which occurred during residency. Most residents (92%) stated coresidents and/or attendings would resent them for asking to do shorter cases during pregnancy, and 66% witnessed negative comments about other pregnant residents during training. An estimated 36% witnessed a colleague make a derogatory comment about breastfeeding/pumping, and accommodations permitting time to pump during the workday was only reported in 54% of respondents.

One in four women would choose another career more accommodating of parenthood than neurosurgery, and 41% would discourage female medical students from pursuing neurosurgery.

Conclusion: Women in neurosurgery face significant challenges in balancing pregnancy and their careers. It is imperative to understand these barriers to implement changes to the field both systematically and socially, for improving the recruitment and success of women in neurosurgery.