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A Model to Predict Level of Prehabilitation Adherence in Older Adults With Frailty Having Cancer Surgery

Shaw, JF[1,2], Hladkowicz, E [3], Bryson, G [4,5], Forster, AJ [6,7], Gagne, S [4], Huang, A [7,8], Lalu, M [4,5], Lavallee, LT [5,9], Moloo, H [5,10], Nantel, J [11], Power, B [7,8], Scheede-Bergdahl, C [12], Taljaard, M [7,2], van Walraven, C [7,13,14], McCartney, CJL [4,1], McIsaac, DI [4,5]

[1]The Ottawa Hospital Research Institute, [2]School of Epidemiology, Population Health and Preventative Medicine, University of Ottawa, [3]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital Research Institute, [4]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, [5] Clinical Epidemiology Program, The Ottawa Hospital Research Institute, [6]Division of General Internal Medicine, The Ottawa Hospital, University of Ottawa, [7]Clinical Epidemiology Program, The Ottawa Hospital Research Institute, [8]Division of Geriatric Medicine, The Ottawa Hospital, University of Ottawa, [9]Division of Urology, The Ottawa Hospital, University of Ottawa, [10]Division of General Surgery, The Ottawa Hospital, University of Ottawa, [11]School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, [12]Department of Kinesiology and Physical Education, McGill University, [13]Department of Medicine, The Ottawa Hospital, University of Ottawa, [14]Institute for Clinical Evaluative Sciences

ABSTRACT

Background: Frailty is a well-established predictor of adverse postoperative outcomes in older surgical patients and is especially common in older people having cancer surgery. Exercise could improve postoperative outcomes for people with frailty; however, little is known about the factors that influence older people's adherence to exercise before surgery (prehabilitation) programs. Our objective was to derive and validate a model to predict prehabilitation adherence in older adults with frailty before cancer surgery.

Methods: This was a nested prospective cohort study of older adults with frailty having cancer surgery who participated in a randomized controlled trial of home-based prehabilitation. We developed a multivariable ordinary least squares linear regression model using pre-specified, prospectively collected covariates to predict adherence (% prescribed exercise sessions attempted). Continuous variables were standardized and assessed for best fit using fractional polynomials. Optimism was estimated through internal validation using bootstrapping.

Results:85 participants were included in the derivation set. Mean percent adherence was 67.3% (SD 29.1%). No pre-specified predictors were significant at the 5% level. The final model explained 27.1% of the variance in adherence, had a root mean square error (RMSE) of 24.7, a mean absolute error (MAE) of 20.1, and 28.3% optimism.

Conclusions: This model helps to explain a moderate degree of variation in prehabilitation adherence in older people with frailty, but no postulated factors were strong predictors individually. This model is an important first step toward personalizing prehabilitation support, but future research is needed to better understand predictors of prehabilitation adherence in older people with frailty.

Risk Factors for Urologic Injury in Women Uundergoing Hysterectomy for Benign Indication

Nayak, A [1,2], Breau, R [1,2,3], Hickling, D [1,2,3], Pascali, D [1,4], Clancy, A [4], Mallick, R [2], Chen, I [2,4]

[1]University of Ottawa, Ottawa, ON, [2]The Ottawa Hospital Research Institute, Ottawa, ON, [3]Division of Urology, Department of Surgery, The Ottawa Hospital, Ottawa, ON, [4]Department of Obstetrics and Gynecology, The Ottawa Hospital, Ottawa, ON

ABSTRACT

Background: Urinary tract injuries are severe complications of hysterectomy. Our objective is to determine the risk factors associated with urologic injury in women undergoing hysterectomy for benign indication.

Methods: A retrospective cohort study (2011-2017) was conducted using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). Women without urologic injury were compared to women with injury, and multivariate logistic regression models were constructed to control for patient demographics and intraoperative variables.

Results: Among 213,980 women who underwent hysterectomy for benign indication, the rate of urologic injury rate was low (0.6%). The majority of injuries involved the bladder (86.2%); 13.8% involved the ureters. Younger age, lower BMI and abdominal hysterectomy were associated with increased injury. Patients who underwent total hysterectomy had increased odds of urologic injury compared to subtotal (adjusted OR 1.54, 95%CI [1.23-1.93]). Patients with Class III obesity had decreased odds of injury compared with patients of normal weight (AOR 0.70, 95%CI [0.55-0.89]). An interaction was observed between surgical approach and indication for hysterectomy. Abdominal compared to laparoscopic approach was associated with urologic injury for women with endometriosis (AOR 3.67, 95%CI [2.35-5.72]), pelvic pain (AOR 4.36, 95%CI [2.06-9.26]), menstrual disorders (AOR 5.71, 95%CI [2.15-15.2]), and fibroids (AOR 2.17, 95%CI [1.59-2.96]). Vaginal compared to laparoscopic approach was associated with increased odds of injury for women with endometriosis (AOR 2.25, 95%CI [1.16-4.40]), menstrual disorders (AOR 14.4, 95%CI [2.28-91.6]), and pain (AOR 54.99, 95%CI [1.24-20.1]). Iatrogenic urologic injury was associated with increased healthcare utilization.

Conclusion: While the risk of urologic injury during hysterectomy for benign indication is low, the risk is dependent on certain patient disease factors and surgical approach.

Safety and Effectiveness of Intratympanic Dexamethasone combined with Other Treatment Regimens in the Management of Sudden Sensorineural Hearing Loss (SSNHL)

Maher, N [1], Little, J [2], Armstong, S [3], Schramm, D [4]

[1]Faculty of Medicine, University of Ottawa, [2]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, [3]Audiology Department, The Ottawa Hospital, [4]Department of Otolaryngology - Head and Neck Surgery, Faculty of Medicine, University of Ottawa

ABSTRACT

Background: Idiopathic sudden sensorineural hearing loss (SSNHL) is defined as the acute onset of hearing loss of ≥30 dB across three consecutive frequencies. Evidence-based therapies for SSNHL include the use of steroids (systemic and/or intratympanic) and hyperbaric oxygen. It has been suggested that a combination of intratympanic and systemic steroids may be more effective than systemic steroids alone in the management of SSNHL.

Purpose: The purpose of this study was to evaluate the safety and effectiveness of intratympanic steroids (dexamethasone) combined with systemic steroids and other treatment regimens for the management of SSNHL.

Methods: A retrospective chart review was conducted of SSNHL patients referred to The Ottawa Hospital Otolaryngology Clinic between July2019 and July2020. Data collected included patient demographics, associated symptoms, therapies received and audiometric outcomes. The primary outcome measure was improvement of audiometric threshold Pure Tone Average. The secondary outcome was Word Recognition Score improvement.

Results: Of 167 patients referred for SSNHL, most patients presented within 2 weeks of symptoms onset and had already been prescribed oral prednisone. Most patients agreed to receive a course of intratympanic steroids. Some patients, usually those with more severe SSNHL underwent hyperbaric therapy. Audiologic results were very variable. Some patients had complete return of hearing. Others had no improvement. Those with milder degrees of hearing loss tended to have better outcomes. Complications of intratympanic dexamethasone therapy such tympanic membrane perforation and infection were very uncommon.

Conclusion: Intratympanic dexamethasone is safe and effective in combination with other treatment regimens in the management of SSNHL.

A Small-Molecule that Binds to the ALS/FTD-Associated C9orf72 Repeat with Potential to Reverse the Mutation

Ripsman, D [1], Lanni, S [2], Nakatani, K [3], Pearson CE [2,4]

[1]Department of Medicine, University of Ottawa, Ottawa, Ontario, [2]Department of Molecular Genetics, University of Toronto, Toronto, Ontario, [3]Department of Chemistry, Osaka University, Osaka, Osaka, [4]Genetics and Genome Biology, The Hospital for Sick Children, Toronto, Ontario

ABSTRACT

Background: Expansion of the d(GGGGCC)n•d(CCCCGG)n repeat in C9orf72 is the most common cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Expansions >90 repeats, where the repeat becomes aberrantly methylated, can cause disease. The repeat can expand in affected tissues over time, driving disease onset and progression, a process that involves DNA synthesis. Arresting or reversing these ongoing expansions poses as a therapeutic avenue. Previously, we published a small molecule that bound the unstable CAG repeat associated with Huntington's disease, could induce contractions of this repeat in the brains of Huntington's mice (Nature Genetics, 2020, PMID:32060489), supporting this therapeutic avenue. Here we show that another small molecule, napthyridine carbamate dimer (NCD), can selectively bind the d(GGGGCC)8 repeat the C9orf72 repeats and block DNA synthesis by DNA polymerases.

Methods: Using a polymerase stop assay we assessed the specificity of NCD for binding and blocking DNA synthesis by DNA polymerases on templates containing d(GGGGCC)8 or d(GGCCCC)8. We also assessed the effect of methylation of the repeats upon NCD's ability to perturb DNA polymerization.

Results: NCD blocked polymerase synthesis through the d(GGGGCC)8 but not the d(GGCCCC)8 repeat. Similarly, NCD blocked polymerase synthesis through the methylated d(GGGGCC)8 but not the methylated d(GGCCCC)8 repeat template.

Conclusions: A polymerase stop assay identified NCD as a selective d(GGGGCC)8 binder and could selectively block polymerase synthesis, on both methylated and unmethylated templates. Our findings support the possibility that small-molecule DNA ligands may be a therapeutic avenue to arrest repeat expansions and thereby arrest ALS or FTD.

Identification of Differentially Expressed Pathways in Breast Cancer Using Protein-Protein Interaction Guided Functional Enrichment Analysis

Nadeau, R [1], Byvsheva, A [1], Lavallée-Adam M [1]

[1]BMI, OISB, University of Ottawa

ABSTRACT

Triple negative breast cancer is a subtype of breast cancer for which the molecular mechanism is largely unknown. It is associated with a poor prognosis, and unlike other breast cancer subtypes, there are currently no targeted and effective treatments. Quantitative proteomics studies have been used in the past to identify proteins that are differential expressed in triple negative breast cancer. Functional enrichment analyses can then detect biological processes that are overrepresented among the proteins to provide insights into the molecular impacts of triple negative breast cancer. However, a biological process may be dysregulated in a condition, while its proteins may not be individually significantly differentially expressed. We propose a novel method using protein-protein interaction networks for the identification of differentially expressed biological processes in the quantitative proteomics analysis of Her2+ and triple negative breast cancer subtypes previously published by Tyanova, et al. Our graph theory-based approach detects Gene Ontology annotations that are both significantly clustered in a BioGRID protein-protein interaction network and differentially expressed across the two experimental conditions, thereby highlighting annotations that may be related to dysregulated pathways. We identified 168 biological processes that are dysregulated between the Her2+ and triple negative breast cancer subtypes and significantly clustered in the network (false discovery rate < 0.001) that would not have been identified by standard methods. This algorithm will provide a better understanding of dysregulated mechanisms in triple negative breast cancer and provide insight into the development of potential therapeutics.and surgical approach.

Systematic Review and Meta-Analysis of the Prevalence of Non-Contrast CT Abnormalities in Adults with Reversible Cerebral Vasoconstriction Syndrome

Gotesman, R [1], Niznick, N [2], Dewar, B [3], Fergusson, D [3], Shorr, R [4], Shamy, M [2, 3], Dowlatshahi, D [2, 3]

[1]Faculty of Medicine, University of Ottawa, [2]Division of Neurology, Department of Medicine, The Ottawa Hospital, [3] Ottawa Hospital Research Institute, The Ottawa Hospital, [4]Learning Services, The Ottawa Hospital

ABSTRACT

Introduction: Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by severe, recurrent thunderclap headaches and vasoconstriction of cerebral arteries that resolve within 3 months. Abnormalities on non-contrast CT (NCCT) such as ischemic strokes, intracerebral hemorrhage (ICH) and subarachnoid hemorrhages (SAH) are frequently observed on brain imaging of RCVS patients though their prevalence varies considerably between studies. We conducted a systematic review and meta-analysis to estimate the prevalence of NCCT abnormalities seen on neuroimaging of adult patients with RCVS.

Methods and Results: We devised a protocol (PROSPERO registration number: CRD42020190637) to provide an a priori outline of the study's methodology. We searched Medline, Embase and the Cochrane Library databases for studies on prevalence of NCCT abnormalities on neuroimaging of RCVS patients. We identified 638 articles and are in the process of screening for eligibility by title and abstract. Suitable studies will be reviewed and relevant data extracted. The studies will be assessed for methodological quality, risk of bias and heterogeneity. Prevalence estimates across studies will be pooled using a random-effects model and subgroup analysis will be performed to assess the impact of age, sex, publication year and study design on prevalence of vascular lesions. Sensitivity analysis will be used to investigate the robustness of the findings. On research day we will present the findings of the full text review and pilot results of the data extraction and analysis.

Conclusion: Through this study we will provide a better appreciation for how RCVS can present and help neurologists detect its presence on imaging.

Patient-centred outcome measures in reperfusion trials for acute ischemic stroke: interim update on an ongoing systematic review and meta-analysis

Kuzmuk, L [1], Field L, Field, T [1,2,3]

[1]Vancouver stroke program
[2]Division of Neurology, University of British Columbia
[3]Faculty of Medicine, University of British Columbia

ABSTRACT

Background: Reperfusion with thrombolysis and/or thrombectomy has been established as the standard of care treatment for appropriate patients with acute moderate-severe strokes, however no consensus has been reached for the use of these therapies in minor strokes. Reperfusion therapy in minor stroke can be associated with rare but serious complications, and it is unclear whether the benefits outweigh the risks in a minor stroke population. The Modified Rankin Scale (mRS) is a commonly used measure of functional outcome in stroke trials, but it does not capture many patient-centred outcomes post-stroke that can significantly impact a patient's quality of life (e.g. mood, cognition, pain, fatigue). This study aims to investigate the effects of reperfusion therapy on patient-centred non-mRS outcomes in acute stroke trials including mild-moderate stroke, as well as to determine how frequently these outcomes are collected as secondary measures in acute stroke trials.

Methods: A systematic review of randomized controlled trials investigating thrombolysis and/or thrombectomy for acute ischemic stroke in which participants with mild-moderate strokes were included (NIHSS ≤ 9). Databases searched: Medline, Embase, PsycINFO, Cochrane, clinicaltrials.gov (January 1995 – August 2019).

Results: 12649 records were identified from initial search, 714 studies eligible for full text review (6%). Full text review is currently in progress. Preliminary results from full-text review will be presented at the meeting.

Conclusions: We predict that reperfusion trials do not frequently include these patient-centred non-mRS outcomes and are hopeful that our results will emphasize the importance of measuring these outcomes in the future.

Overview and Study Design: Novel MRI Tools Tracking Developmental Change Within the Dopamine System in Children

Al Haddad, R [1,2], Cassidy, C [1,2]

[1]CMM, University of Ottawa
[2]The Royal's Institute of Mental Health Research

ABSTRACT

It has been recently shown that neuromelanin MRI can be used as a non-invasive measure of dopamine function in the brain. Unlike traditional invasive dopamine PET imaging, NM-MRI can be used for longitudinal studies in youth. Neuromelanin is synthesized from dopamine and accumulates gradually over the lifespan within dopamine neurons in the substantia nigra, a nucleus in the midbrain, providing a good marker of developmental change. Since neuromelanin is paramagnetic, its content can be detected with special NM-MRI sequence. Dopamine is involved in a number of brain processes, including locomotion, cognition, memory and reward mechanisms. It is therefore beneficial to understand its role in human brain development using NM-MRI is beneficial, since abnormal dopamine homeostasis has serious implications in many neurological disorders such as ADHD, risk of addiction and psychosis. This unique study will capture developmental changes in children and link them to the development of the dopamine system. NM-MRI scans will be acquired from 50 children between 6-12 years old over a 3 years period, with 9-12 month interval between scans. During each time point, dopamine related functions, as well as lifestyle and social factors will be assessed. We aim to generate a longitudinal cohort by engaging the community in the study by recruiting participants through schools and community organizations. This study aims to reveal the normal pattern of developmental change in NM-MRI signal as a proxy for dopamine function in healthy children. We can then correlate this measure to behaviour and environmental influences to better understand its significance. Moreover, establishing this normal range could ultimately identify risk of pathology for individuals outside of this range.

Neuromelanin-sensitive MRI as a Probe to Measure In Vivo Functioning of the Locus Coeruleus Norepinephrine System

McCall, A [1,2], Haddad, R [1,2], Cassidy, C [1,2]

[1]Institute for Mental Health Research (IMHR), The Royal Mental Health Centre, The University of Ottawa
[2]Faculty of Medicine, Department of Cellular & Molecular Medicine, University of Ottawa

ABSTRACT

The locus coeruleus (LC) is the primary source of norepinephrine (NE) in the central nervous system. Dysregulation of this system has been implicated in numerous disease states and more recently, dysfunction of this system has been linked to hyperarousal symptoms commonly seen in post-traumatic stress disorder (PTSD). Neuromelanin-sensitive MRI (NM-MRI) is a novel, in vivo imaging method which can be used as an alternative imaging method to overcome challenges faced by researchers studying the LC-NE system. To date, NM-MRI has not been utilized in PTSD research. Furthermore, our current research demonstrates the validity of this method for capturing the function of the LC-NE system in vivo. We hypothesized that the NM signal of the LC would positively correlate with hyperarousal symptoms experienced by veterans of the Canadian Armed Forces (CAF) with PTSD. 24 veterans from the CAF were recruited from the Operational Stress Injury clinic at The Royal. 19 of these individuals met DSM-5 criteria for PTSD. Specifically, we demonstrate that after NM imaging, individuals with PTSD did in fact show a significant, positive correlation between their caudal LC NM signal and their hyperarousal symptom cluster score on the Clinician Administered PTSD Scale for DSM-5 compared to controls ($r=0.52$, $p=0.02$, partial correlation controlling for depression severity, age, sex, and PTSD diagnosis).
To conclude, our results are consistent with previously published results demonstrating a link between hyperactivity of the LC and hyperarousal symptomology in PTSD. We also show that NM-MRI can be used to measure in-vivo functioning of the LC-NE system.

Cell-type Specific Dissection of Long-Range Inputs to Layer 2/3 of the Motor Cortex

Bezuidenhout, B. [1], Lee, C. [2], Chen, S.X. [2]

[1]Translational and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada
[2]Department of Cellular Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada

ABSTRACT

Mapping neural connections in mammalian brains can provide insight on the function of neural circuits and therefore remains an important goal in neuroscience. Currently the role of excitatory neurons in motor learning is well understood, but the role of GABAergic inhibitory interneurons is unclear. Previous research from our lab has demonstrated that in the motor cortex (M1), Somatostatin-expressing (SOM), Parvalbumin-expressing (PV), and Vasoactive intestinal peptide-expressing (VIP) interneurons, three major subtypes of GABAergic interneurons, are involved in regulating local circuit plasticity during motor learning. To understand the role of these inhibitory microcircuits in motor learning, we are using a newly engineered rabies virus tracing method which allows tracing of monosynaptic inputs to the M1 in a cell-type specific manner. We expect that different GABAergic subtypes in M1 receive overlapping, but distinct inputs that contribute to their unique roles in motor learning. Understanding the anatomical connectivity of the motor system, with cell-type specificity, is an essential step in improving our understanding of the cortical mechanisms enabling motor movements and motor learning.

Effects of a 12-Week Aerobic Exercise Intervention on Clinical and Cognitive Symptoms of Depression in Transitional-Aged Youth

Staff, C [1,2], Piche, J [1,2], Ogunlana, A [2], Jaworska, N [1,2]

[1]Department of Cellular & Molecular Medicine; Faculty of Medicine, University of Ottawa
[2]Institute of Mental Health Research, affiliated with the University of Ottawa

ABSTRACT

The putative pro-cognitive and mood-elevating effects of exercise have become increasingly investigated in the adult population, though research in youth is in its infancy. Of particular interest are the potential effects of long-term aerobic exercise interventions on symptoms of depression, anxiety, self-esteem, and cognitive impairments in youth with depression. As part of a larger pilot study, transitional aged youth (TAY; 16-24yrs), with depression were tested (N=14) to examine the effects of a 12-week (3x/week) exercise intervention on self- and researcher-rated depression; self-reported anxiety, daily functional impairment, self-esteem, and mastery scores; as well as cognitive performance. Electroencephalographic (EEG)-derived P3 and N2 event-related potentials (ERPs) were examined during a flanker task as measures of attention and inhibitory control, respectively. Baseline ERP measures (amplitude and latency) were correlated with clinical indices. The ERPs were also assessed in order to ensure task validity; wherein ERPs to incongruent trials versus congruent were expected to have greater amplitudes and latencies. A reduction from pre- to post-intervention scores of depression and functional impairment scores, as well as an increase in cognitive performance, were found. Positive correlations existed between congruent and incongruent P3 amplitudes and self-mastery scores. As hypothesized, incongruent versus congruent P3 amplitudes and latencies as well as N2 amplitudes were greater, indicating increased attention and inhibition during the processing of incongruent trials. While preliminary, these results suggest that exercise intervention can increase cognition and reduce symptoms of depression in youth. Further research is necessary on the effects of exercise on ERPs in the context of depression.

Decreasing alpha-Synuclein Levels Through Reduction of PFTK1: A Novel Approach to Treating Parkinson's Disease

Parmasad, J [1,2], Geertsma, H [2,3], Callaghan, S [2,3], Rousseaux, M [2,3,4]

[1]Translational and Molecular Medicine, University of Ottawa, [2]University of Ottawa Brain and Mind Research Institute, [3]Department of Cellular and Molecular Medicine, University of Ottawa, [4]Ottawa Institute for Systems Biology, University of Ottawa

ABSTRACT

Parkinson's Disease (PD) is a debilitating neurodegenerative disease characterized by the abnormal aggregation of alpha-Synuclein (a-Syn) in Lewy bodies and neurites. Overexpression of a-Syn is sufficient to drive toxicity in patients and model organisms, and its reduction is neuroprotective. Therefore, reducing a-Syn levels may be a promising therapeutic approach to treating PD. We previously identified PFTAIRE protein kinase 1 (PFTK1), a kinase of largely unknown function, as a robust regulator of a-Syn levels. In order to study the functional relationship between a-Syn and PFTAIRE1, we created a double-mutant mouse line (Pftk1+/-; mThy1-SNCA Tg/y) by crossing Pftk1+/- mice to a-Syn overexpressing (mThy1-SNCA Tg/y) mice. Preliminary data suggest that the double mutant mice may show mild improvements in locomotion, initiation of movement, procedural ability and gut motility, through pole, nesting, and fecal count tests. Biochemical analysis of a-Syn overexpressing mouse brain suggests that knocking-down PFTK1 decreases transgenic a-Syn levels by 30% but paradoxically increases "pathogenic" pSer129 a-Syn levels by as much as four-fold. Moreover, PFTK1 reduction has prolonged the survival of mThy1-Snca Tg/y mice by roughly 40%. Thus far, our results support the potential of PFTK1 reduction in decreasing a-Syn levels and the effects of its overexpression in a mouse model of PD. Further testing will shed light on the potential of PFTK1 as a clinically relevant target for reducing a-Syn toxicity and ultimately treating PD.

Diffusion Tensor Imaging Analysis in Suicide Attempters Versus Ideators Using TBSS

Vandeloo, KL [1], Burhunduli, P [1], Fang, Zhuo [1], Van Geel, A [2], Norris, S [2], Blier, P [2], Phillips, JL [2]

[1]University of Ottawa
[2]University of Ottawa Institute of Mental Health Research

ABSTRACT

Background: Suicide is a significant global concern, with over 800,000 suicide-related deaths reported annually. Diffusion Tensor Imaging (DTI) provides a unique opportunity for the study of white matter microstructure in the context of Major Depressive Disorder (MDD) and suicide.

Methods: DTI data for N=30 participants (N=12 suicide attempters and N=18 suicide ideators; mean age 43 ± 14; 17M/14F) with MDD were analyzed using Tract-Based Spatial Statistics (TBSS) in FMRIB Software Library. Images were acquired on a 3T Siemens MR-PET system using a single-shot 2D diffusion tensor echo planar sequence in the axial plane, over 64 diffusion directions. Clinical associations were explored using bivariate Pearson correlations in IBM SPSS Statistics v.26.

Results: Preliminary TBSS analysis revealed reduced fractional anisotropy (FA) in the left cingulum adjacent to the hippocampus in suicide attempters compared to suicide ideators (CGH; p=0.01, uncorrected). Extracted mean left CGH FA values were negatively associated with self-reported suicidal ideation severity (r=-0.49, p=0.028), however, no significant correlations between cingulum FA and depression severity were identified.

Conclusions: These preliminary imaging results highlight the relevance of white-matter microstructure in the context of suicide, which may be independent of depression severity. Further study in a larger sample is warranted.

Longitudinal Exploration of Sexually Dimorphic Differences in an Alzheimer's Disease Mouse Model

Sarwal, P [1, 2], Alecu, I [1, 2], Bennett, SAL [1, 2]

[1]Neural Regeneration Laboratory, Ottawa Institute of Systems Biology, University of Ottawa Brain and Mind Research Institute
[2]Department of Biochemistry, Microbiology, and Immunology, University of Ottawa

ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by the presence of neurofibrillary tangles and amyloid plaques formed by the accumulation of toxic amyloid β (Aβ) fragments. Males and females exhibit differences in susceptibility to AD due to variations in cognitive reserve, which is the adoption of cognitive strategies to cope with Aβ toxicity. To better understand sexually dimorphic differences in AD, we used behavioural tests to longitudinally explore differences in learning, memory, and overall cognition in the N5 TgCRND8 (Tg) mouse model of AD. Y-maze results indicate that at 2 months of age, only Tg males exhibited working memory impairments. At 6 months of age, Tg males and females exhibited impaired working memory, and at 13 months of age, all aged wild-type and Tg mice showed behavioural indices of impaired working memory function. Results for general behavioural impairment using nest building found that Tg females exhibited statistical impairment at 6 months of age, while decline in Tg males was first observed at 8 months of age. Our findings differentiate sex-specific differential decline in behavioural indices of learning and memory that accompany cognitive and behavioural symptoms of AD. These sexually dimorphic differences in the Tg model of AD can help analyze preclinical models of AD dementia and contribute to the development of targeted therapies for this disease.

The Effects of Fasting on the Circulating Lipidome of an Alzheimer's Disease Mouse Model

Bojic, S [1,2], Alecu, I [2], Bennett, S [2]

[1]Faculty of Health Sciences, University of Ottawa, Ottawa, ON, Canada
[2]Neural Regeneration Lab, Ottawa Institute of Systems Biology, Brain and Mind Research Institute, Department of Biochemistry, Microbiology, and Immunology, University of Ottawa, Ottawa, ON, Canada

ABSTRACT

Growing evidence suggests that altered lipid metabolism is implicated in the pathogenesis of Alzheimer's disease (AD). Specifically, changes in circulating glycerophospholipidomes have been observed within three years of patients phenoconverting; however, this could be in large part due to the collection of samples at different times of the day or in different fasting states. Thus, the aim of this study is to examine whether and how fasting affects the circulating plasma phospholipidome in an AD mouse model (N5 TgCRND8 (Tg)), and whether there are sexually dimorphic differences. We will investigate this research question by profiling extracted glycerophospholipids and searching for underlying patterns and statistical differences between groups. We have observed significant decreases in various lipid subclasses in fasted NonTg males compared to fed NonTg males, with some, but not all, of these differences also present between fed and fasted NonTg females. Most of these decreases were not observed in either Tg males or Tg females when fasted. The decreases observed could be due to cells differentially taking up these lipids from circulation in the NonTg mice versus the Tg mice to make up for the reduction of ingested fatty acids necessary for glycerophosphocholine synthesis. The results of this study could help to improve AD diagnosis and monitoring of disease progression.

Emergency Department Visits Among Pediatric Patients with Comorbid Substance Misuse and Mood Disorders

Hanzal, N[1], Polihronis[2], Jabbour[2,3,4]

[1]University of Ottawa, Faculty of Medicine, Ottawa, Ontario, [2]CHEO RI, Ottawa, Ontario, [3]CHEO, Emergency Department, Ottawa, Ontario, [4]University of Ottawa, Department of Pediatrics, Ottawa, Ontario

ABSTRACT

Background: Emergency department (ED) visits with mental health (MH) concerns as the primary complaint have significantly increased in Canada over the last decade in pediatric populations, of which a substantial portion are attributed to substance use. In characterizing these visits, it is important to consider that mood disorders are the most common psychiatric comorbidities among patients with substance use disorders.

Objectives: This study aims to characterize features of comorbid substance use and mood disorder ED presentations in a pediatric population such as, the frequency of ED visits, access to MH services, and psychopathologic comorbidities.

Methods: A retrospective chart review of patients aged 6-17 years who presented to the CHEO ED with substance use and/or a mood disorder as their primary complaint, as identified using ICD-10 codes and presenting problems at triage, between June 2017 and March 2018 was conducted. Data were collected using hospital administrative patient records.

Results: Preliminary findings showed that of the 1299 analyzed ED visits from 1032 patients (68.3% female; 90.4% English-speaking), the three most commonly logged chief complaints at triage were 1) depression/suicidal/deliberate self-harm (53.7%); 2) overdose ingestion (17.4%); and 3) substance misuse/intoxication (14.8%). Of these analyzed ED visits, 267 (20.6%) were repeat visits. Risk factors associated with an increased likelihood of repeat ED visits are to be analyzed further.

Conclusion: Findings could aid in the identification of specific risk factors affecting MH-related ED visits and the development of a clinical pathway aimed at decreasing ED use as a primary access point for MH services.

Characterization of a Novel Viral Sensitizer that Enhances Oncolytic HSV1 and VSV Infection in Cancer Cells

Gilchrist, V [1,2], Watson, M [1,2], Yang-Ping Apperley, K [4], Hoang, HD [1,2], Yelle, N [1,2], Jia, JJ [1,2], Bo, Y [1], Fonseca, BD[1,2], Graber, TE [1,2], Côté, M [1], Gadde, S [1], Roffé, R [3], Boddy, CN [4], Alain, T [1,2]

[1]Department of Biochemistry, Microbiology and Immunology, University of Ottawa, [2]Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada, [3]Brazil National Institute of Science and Technology in Oncogenomics (INCITO), São Paulo, Brazil, [4]Department of Chemistry and Biomolecular Sciences, University of Ottawa.

ABSTRACT

A oncolytic herpes simplex virus-1 (HSV1) platform is FDA-approved for the treatment of advanced melanoma, while rhabdoviruses (e.g. Vesicular Stomatitis Virus (VSV)) are undergoing clinical trials for head and neck cancer. Poor viral replication in tumour tissue remains a significant obstacle that limits the clinical efficacy of oncolytic virus therapeutics. The identification of compounds capable of improving viral replication is therefore perceived to be of great clinical value. Using pharmacoviral combination of HSV1 with a library of BI-D1870 structural analogs, we identified KA-019 as a novel compound that effectively enhances dose-dependent oncolytic HSV1 and VSV-infection in a range of human and murine cancer cell models. We characterized the effect of this compound against the parental drug by examining viral spread, replication and viral protein synthesis within cancer cells. Here, we show that KA-019 potentiates HSV1- and VSV-infection to a greater extent than the parental drug. Moreover, we present evidence of a potential mechanism by which this class of compounds synergies with oncolytic viruses in cancer cells.

COVID-19 Spike Protein Fragments Expressed in Rice for use in a Nasal Spray Vaccine

Provost, Z [1]

[1]Undergraduate Biotechnology Student

ABSTRACT

By taking advantage of the millennia of experience humans have with cultivating rice and making use of it to solve complex problems such as viral pandemics like COVID-19 interesting solutions can arise. This poster presents a method of producing a vaccine that could solve many problems that exist with current vaccine products, such as the inability for patients to self administer. Not exposing themselves to the possibility of adverse events related to the administration of the vaccine itself is another problem. The COVID-19 Spike Protein is of particular interest due to its involvement with host infection and attachment. Puroindolines have a high affinity for rice starch granules and this property makes it possible to produce large amounts of an API by using Pin+ transgenic rice seeds followed by performing extraction from the starch granules in order to obtain the recombinant protein of interest. Introduction is performed via puroindoline tethering. Processing the harvested rice consists of traditional food grade rice processing followed by air classification and chemical isolation. The nasal delivery product could make use of existing formulations and devices.

Management of Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19- A Comprehensive Literature Review

Kiss, A [1], Mondal, T [2]

[1]Faculty of Medicine, University of Ottawa
[2]Department of Pediatrics, McMaster University

ABSTRACT

Introduction: The prevalence of COVID-19 is low in children and the severity mild to asymptomatic. Yet, some pediatric patients develop a syndrome resembling Kawasaki Disease (KD) post-SARS-CoV-2 infection, termed Multisystem Inflammatory Syndrome in Children (MIS-C), with an estimated incidence of 2/100,000 children. Clinical features can include fever, hyperinflammatory state, gastrointestinal symptoms, myocardial dysfunction, and shock. The pathogenesis of MIS-C is yet to be elucidated but is distinct from KD (e.g. significantly older population, more severe course, different biochemical profile).

Methods: This comprehensive review searched AMED, EBM Reviews, Embase, Healthstar, MEDLINE, ERIC, and Cochrane for studies that reported treatments and outcomes of MIS-C and met inclusion criteria (n≥ 1, children with MIS-C, detailed treatment description, treatment outcome discussion).

Results: The search strategy yielded 42 papers, from which 15 underwent full-text review (n=386). A majority of children received intravenous immunoglobulin (77%) and some form of anticoagulation (63%). Steroid use was also common (44%). Immunotherapy was used in severe cases (n=72). Outcomes reported included PICU admission (77%), need for extracorporeal membrane oxygenation (5%), and mortality (1.3%). Although efficacy of treatments for MIS-C is not yet investigated, we propose close monitoring by a multidisciplinary team, symptomatic treatment (e.g., intravenous immunoglobulin for KD-like symptoms, steroids/immunotherapy for multisystem inflammation), and long-term follow up.

Conclusion: Although outcomes are largely favourable, management is based on a different disease entity (KD), which may not be appropriate given the likely pathophysiologic differences. Further research is required to evaluate the effectiveness of current MIS-C treatments and to determine more targeted therapies.

Luciferase-Based Cytotoxicity Assay Performed on A375 Melanoma Cell Line

Fernandez, C [1,3], Cortes-Kaplan, S [2,3], Ardolino, M [2,3]

[1]Translational and Molecular Medicine, Faculty of Medicine, University of Ottawa
[2]Department of Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa
[3]Cancer Therapeutics Program, Ottawa Hospital Research Institute

ABSTRACT

Natural killer (NK) cells are innate lymphocytes that play an important role in innate immunity. They express many activating receptors, which allow them to recognize and kill cancer cells. NK92 is a human NK cell line that is used to study NK cell cytotoxicity. Here, we test ligand expression on A375, a human melanoma cell line, to determine if this cell line is a suitable target cell line for NK92 cytotoxicity experiments. By immunostaining and flow cytometry, we show that that A375 cell line expressed the following ligands for NK activating receptors: ULBP and B7H6 ligands, but not CD48 or MICA/B. Next, we transduced A375 cells with a lentivirus encoding nanoluciferase for use in luciferase-based cytotoxicity assays. Results showed that the transduced cells expressed luciferase as detected by higher luminescence compared to untransduced cells. To conclude, these results are helpful in order to further understand ligand/receptor interactions, which could potentially help synthesize cancer drugs with higher specificity for their target.

Vector-Borne Illnesses in Your Area? It's More Likely Than You Think! Analyzing the Prevalence of Tick-Borne Pathogens at Murphys Point

Luu, N [1], Slatculescu, A [2,3], McKay, R [2,3], Kulkarni, M [2,3]

[1]Faculty of Medicine, University of Ottawa
[2]SEPH, University of Ottawa
[3]Interdisciplinary Spatial Informatics for Global Health (INSIGHT) Research Lab

ABSTRACT

Ixodes scapularis is a species of hard-bodied tick commonly found in Ontario. These ticks can be carriers of various pathogens that can cause infectious diseases such as Lyme disease and anaplasmosis. Pathogens are transmitted to humans by tick bites. The occurrence of ticks in Ontario is increasing due to climate and environmental changes, making these vectors a growing risk to public health. Our objective was to identify the prevalence of tick-borne pathogens in a known endemic region: Murphys Point Provincial Park in Perth, Ontario. Ticks collected from field surveillance activities in July 2019 were identified by species and life stage using taxonomic keys. Then, nucleic acid extractions on nymph and adult I. scapularis were used for qPCR screening and confirmatory assays. These assays determined the presence of pathogen genetic material using primers that were specific to genes of certain pathogen species. We screened for four pathogens: Borrelia burgdorferi, Anaplasma phagocytophilum, Borrelia miyamotoi, and Babesia microti. Of the 130 I. scapularis collected, 104 were nymphs, 23 were adults, and 3 were larva. 111 nymphs and adults were tested with qPCR assays with 33% positive for B. burgdorferi and 11.7% for A. phagocytophilum. We did not detect the presence of B. miyamotoi and B.microti. Further testing is required to conclude if there were other pathogen species present. In summary, it is vital to continue monitoring known endemic areas and tracking tick populations. Identifying potential risk areas and the prevalence of tick-borne pathogens are crucial steps to detect risk early and prevent disease.

Impact of Coronavirus Disease 2019 on the Clinical Outcomes and Placental Pathology of Pregnant Women and Their Infants: A Systematic Review

Oltean, I [1], Tran, J [2], Lawrence, S [1,2,3], Ruschkowski, BA [2], Zeng, N [2], Bardwell, C [2], Nasr, Y [2], de Nanassy, J [1,2,3], El Demellawy, D [1,2,4]

[1]Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada, K1H 8L1, [2]Department of Medicine, University of Ottawa, Ottawa, Ontario Canada, K1H 8M5, [3]Department of Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada, K1H 8L1, [4]Department of Pathology, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada, K1H 8L1

ABSTRACT

Background: Pregnant women are susceptible to viral infections due to physiological changes such as depressed cell-mediated immunity. At the time of the facilitation of this review, no severe adverse pregnancy or neonatal outcomes had been consistently reported in COVID-19 positive pregnancy cases, and the role of COVID-19 during pregnancy remains to be elucidated.

Methods: A systematic review was conducted to examine clinical maternal and neonatal clinical outcomes. Studies were included if they reported COVID-19 infection among pregnant women and/or COVID-19 positive neonates, as validated by positive antibody testing or viral testing using Polymerase Chain Reaction. Case series, case reports, case-control studies, and comparative studies were included.

Results: 837 records were identified, resulting in 525 records for level I screening. 41 were included after full-text review. Results suggest elevated rates of ICU admission, gestational diabetes, preeclampsia, C-sections, pre-term birth, and CRP in comparison to pregnant women without SARS-CoV-2. When compared to non-pregnant patients with SARS-CoV-2, rates of viral pneumonia, lung abnormalities, and lower lymphocyte counts were similar, while fewer cases of thrombocytopenia were reported in this review.

Conclusions: This review advances limited knowledge around maternal and neonatal outcomes regarding placental pathology, radiology, and laboratory findings in the context of a global pandemic. Careful monitoring of pregnancies with SARS-CoV-2 to minimize adverse clinical outcomes is recommended.

Risk of Infections in Infants Delivered by Caesarean Section on Maternal Request Compared to Vaginal Delivery: A Systematic Review

Nguyen, L [1,2], Kong, G [1,3], Guo, Y[1,4,5,6], Wen, SW [1,4,7]

[1]OMNI Research Group, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, [2]Faculty of Medicine, University of Ottawa, Ottawa, Ontario, [3]Department of Mathematics and Statistics, Queen's University, Kingston, Ontario, [4]School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, [5]Better Outcomes Registry & Network Ontario, Ottawa, Canada, [6]Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, [7]Department of Obstetrics and Gynecology, University of Ottawa, Ottawa, Ontario

ABSTRACT

Background: Caesarean delivery on maternal request (CDMR) refers to a caesarean section (CS) performed on maternal request in the absence of medical indications. Current knowledge of risks and benefits of CDMR are minimal and mostly based on moderate and weak evidence (indirection comparison). Given the large disease burden of infections in infants, the aim of this systematic review is to summarize the available evidence on the risk of infant infection in CDMR and vaginal delivery.

Methods: Two reviewers have conducted a search of Medline, Embase, Cochrane Library, PubMed, SCOPUS and Web of Knowledge for all English-language studies from inception to June 2020. The Preferred Reporting Items for Systematic Reviews (PRISMA) Statement were followed. All observational studies and randomized-controlled trials have been included.

Results: The search revealed 3964 studies, and 11 fulfilled the inclusion, which compared risk of infant infection between medically non-indicated or low-risk elective CS, and vaginal delivery. All included studies looked at infant infections at the neonatal period. 81.8% (9/11) studies reported non-significant differences between the two groups, while 11.1% (2/11) reported significant decreased risk of neonatal infection in the CS group.

Conclusions: Majority of studies suggest there are no significant differences in risk of infection between CDMR and vaginal deliveries. Findings from this review suggest there is very little evidence for long-term outcomes in infants delivered by CDMR. Further high-quality, population-based studies are needed to guide clinical practice relating to CDMR.

Optimizing Yield and Immunogenicity of Plant-Based Vaccines: A Guide for SARS-CoV-2

Bradbrook, A [1], Altosaar, I [2]

[1]BMI, Faculty of Medicine, University of Ottawa. South Carleton High School
[2]BMI, Faculty of Medicine, University of Ottawa

ABSTRACT

The emergence of SARS-CoV-2 Novel-2019 virus has led to the race to find a vaccine. Currently, the WHO recognizes 167 vaccines that are in production, 29 of which are in clinical evaluation. Out of these 167 vaccines, only 3 are plant-based. These are being produced by Medicago Inc. (in clinical evaluation), iBio and CC-Pharming (in preclinical evaluation), Baiya Phytopharm and Chula Vaccine Research Center (in preclinical evaluation). Why is this important? Plant-based vaccines present numerous advantages including easy scalability and lower costs. If a SARS-CoV-2 Novel-2019 vaccine was plant-based, distribution would be much easier due to these benefits. Of course, a plant-based vaccine created to combat a global pandemic would require both optimized yields and immunogenicity. Therefore, this review will summarize previous attempts at SARS-CoV plant-based vaccines, and how yields and immunogenicity were optimized for other similar vaccines such as those for influenza and HIV.

Term-Dependent Changes in Human Milk Exosome Composition: Immunomodulatory Effects In Vitro

Vahkal, B [1], Ferretti, E [2], Beaulieu, JF [3], Kraft, J [4], Altosaar, I [1]

[1]University of Ottawa, Department of Biochemistry, Microbiology and Immunology, [2]Children's Hospital of Eastern Ontario, Department of Pediatrics, Division of Neonatology, [3]University of Sherbrooke, Department of Anatomy and Cell Biology, [4]University of Gothenburg, Department of Molecular and Clinical Medicine

ABSTRACT

The leading cause of death among infants in neonatal intensive care units is necrotizing enterocolitis (NEC). The contributing factors to the inflammatory cascade causing NEC include premature birth, formula feeding and an imbalance in the intraluminal bacteria. Human milk has been proposed to have preventative effects on NEC, potentially via its immune-related exosomal cargo. Mothers birth infants at very different times and prior studies have established that milk composition differs based on infant's gestational age. We propose that the differences extend to human milk's exosomal cargo. We hypothesize that term and preterm human milk exosomes contain unique proteins that promote immune tolerance in intestinal epithelial cells. To investigate this, exosomes from term and preterm milk were isolated. Exosomal proteomes were detected using liquid chromatography–mass spectrometry and functionally characterized. To measure immunomodulatory effects of exosomes, Caco-2 intestinal cells were first treated with heat-killed bacteria for inflammatory activation, followed by exosomes. Following treatment, RNA expression of select cytokines was measured using qPCR. Following proteomic analysis, significantly higher total protein count was detected in preterm milk exosomes in comparison to term. Unique proteins in exosomes corresponded to anatomical development for preterm milk and metabolic processes for term milk. In vitro, both term and preterm milk exosomes significantly reduced inflammatory cytokines. These results indicate that preterm milk exosomes are equipped with unique cargo to aid the development of an infant born too early. Ultimately, this research provides novel insights into exosomal cargo that could be targeted for therapeutic development against infant inflammatory diseases.

Effect of In-Patient Antibiotic Treatment Among Delirious Older Adults Found with a Positive Urinalysis: A Retrospective Cohort Study

Joo, P [1,2,3], Grant, L [4], Ramsay, T [2], Nott, C [1,3], Zvonar, R [1], Jia, J [3], Eagles , D [1,2,3], Yadav, K [1,2,3], Mollanji, E [3]

[1]The Ottawa Hospital, Ottawa, Canada, [2]Ottawa Hospital Research Institute, Ottawa, Canada, [3]The University of Ottawa, Ottawa, Canada, [4]McGill University, Montreal, Canada

ABSTRACT

Doctors often look for urinary tract infections (UTIs) in elderly patients presenting with newfound confusion – even when the symptoms usually associated with UTI are absent. There is, however, little evidence showing UTIs can produce confusion without these symptoms. Furthermore, a corresponding abnormal urine test may also not reflect true infection – due to the high prevalence of asymptomatic bacteriuria among older adults. There is little evidence that antibiotic treatment for such suspected UTIs improves patients' confusion any faster than otherwise. On the other hand, antibiotic treatment can cause side effects such as C. difficile infection. This study reviews The Ottawa Hospital records of elderly patients admitted after presenting to the Emergency Department with an abnormal urinalysis and positive Confusion Assessment Method (CAM) test. By comparing the proportion of patients whose confusion resolved when they received antibiotics and those who did not, and between those who did not have UTI symptoms and those who did, we aim to clarify the impact of antibiotics in this selection population. In addition to other secondary outcomes, data characterizing patient presentation was also collected – including laboratory tests, culture results and comorbidities. Statistical analysis showed no significant difference in the proportion of positive CAM on day 7 of admission, when comparing patients who received antibiotics to those who did not (OR 0.65 (95% CI 0.013–6.9); p=1). Subgroup analysis was also conducted – to characterize circumstances in which antibiotics are beneficial. Overall, preliminary findings suggest that providing antibiotics to this patient population does not significantly improve confusion symptoms.

Timing of HIV Diagnosis Prior to Pregnancy: A Canadian Perspective

Shoemaker, E [1,2,3], Merritt, K [1,4], Smith, S [1], Loutfy, M [2,5,6], Kendall, C [1,2,3,4,7]

[1]C.T. Lamont Primary Health Care Research Centre, Bruyère Research Institute, [2]ICES Toronto, [3]The Ottawa Hospital Research Institute, [4]Faculty of Medicine, University of Ottawa, [5]Women's College Research Institute, Women's College Hospital, University of Toronto, [6]Faculty of Medicine, University of Toronto, [7]Li Ka Shing Knowledge Institute, St. Michael's Hospital

ABSTRACT

In Canada, as is found globally, women of reproductive age represent one of the growing demographics of persons living with HIV. Fortunately, advances in the availability and effectiveness of antiretrovirals during pregnancy has led to a significant reduction in perinatal HIV transmission. In fact, recent guideline changes suggest that initiating antiretrovirals prior to conception can lead to an overall negligible risk of transmission. To achieve this possibility, and thereby virtually eliminate perinatal HIV transmission, it necessitates that all women living with HIV are aware of their HIV status prior to pregnancy. Using a Canadian perspective, we highlight the importance of diagnosing HIV prior to pregnancy and call for a global strategy to aid in pre-conception screening for women of reproductive age and specifically for women who might be at high risk for HIV. We further draw on results from Ontario, which demonstrate a significant proportion of women living with HIV are already diagnosed prior to pregnancy and we use this as a model to inspire equitable and early access to HIV testing across all communities. Rather than relying on prenatal HIV screening during the first or second trimester, which is typically the standard of care globally, we hope that our findings help healthcare providers see the value in promoting HIV screening prior to conception.

CD8+ T Cell Hyperfunction Facilitates Cancer Development in a Murine Model of Liver Fibrosis

Madani, J [1,2], Vranjkovic, A [2], Hasim, MS [1,3], Li, J [1,2] Ardolino, M [1,3,4], Crawley, AM [1,2,4,5]

[1]University of Ottawa, Dept. Biochem., Microbiol., and Immunol., Ottawa, ON, [2]Ottawa Hospital Research Institute, Chronic Disease Program, Ottawa, ON, [3]Ottawa Hospital Research Institute, Cancer Therapeutics Program, Ottawa, ON, [4]Center for Infection, Immunity and Inflammation, Faculty of Medicine, University of Ottawa, Ottawa, ON, [5]Carleton University, Dept. Biol., Ottawa, ON

ABSTRACT

Advanced liver fibrosis in chronic hepatitis C virus (HCV) infection is associated with immune dysfunction, including bulk CD8+ T cell hyperfunction, which may contribute to adverse clinical outcomes such as liver cancer. To CD8+ T cell dysfunction and liver fibrosis and cancer development, we used a hepatotoxin-induced murine model of liver fibrosis. Mice (C57BL/6) were injected twice weekly with carbon tetrachloride (CCl4) for 12-16 weeks. We observed robust liver fibrosis resembling chronic HCV-infection. After stimulation of peripheral blood mononuclear cells, the proportions of granzyme B+, IFN-γ+ and PD-1+ CD8+ T cells in fibrotic mice were significantly higher than controls, particularly in naïve and central memory cell subsets. This hyperfunction was sustained after removing the CCl4 liver insult. Finally, ectopic tumor growth was significantly greater in fibrotic mice and responses to immunotherapy were delayed. In this model, we also observed time-dependent changes in CD8+ T cell function as well as sex effects. We show for the first time that CD8+ T cells are hyperfunctional in a murine model of chronic liver fibrosis resulting in impaired extrahepatic immune responses. This also validates the utility of this model for future studies to identify mechanistic targets to restore immune function in advanced liver disease.

COVID-19 in a University Affiliated Obstetrical Unit: Maternal and Fetal Morbidity in a Pandemic

Ferreira, A [1], Saginur, M [2], Gravelle, A [1,2], Palerme, S [2]

[1]Faculté de médecine, Université d'Ottawa
[2]Département d'Obstétrique et Gynécologie, Hôpital Montfort

ABSTRACT

Background: The COVID-19 pandemic was declared on March 11, 2020 by the World Health Organization. This virus is primarily spread by respiratory droplets and direct contact with infected body fluids. There are numerous clinical manifestations such as fever, fatigue or pneumonia. However, many COVID-19 carriers may be asymptomatic. Diagnosis is based on the clinical presentation and on the detection of virus.

Objectives: This research aim to identify rates of asymptomatic carriers of COVID-19 in the obstetrical population at the Montfort Hospital, as well as to determine whether the COVID-19 environment ante and intra partum have an impact on maternal and fetal morbidity.

Methods: A retrospective cohort design will be used in this study and electronical chart review will be performed to obtain patient information. Data from April to September 2019 will be compared to the pandemic period from April to September 2020. Analysis will be conducted in order to compare parameters between the five risk categories for COVID-19.

Conclusion: Obstetrics is a field particularly affected by the COVID-19 pandemic. Pregnant women require ante and intra partum care, despite reduced access to health care. Better understanding the impacts of the pandemic on our population would help refine risk categories and ways to improve their experience.

Characterizing the Involvement of the Lysophosphatidic Acid Receptor 1 Pathway in Impaired Adult Neurogenesis of an Alzheimer's Disease Mouse Model

McNicoll, M [1,2], Fong, B [1,2], Liu, Y [1,2], Slack, R [1,2]

[1]CMM, University of Ottawa
[2]Brain and Mind Research Institute, University of Ottawa

ABSTRACT

Defects in neurogenesis have been shown to exist in Alzheimer's Disease (AD) and aggravate the neuropathology and cognitive deficits associated with the disease. Study of the underlying mechanisms behind these defects can reveal promising and novel avenues of therapy. We performed immunohistochemistry and bulk RNA sequencing analysis to identify the defects in the neural stem cells (NSCs) of triple transgenic Alzheimer's disease (3xTG) mice and the differential expression profiles that may account for these defects. The transcriptome analysis revealed that the lysophosphatidic acid receptor 1 (LPAR1) pathway was heavily dysregulated in 3xTG mice, and given its role in cellular proliferation and survival, we propose that it could be a potential cause in the defects of 3xTG NSC function. Through qPCR and immunohistochemistry analysis of LPAR1 expression in vivo, we attempt to validate trends of LPAR1 downregulation in 3xTG mice. We propose here that LPAR1 is a promising target for future studies on restoring 3xTG neurogenesis, and in vivo characterization and assays are better tools to gain more insight on its expression and function.

Efficacy and Safety of Mesenchymal Stem Cell Therapy in Preclinical Animal Models of Sepsis: A Systematic Review and Meta-Analysis Protocol

Tahir, U [1], Hum, C [2], Mei, S [3], Champagne, J [2], Strauss, A [2], Fergusson, D [2], Stewart, D [3,4], Walley, K [5], Marshall, J [6], Winston, B [7], McIntyre, L [2,8,9]

[1]Department of Medicine, University of Ottawa, Ottawa, ON, Canada, [2]Clinical Epidemiology Program, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [3]Regenerative Medicine Program, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [4]Department of Cell and Molecular Medicine, University of Ottawa, Ottawa, ON, Canada, [5]Department of Medicine, Centre for Heart Lung Innovation, University of British Columbia, Vancouver, Canada, [6]Department of Surgery (Critical Care), University of Toronto, Toronto, Canada, [7]Department of Critical Care Medicine, University of Calgary, Calgary, Canada, [8]Department of Medicine (Division of Critical Care), University of Ottawa, Ottawa, ON, Canada, [9]Department of Medicine (Critical Care), Ottawa Hospital, Ottawa Hospital Research Institute, Centre for Transfusion and Critical Care Research, Canadian Blood Services, 501 Smyth Road, Box 201, Ottawa, ON K1H 8 L6, Canada.

ABSTRACT

Introduction: Sepsis is a maladaptive immune response to infectious pathogens triggered by an excessive production of inflammatory cytokines causing cellular dysfunction, compromised endothelial permeability, and coagulopathies; eventually leading to progressive organ failure and death. In animal models, mesenchymal stem cells (MSCs) have been shown to attenuate the immune system, rid infection-causing organisms, restore organ function, and reduce death.

Objectives: To perform a systematic review that examines MSCs' effects on death, organ dysfunction, pathogen clearance, and systemic inflammation in in-vivo pre-clinical animal models of sepsis.

Methods: We will include pre-clinical controlled trial studies that use in-vivo sepsis models that administer MSCs systemically. Studies that use engineered MSCs, multiple doses of MSCs, and co-treatments with other therapies or cell types will be excluded. Primary outcome is death; secondary outcomes include organ dysfunction, systemic inflammation, and pathogen clearance between the following intervals <6h, 12h, 24h, 48h, 72h, 96h, and >96h post-MSC administration. Electronic databases will be screened independently by two reviewers using predefined search terms to identify relevant studies. A meta-analysis will be undertaken of the pooled outcome measures. Dichotomous outcomes will be reported as odds ratios and 95% confidence intervals. Continuous outcomes will be expressed as ratio of means and 95% confidence intervals. The quality of evidence will be evaluated using the SYRCLE risk of bias tool5.

Discussion: Data generated from our systematic review will provide a systematic update on the existing pre-clinical evidence of MSCs in sepsis and identify potential research gaps for future research considerations.

The Role of Long-Term Exercise and Obesity on the Hematopoietic Stem Cell Niche Following Radiation Treatment in Mice

Bojic, D [1], Farber, E [2], De Lisio, M [2,3]

[1]Translational Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, K1H 8L1, Canada, [2]School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, K1H 8L1, Canada, [3]Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, K1H 8L1, Canada

ABSTRACT

The number of long-term Canadian cancer survivors exposed to radiation therapy is increasing. Furthermore, obesity and physical inactivity are prevalent, modifiable, risk factors in this population. Unfortunately, all of these factors have been linked to increased secondary hematological cancer risk. Work from our lab has indicated that obesity and exercise differentially regulate radiation-induced alterations to hematopoietic stem cells (HSCs) and their niche in acute interventions. However, it remains unknown whether these changes persist with lifelong exercise and obesity interventions following radiation. As such, this study will assess the long-term impact of exercise and obesity on the HSC niche following radiation exposure in mice. Femurs are currently being analyzed from male CBA mice who have been exposed to a cancer inducible dose of whole body ionizing radiation (3 Gy) and randomly divided into either a control diet/sedentary group (CTRL/SED), 45% high fat diet/sedentary group (HFD/SED), control diet/exercise group (CTRL/EX) or 45% high fat diet/exercise group (HFD/EX). Bone morphometry and marrow adipose tissue (MAT) is being assessed using MicroCT; changes to adipocyte primed mesenchymal stem cells are being assessed using immunofluorescence; and myeloid skewing is being assessed by complete blood cell count. We expect the exercise intervention to promote sustained positive changes in the niche including greater bone volume, reduced MAT volume, and decreased myeloid skewing in mice when compared to the sedentary intervention. This data will provide key information to both cancer survivors and clinicians to support exercise and dietary interventions as potential protective strategies against secondary cancer development following radiation.

Efficacy of Intravitreal Dexamethasone Implant Monotherapy as the Treatment of Macular Edema in Non-Infectious Uveitis

Gupta, R [1,2,3], Ilin, J [1,2,3]; Gottlieb, C [1,2,3]

[1]Ottawa Hospital Research Institute, Ottawa, Ontario, Canada
[2]Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[3]University of Ottawa Eye Institute, Ottawa, Ontario, Canada

ABSTRACT

Purpose: This study investigates the efficacy of dexamethasone (DEX) intravitreal implants as monotherapy for the treatment of macular edema in non-infectious intermediate, posterior or panuveitis.

Methods: A retrospective chart review from the University of Ottawa Eye Institute, Ottawa, Ontario, Canada was conducted. Patients for inclusion in the study were identified by a database search. Thirty patients seen at an academic tertiary care centre for the treatment of intermediate, posterior and panuveitis with DEX were included in the study. The outcomes measured were central retinal thickness (CRT) and best corrected visual acuity (BCVA). Baseline measurements of CRT and BCVA were measured within 1 month prior to intravitreal DEX implant, and follow up measurements were collected at 1-month and subsequent 3-month intervals up to 12 months after each injection.

Results: A total of 39 implants on 39 eyes of 30 patients were included in the analysis of this study. Of these, 64.1% had an improvement in BCVA and 65.4% had a reduction in CRT. BCVA improved from 0.285µm at baseline to 0.172µm at 3 months and 0.182µm at 12 months. Preliminary CRT data showed a decrease from 392µm at baseline to 305µm at 1 month and 326µm at 12 months.

Conclusion: The DEX implant as monotherapy for macular edema in non-infectious uveitis was associated with a reduction in CRT and improvement in BCVA. The DEX implant, used as a monotherapy in eyes with intermediate, posterior and panuveitis, has the potential to treat uveitis without oral corticosteroid or other immunomodulatory therapy.

Embryonal Tumour with Multilayered Rosettes in the Parietooccipital Region – A Case Report

Horwitz, J [1], Huang, A [2], McAuley, D [3], Johnston, D [4]

[1]Faculty of Medicine, University of Ottawa, [2]Division of Pediatric Hematology/Oncology, The Hospital for Sick Children, [3]Division of Pediatric Neurosurgery, The Children's Hospital of Eastern Ontario, [4]Division of Pediatric Hematology/Oncology, The Children's Hospital of Eastern Ontario

ABSTRACT

Embryonal tumour with multilayered rosettes (ETMR) is a rare and highly aggressive brain tumour that predominantly affects children under the age of 3. These primitive central nervous system lesions can vary morphologically but each subtype demonstrates amplification of the 19q13.42 chromosome locus, which serves as the unifying diagnostic feature of ETMR. Despite intensive treatment attempts, the prognosis for ETMR remains poor with a median survival time of 12 months post-diagnosis. Few cases of this rare tumour have been extensively described in the literature to date. This report is a case of ETMR diagnosed in the parietooccipital region of a 2-year-old girl who presented with features of raised intracranial pressure and subsequent coma. Treatment was multimodal and included 3 surgical resections followed by adjuvant chemotherapy with stem cell rescue and focal radiotherapy. The patient was treated per the CCG 99703 protocol, although several non-standard agents were added on that have not been extensively described for their use in ETMR. Notably, the patient received intrathecal cytarabine and topotecan, as well as the biologic agents vorinostat and isotretinoin. The patient also received 1 year of maintenance chemotherapy and focal radiotherapy to manage residual disease. At the completion of therapy, the patient was in radiographic and clinical remission and has sustained this outcome at 2 years' follow-up. This therapeutic approach might help to achieve similar outcomes in future patients, noting that the non-standard use of focal radiotherapy in this young patient population may be of particular benefit.

Visualisation of MMP Activity in Aortic Valves using In Situ Zymography

Prabhune, R [1], Rotstein, B [1,2], Farber, G [1,2]

[1]University of Ottawa Faculty of Medicine
[2]University of Ottawa Heart Institute

ABSTRACT

Calcific Aortic Valve Disease (CAVD) affects up to 5% of the population over 70 years old. It is a serious complication associated with genetic disorders such as Marfan syndrome and is characterised by aortic stenosis and sclerosis through calcification and leaflet fusion. It was found that matrix metalloproteinases (MMPs) have an enzymatic role in extracellular matrix remodelling and calcification. Phenanthroline functions as a pan-MMP inhibitor, though its effects in aortic calcification have yet to be established. In situ zymography was performed to confirm the efficacy of phenanthroline on aortic valve tissue harvested from ApoE-/- mice. When dissolved in water, phenanthroline had no effect on MMP enzyme activity, but demonstrated a dose-dependent increase in inhibitory activity when dissolved in 100% ethanol. We propose that phenanthroline requires an aprotic solvent to fully dissolve and interact with the tissue due to its cyclic structure. However, different solvents should be tested to refine the protocol as 100% ethanol caused tissue dehydration during incubation. These findings can be used to optimize in situ zymography protocols for the study of MMPs in calcified aortic valve tissue.

Audit of Cardiac Implantable Electronic Device Outcomes at a Large Tertiary Care Hospital

Odabashian, R [1],Unni, RR [1], Sadek, M [2], Nery, PB [2], Nair, GM[2], Davis, DR[2], Redpath, CJ [2], Birnie, DH [2], Klein, A [2], Alqarawi, WAA[2], Aydin, A [2], Green, M [2], Golian, M [2]

[1]Department of Medicine, University of Ottawa, Ottawa, Canada
[2]University of Ottawa Heart Institute, Ottawa, Canada

ABSTRACT

Background: Cardiovascular electronic implantable device (CEID) implantation in

Canada is rising in frequency, reflecting an aging population and increasing prevalence of heart disease. Accompanying the rise in implantation procedures is the number of periprocedural complications. With more frequent implants, it is important to evaluate recent real-world device complication rates as quality indicators.

Objective: This study sought to determine the incidence of complications post CEID implantation at a large tertiary centre.

Methods: We conducted an audit of all patients receiving a CEID between April 2019 and March 2020 at a large Canadian tertiary care center. Complications and device data were extracted using electronic medical records and PACEART. Complications evaluated include pneumothorax, pocket infections, hematomas, venous thrombosis, lead perforation, and dislodgements.

Results: There were 11 experienced operators. A total of 1365 CEIDs were implanted with all patients receiving first post-procedure follow up at the implanting center. These included 204 (15%) cardiac resynchronization therapy devices (CRT), 841 (62%) pacemakers (PPM), and 269 (19%) implantable cardioverter defibrillators (ICD) implanted.

The overall complication rate was 4.25% (58/1365 events). The incidence of pneumothorax was 0.81%. The rate of CIED pocket infection was 1.2%. A total of 18 patients had lead dislodgement (1.32%). The rate of lead perforation was 0.81%. Clinically significant hematomas were seen in eight patients (0.6%).

Conclusion: This audit provides a contemporary report of clinically significant post device complication rates. Current reported rates are lower than previously published rates, likely due to experience, better surgical techniques, and guideline-directed postoperative care. Ongoing evaluation of CEID complications is an important quality indicator and should be performed annually.

Value of CT angiographic Carotid Plaque Assessment in Stroke Patients with No Significant Stenosis

Sypkes, C [1], Mawi, H [2]; Quateen, A [2], Chakraborty, S [2]

[1]Faculty of Medicine, University of Ottawa
[2]Department of Radiology, University of Ottawa

ABSTRACT

Objective: The degree of carotid artery stenosis informs patient risk stratification and management. However, there remains a large number of ischemic stroke patients without significant carotid stenosis. Further, plaque characteristics including composition and surface morphology play a key role in symptom occurrence. CTA remains the initial modality for assessment of acute cases of stroke/TIA. The aim of this study was to evaluate carotid plaque characteristics using CT angiography in ischemic stroke patients to identify potential active thrombogenic plaque.

Materials and Methods: A retrospective search of PACS for CT angiograms was conducted using the key words stroke and TIA. Patients with confirmed thrombus in the form of a cut-off or established stroke were included. Exclusion criteria included patients with >70% stenosis and patients with risk factors for proximal embolism. The control group included patients without confirmed stroke or thrombus. Clinical data was then gathered, and CT angiograms were evaluated for the presence of atherosclerotic plaque, stenosis, calcification, surface irregularity, plaque ulceration, adherent thrombus and napkin-ring sign. Post-processing reconstructions and analysis were performed with TeraRecon to calculate plaque density for a segment measuring 5 cm around the carotid bifurcation.

Results: The study included 18 ischemic stroke patients at The Ottawa Hospital with a mean age of 72 ± 17. All patients had <30% stenosis but were positive for intracranial thrombus. Ulceration is noted in 20% and surface irregularity is seen in 66% of cases. Napkin- ring sign is noted in 2 symptomatic carotid arteries. No adherent thrombus was seen. Low density plaque was 31% of total plaque volume measured in this cohort.

Conclusion: Surface irregularity and ulceration are important additional findings in the etiology of thrombus formation. Low density plaque component is a potential marker for active thrombogenic plaque in CT angiogram.

Direct Oral Anticoagulants and the Risk of Hemorrhage when Used in Combination with Amiodarone, Verapamil or Diltiazem

Hill, K [1], Sucha, E [2], Rhodes, E [2], Carrier, M [1], Hundemer, G [3], Batistella, M [4], Knoll, G [2,3], Sood, M [1,2,3,5]

[1]Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada, [2]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada, [3]Division of Nephrology, Department of Medicine, The Ottawa Hospital, Ottawa, Ontario, Canada, [4]Division of Nephrology, Department of Medicine, St Michael's Hospital, Toronto, Canada, [5]Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, Ontario, Canada.

ABSTRACT

Background: Direct oral anticoagulants (DOACs) are used for stroke prevention in atrial fibrillation and to treat or prevent venous thrombosis. Verapamil, diltiazem and amiodarone are common antiarrhythmics used in the management of atrial fibrillation. These antiarrhythmics alter DOAC metabolism by acting on P-glycoprotein and the cytochrome P450 3A4 pathway. Several studies have demonstrated that the combination of these medications, with DOACs, can increase DOAC serum levels, placing patients at risk of bleeding. However, the clinical significance of this interaction is unknown.

Methods: We conducted a retrospective cohort study of patients prescribed a DOAC (dabigatran, apixaban or rivaroxaban) in Ontario, from 2009-2016. Our primary outcome was major hemorrhage requiring admission to hospital or visitation to an emergency room, within 30-days after antiarrhythmic initiation. The association between each antiarrhythmic, when compared to its active control (metoprolol or amlodipine), and hemorrhage was examined using inverse probability treatment weighted Cox proportional hazards models

Results: 20,794 eligible patients were prescribed either amiodarone (n=4,872), verapamil (n=1,284) or diltiazem (n=14,638), while on a DOAC. The 30-day adjusted risk of major hemorrhage was not significantly different between amiodarone (HR 0.77 95%CI 0.61-0.97), verapamil (HR 1.32 95%CI 0.88-1.98) or diltiazem (HR 0.99 95%CI 0.85-1.15), relative to their respective active comparators. This result was consistent when a broader definition of bleeding was adopted, when adjusted for renal function and when we assessed for differences based on DOAC type or dosage.

Conclusion: Administration of a DOAC with verapamil, diltiazem or amiodarone did not result in a higher 30-day risk of bleeding.

The Impact of Hepatitis C Antiviral Therapy on Cardiovascular Outcomes: A Systematic Review

Shamsudeen, I [1], Doyle, MA [2]

[1]Faculty of Medicine, University of Ottawa
[2]Division of Endocrinology and Metabolism, University of Ottawa

ABSTRACT

Background: Recent studies suggest Hepatitis C virus (HCV) antiviral therapy may have a protective effect on cardiovascular outcomes. However, there is conflicting evidence to support this and there have been no systematic reviews done. The objective of this study is to evaluate the effects of HCV treatment and sustained virologic response (SVR) on cardiovascular outcomes. This knowledge will aid in informing long-term HCV management strategies and improving outcomes in this population.

Methods: A comprehensive, systematic literature search was conducted using MEDLINE and EMBASE between 1989 and April 2019 to identify all relevant studies. Titles and abstracts were screened for inclusion/exclusion criteria. The Newcastle-Ottawa Scale was applied to assess for risk of bias. A qualitative analysis was performed to synthesize the results.

Results: The literature search yielded 1256 studies. 12 studies met inclusion criteria. Four studies demonstrated that HCV treatment reduced the risk of acute coronary syndrome (RRR 8-64%) and five studies, ischemic stroke (RRR 9-66%). One study showed that direct-acting antiviral (DAA) therapy was associated with a 43% reduction in the risk of any cardiovascular outcome, compared to 22% for pegylated-interferon and ribavirin (PEG-RBV) therapy. Three studies demonstrated that SVR reduced the risk of any cardiovascular outcome (RRR 30-65%).

Conclusion: This study suggests that HCV antiviral therapy and SVR lead to improved cardiovascular outcomes. The data also suggests DAA may reduce cardiovascular risk more than PEG-RBV. Further studies are needed to explore the association between HCV antiviral therapy and cardiovascular outcomes based on viral load, genotype and HIV co-infection.

Manual Motion-Correction for SPECT Myocardial Blood Flow and Myocardial Flow Reserve Quantification

Han, L [1], Carey, C [2], Brenande, J [2], Wells, RG [2], Ruddy, T [2]

[1]Faculty of Medicine, University of Ottawa
[2]University of Ottawa Heart institute

ABSTRACT

Background: Myocardial blood flow (MBF) and myocardial blood flow reserve (MFR) measurements provide additional prognostic and diagnostic information to relative perfusion imaging. However, MBF data are rarely obtained in routine single photo emission computed topography (SPECT) myocardial exams with conventional cameras. Recent innovations in solid-state CZT cardiac SPECT cameras make it feasible to obtain MFR and MBF measurements. We study the inter-observer variability of SPECT MBF and MFR using commercial 4DM analysis software.

Methods: SPECT 99mTc-tetrofosmin rest-stress dynamic images were retrospectively processed by two operators using 4DM software. Manual motion-correction was applied to each frame of the dynamic image series to align with the myocardial border contours. A 1-tissue-compartment model with a previously obtained extraction-fraction correction was used to determine MBF and MFR (ratio of stress MBF to rest MBF). MBF and MFR were measured globally and in each vascular territory. The inter-observer variability was measured as the standard deviation of percent difference in MBF or MFR between observers.

Results: 9 repeated studies were analyzed. The global MBF inter-observer difference was 65% +/-13%. The regional MBF inter-observer differences were 64% +/-7%, 79% +/- 14%, 59% +/-2% for LAD, LCx, and RCA territories respectively. For MFR, the global difference was 42% +/- 58% and the regional differences were 36% +/- 57%, 45% +/- 7%, 31% +/- 4% for LAD, LCx, and RCA territories respectively.

Conclusion: Processing with currently available commercial software leads to high inter-user variability. Increased automation to reduce user interactions may be needed to improve reliability of MBF.

Respiratory Motion Correction of SPECT Myocardial Perfusion Images

Zeghal, M [1], Brenande de Oliveira Brito, J [2], Carey, C [2], Dubie, K [2], Han, L [1], Mahmood, F [1], Small, G [2], Ruddy, TD [2], Glenn Wells, R [2]

[1]Undergraduate Medical Education, Faculty of Medicine, University of Ottawa
[2]Division of Cardiology, University of Ottawa Heart Institute, Ottawa, Ontario, Canada

ABSTRACT

Background: Current ASNC guidelines for SPECT myocardial perfusion imaging (MPI) require a 30-45 minutes delay between radiotracer injection and acquisition of SPECT MPI scans to reduce the impact of extra-cardiac interference. During acquisition, respiratory motion contributes significantly to motion-blurring of images and extra-cardiac interference. In this study, data-driven respiratory motion correction (RMC) software was evaluated in its effectiveness to reduce extra-cardiac interference in SPECT myocardial perfusion images and thereby improve the correspondence between images acquired starting 5 minutes after injection (immediate) and at a standard time (delayed).

Methods: SPECT MPI studies were retrospectively evaluated and processed using data-driven RMC software for a sample of 20 patients. Immediate and delayed images without (NoMC) and with RMC were assessed using standard clinical software. Normalized myocardial perfusion value differences between delayed and immediate time-points were computed for each myocardial segment, based on a 17-segment left ventricle (LV) model. Differences between immediate and delayed values derived from NoMC and RMC data were compared, for stress and rest scans, using a Wilcoxon signed-rank test ($\alpha = 0.05$).

Results: RMC mean differences tended to decrease at stress and increase at rest. Changes in most LV segments were not significant but there were significant decreases at stress for the basal anteroseptal, mid inferoseptal, and apical septal segments ($P < 0.05$).

Conclusion: Preliminary results demonstrate that motion-correction can reduce the change in myocardial uptake between immediate and delayed imaging in septal segments at stress.

Roles of xCT (SLC7A11) in the Crosstalk Between Metabolic Regulation and Oxidative Stress

Elkhatib, H [1], Parmar, G [1], Harper ME [1]

[1]BMI, University of Ottawa

ABSTRACT

Skeletal muscle contains the largest pool of glutathione (GSH) in the human body. GSH is a tripeptide that has a major role in the antioxidant system of the cell. GSH evokes an action on regulating responses to oxidative stress, but its metabolic role has not yet been fully characterized. GSH is synthesized in a pathway controlled by glutamate cysteine ligase (GCL), and GCL is dependent on plasma membrane xCT (SLC7A11) importation of the rate-limiting amino acid cysteine. Buthionine sulfonimine (BSO) is an irreversible inhibitor of the GCL enzyme, consequently decreasing cell GSH concentration. To further our understanding on the effects of impaired GSH on metabolic function, we first silenced xCT expression in C2C12 myoblasts and verified knockdown efficacy. We then conducted an acute pharmacological inhibition of GCL by treating C2C12 cells with BSO for 24 hours. After analytically confirming the drug's efficacy on GSH depletion using high performance liquid chromatography, we measured oxygen consumption rate and extracellular acidification rate of the treated cells using a Seahorse XFe96 analyzer. While selective siRNA silencing did not efficiently decrease xCT expression in C2C12 myoblasts, BSO treatment fully depleted GSH production in these cells.

Prediction of Mouse Main Olfactory Bulb Spatial Transcriptomics Expression via Deep Learning on H&E Images

Dilanni, C [1, 2, 3, 4], Mamun, M [1, 2, 3], Perkins, T [1, 2, 3]

[1]Translational and Molecular Medicine, Faculty of Medicine, University of Ottawa, [2]BMI, University of Ottawa, [3]Ottawa Hospital Research Institute, [4]Computer Science, Carleton College

ABSTRACT

Spatial transcriptomics (ST) is an in situ RNA sequencing technology used to sequence tissue while maintaining the reads' spatial resolution. It implements a slide consisting of thousands of barcoded spots, each of which captures the mRNA of cells with which it is in direct contact. Although ST can provide quantification and visualization of the overall transcriptome in tissue samples, the unsequenced tissue between the slide's spots compromises ST's molecular resolution. Here we develop a convolutional neural network (CNN), using the convolutional layers from the DenseNet-121 network, to predict localized gene expression levels from haematoxylin-and-eosin-stained (H&E) images. As a performance benchmark, we trained our model using the most expressed genes of 2 breast cancer samples with 7,785 total spots from 10x Genomics. The weights were retrained for both highly expressed and highly variable genes on 12 mouse main olfactory bulb (MOB) samples with 3,116 total unique spots. The model achieved a maximum of 35.1% expression variance explained using the breast cancer samples and 15.0% using MOB samples. Highly variable and highly expressed genes had similar percentages of variance explained by the network. When trained on the MOB, the network accurately predicted Snap25, a highly variable gene which encodes a synaptosomal-associated protein. Our analysis suggests a CNN is able to identify spatial transcriptomic signatures within H&E images for both highly variable and highly expressed genes. The datasets' difference in performance is attributed to the reduced read depth and spot count of the MOB dataset.

A Deep Learning Algorithm to Predict Spatial Gene Expression from Fetal Heart Haematoxylin-and-Eosin-stained (H&E) Images

Mamun, M [1, 2, 3], Dilanni, C [2, 3, 4], Perkins, T [2, 3]

[1]Translational and Molecular Medicine, Faculty of Medicine, University of Ottawa, [2] Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa, [3]Ottawa Hospital Research Institute, [4]Computer Science, Carleton College

ABSTRACT

Studying the spatial distribution of gene expression in tissues is an integral part of understanding diseases and biological processes. RNA-seq technologies such as Spatial transcriptomics (ST) use slide arrays containing thousands of barcoded spots to measure mRNA levels in individual tissue samples, providing us with a better understanding of tissue function. Although ST provides an overall representation of a tissue section's transcriptome, it compromises molecular resolution as it is unable to sequence regions outside of a spot. Here we evaluate the performance of a convolutional neural network (CNN) using the DenseNet-121 network to predict gene expression from fetal heart H&E images, using 19 fetal heart samples from 3 key stages of development, 4.5, 6 and 9 weeks post conception and 3175 spatially resolved spots. The model achieved a maximum percent of variance explained (POVE) of 20% when predicting the top ten most highly expressed genes, and both highly variable and highly expressed gene predictions had similar POVE values. For example, the CNN was able to predict the expression of MYL7, a gene involved in calcium ion binding in the heart. Lastly, we found a weaker predictive power of the network in comparison to previously tested datasets using breast cancer tissue sections. Our analysis suggests that a tissue sample's sequencing depth, tissue morphology and amount of spatially resolved spots may impact the predictive performance of the neural network. A generalized, automated method to predict gene expression in histological images can make medical diagnoses quick and efficient.

Targeted Therapies for Metabolic Myopathies Related to Glycogen Storage and Lipid Metabolism: A Systematic Review and Steps Towards a 'Treatabolome'

Manta A[1,2], Thompson R[1], Spendiff S[1] and Lochmüller H[1,2,3]

[1]Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada, [2]Children's Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada, [3]Department of Neuropediatrics and Muscle Disorders, Medical Center – University of Freiburg, Faculty of Medicine, Freiburg, Germany; Centro Nacional de Análisis Genómico (CNAG-CRG), Center for Genomic Regulation, Barcelona Institute of Science and Technology (BIST), Barcelona, Catalonia, Spain; Division of Neurology, Department of Medicine, The Ottawa Hospital; and Brain and Mind Research Institute, University of Ottawa, Ottawa, Canada

ABSTRACT

Metabolic myopathies are a heterogenous group of muscle diseases typically characterized by exercise intolerance, myalgia and progressive muscle weakness. Often these features are accompanied by other multisystemic symptoms depending on the affected metabolite and the expression of the variant gene. While our understanding of the pathogenesis of metabolic myopathies related to glycogen storage, lipid metabolism and β-oxidation have been well established, consensus on the best therapeutic management of these patients is lacking. The objective of this study was to collate all the evidence on therapeutic pharmacological therapies for the aforementioned metabolic myopathies specific to the genetic mutation. A systematic review was conducted to retrieve all levels of evidence examining the therapeutic efficacy of pharmacological treatments on metabolic myopathies related to glycogen storage and lipid metabolism. A key inclusion criterion was the genetic variant of the patients must be stated to link the outcomes to the specific genetic mutation. Of the 1,085 articles initially identified, 268 full-text articles were assessed for eligibility, of which 87 were carried over into the final data extraction. The most studied metabolic myopathies were Pompe disease (45 articles), Multiple Acyl-CoA dehydrogenase deficiency related to ETFDH mutation (15 articles) and systemic primary carnitine deficiency (8 articles). The most studied therapeutic management strategies for these diseases were enzyme replacement therapy, riboflavin and carnitine supplementation, respectively. The goal of the future analysis is to link the 'treatable' gene variants identified in this review to a computer-aided system to alert clinicians to all management strategies at the time of genetic diagnosis of a metabolic myopathy.

Development and Validation of Biomarkers in Huntington's Disease (HD): A Systematic Review and Critical Appraisal Scheme to Support Therapeutic Development of Transforming Disease-Modifying Therapies

Tang, H [1], Mestre, T [2], van Eimeren, T [3,4], Sampaio, C [5]

[1]Faculty of Medicine, University of Ottawa, [2]Parkinson's disease and Movement Disorders Center, Division of Neurology, Department of Medicine, The Ottawa Hospital Research Institute, University of Ottawa, Canada, [3]University of Cologne, Departments of Nuclear Medicine and Neurology, Cologne, Germany, [4]German Center for Neurodegenerative Diseases (DZNE), Bonn-Cologne, Germany, [5]CHDI Management/ CHDI Foundation, Princeton, NJ, USA

ABSTRACT

HD is a fatal neurodegenerative condition. There are promising novel gene-based therapies developed with an intent to modify the disease trajectory in the presence of clinical disease and, ideally, at a premanifest stage. Valid biomarkers are urgently needed to facilitate the development of these disease-modifying therapies specially in premanifest HD. There is no study characterizing the quality of research for the development and validation of biomarkers in HD. A systematic review of all HD biomarker studies up to June 2020 was conducted with the goal of characterizing the landscape of biomarker development in HD and providing a standardized appraisal of their methodological quality. To that effect, a 24-item checklist (item score: 0 or 1) was developed based on available tools (e.g.,STARD checklist for diagnostic accuracy). We included 218 biomarkers studies divided into clinical, imaging, genetic, biochemical, and mixed biomarker. Only 78 (35.8%) studies had a longitudinal design. On average, 10 items (s.d. = 3) scored 1 for each study. The checklist items that more frequently scored 0 were assessment of biomarker validity and reliability, sampling method, report of adverse events, power calculation and appropriateness of study enrollment. Publications from 2016 to 2020 had a better methodological quality than publications prior to 2016 ($p = 0.035$). Genetic and biochemical biomarkers scored less than the mixed, clinical, and imaging biomarkers ($p < 0.001$). Better designed studies are necessary for a validated use of biomarkers that can aid the successful therapeutic development in HD, with application in other chronic neurodegenerative disorders.

The Role of Staufen1 in Rhabdomyosarcoma Progression and Treatment via the Modulation of Autophagy Degradation and Mitochondrial

Almasi, S [1], Crawford Parks, TE [1], Marcellus, KA [1], Jasmin, BJ [1]

[1]CMM, Faculty of Medicine, University of Ottawa

ABSTRACT

Staufen1 (STAU1) is a multifunctional RNA binding protein involved in the regulation of different aspects of RNA metabolism including RNA transport, localization, splicing, translation, decay, etc. Our laboratory has been recently reported the oncogenic role of STAU1 in muscle-like cancer Rhabdomyosarcoma (RMS). Our previous findings indicated high expression of STAU1 in RMS tumours and cell lines, therefore STAU1 downregulation was shown to be associated with reduced RMS tumorigenesis. However, the underlying mechanisms of STAU1-induced oncogenesis remained to be discovered. In this research, we identified the key signaling pathways and cellular processes that STAU1 regulates in RMS. Using RMS cell lines, RH30 and RD cells expressing shSTAU1, we showed the negative impact of STAU1 silencing on autophagy and mitochondrial metabolism. Our results revealed that STAU1 silencing downregulates JNK signaling and leads to autophagy inhibition in RH30 cells. On the other hand, a decrease in the expression level of oncogenic c-Myc in STAU1-depleted cells attenuates mitochondrial metabolism in RD cell line. A similar effect was observed in the TA muscle tissues obtained from 4-week old STAU1-transgenic mice. More specifically, elevated levels of STAU1 in TA muscles was associated with an increase in the expression level of autophagy and mitochondrial markers. Therefore, we demonstrated for the first time the positive role of STAU1 in autophagy and mitochondrial metabolism in cancer cells.

Prevalence Of Infectious Complications Among Inpatients With Cirrhosis on Proton Pump Inhibitors

Yau, M [1], Tan, P [2], Ukos, M [1], Miller, C [1], Lombardi, J [1], Kelly, E [2]

[1]UGME, Faculty of Medicine, University of Ottawa
[2]Division of Gastroenterology, Faculty of Medicine, University of Ottawa

ABSTRACT

Background: Proton pump inhibitors (PPIs) are prescribed for various gastrointestinal diseases. There is some evidence that PPIs may increase the risk of infectious complications in patients with cirrhosis, however this is controversial. Hence, we aim to examine the prevalence of infectious complications among inpatients with cirrhosis on PPIs.

Methods: This is a retrospective, single center cohort study on adult patients with cirrhosis admitted to the Ottawa Hospital between January 1st, 2011 and December 31st, 2015. A chart review was conducted. Relevant information was extracted.

Results: 953 patients were included in this study (mean age=62, SD 12; 635 male, 318 female; median MELD-Na score=16, IQR=12-22). 45% (n=397) were on PPI on admission, while 70% (n=664) were on PPI in-hospital. No significant differences were found between types of infections and in-hospital PPI exposure (PPI versus no PPI: spontaneous bacterial peritonitis 10.3% versus 8.0%, p=0.2; urinary tract infections 9.2% versus 6.6%, p=0.18; clostridium difficile 3.8% versus 2.1%, p=0.2; bacteremia 8.6% versus 7.6%, p=0.6; pneumonia 12.7% versus 12.5%, p=0.9; any infection 32.1% versus 31.6%, p=0.9). Patients on PPI in-hospital were more likely to die in-hospital (22.0% versus 13.5%, p=0.002), however death from infectious complications were similar (18.5% versus 23.1%, p=0.5).

Conclusions: We did not identify significant associations between PPI use and infectious complications. Patients on PPI were more likely to die in-hospital, which may reflect the acuity of their in-hospital illness. Further studies would be warranted, given its potential impact on the mortality and morbidity of this vulnerable population.

An Integrated Proteomic Approach to Mapping the ALS-linked TDP-43 Interactome

Patel, A [1,2,3], Suk, T [1,2,3], Callaghan, S [2], Hashimoto-Roth, E [4,5], Lavallée-Adam, M [4,5], Ngsee, J [1,2,6], Rousseaux, M [1,2,3,4,5]

[1]Department of Cellular and Molecular Medicine: Neurosciences Graduate Program, University of Ottawa, [2]Brain and Mind Research Institute, Ottawa ON, [3]Eric Poulin Centre for Neuromuscular Disease, Ottawa ON, [4]Department of Biochemistry, Microbiology & Immunology, University of Ottawa, [5]Ottawa Institute of Systems Biology, Ottawa ON, [6]Ottawa Hospital Research Institute, Ottawa ON

ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a progressive and incurable neurodegenerative disease in which protein aggregates pathologically accumulate. A major component of these aggregates is TDP-43, an RNA binding protein, which is sequestered from its normal nuclear locale to the cytoplasm. Using CRISPR/Cas9, our lab has generated knockin cell lines expressing GFP-tagged wildtype (WT) and an ALS-causing mutant (Q331K), in the endogenous TARDBP locus (coding for TDP-43). The nuclear expression of TDP-43 is tightly regulated and its cytosolic accumulation in ALS may be indicative of perturbations in mechanisms needed for normal function. On the cellular level, we have shown that the Q331K mutation causes loss-of-function and mislocalization of TDP-43. Given that the subcellular location of a protein is highly dynamic and affected by protein-protein interactions (PPIs), we posit that identifying novel interactors of wild-type and mutant TDP-43 could reveal insight into networks involved in driving neurodegeneration. Using these cells, we have performed immunoprecipitation coupled to mass spectrometry (IP-MS) to elucidate interactors of WT- and Q331K, TDP-43. Our IP-MS experiments and subsequent bioinformatic and literature analyses have revealed a list of protein candidates that we are validating (using confocal microscopy and IP-western blot), and will characterize (to test the consequences of disrupting these interactions on TDP-43 function) through cellular and biochemical methods. Using this unbiased approach, we will identify novel interactors that give insight into pathways that can be targeted for therapeutic intervention.

An In Vitro Model of Exercise for Human Primary Muscle Cells

Ahsan, M [1], Garneau, L [1,2], Aguer, C [1,2]

[1]University of Ottawa, Department of Biochemistry, Microbiology, and Immunology
[2]Institut du Savoir Montfort –Research

ABSTRACT

Skeletal muscle insulin resistance is a characteristic feature of type 2 diabetes mellitus (T2DM), which affects 1 in 10 Canadians and nearly 500 million individuals worldwide. On a molecular level, it prevents insulin-induced GLUT4-mediated glucose uptake. However, exercise has been found to subvert this molecular impotence and facilitate GLUT4-mediated glucose uptake in skeletal muscle. Long-term exposure to electrical pulse stimulation (EPS), as an in vitro model of exercise, elicited defective metabolic responses in muscle cells from T2DM patients, demonstrating altered metabolism. While long-term EPS exposure has been studied extensively, the effects of short-term exposure remains unknown We intend to develop an in vitro model of exercise for human primary muscle cells by monitoring GLUT4 translocation and other molecular markers of muscle metabolic adaptations to exercise in muscle cells extracted from healthy and obese participants with and without T2DM in response to 1 hour of EPS. Our preliminary results using muscle cells from one patient with obesity and T2DM is presented here. In response to 1-hour EPS, we observed increased pAMPK and consistent pGLUT1, but consistent pACC and decreased membrane GLUT4. The latter results are unexpected but support the idea of T2DM altering metabolic responses to EPS, as previously observed in samples from patients with T2DM. However, this is only one sample and more work must be done to draw any conclusions. Ultimately, the model will be verified by measuring myokine expression, establishing a reliable standard of in vitro research into the effects of short-term exercise on human skeletal muscle metabolism.

Impact of White and Dark Red Kidney Beans on Intestinal and Metabolic Health in C57Bl/6 Male Mice

Rodrigue, A.F [1,2], Aly, M [1,3], Mahmoudian, L [1], Pereira B.B [1,4], Minicucci, M.F [4], Buteau, S [1], Adeli S.R [1], Power, K.A [1,2]

[1]School of Nutrition Sciences, Faculty of Health Sciences, University of Ottawa, Ottawa ON, Canada, [2]Department of Biochemistry, Immunology, and Microbiology, Faculty of Medicine, University of Ottawa ON, Canada, [3]School of Science, Health and Criminal Justice, The State University of New York, Canton NY, USA, [4]Internal Medicine Department, Botucatu Medical School, São Paulo State University (UNESP), Botucatu, Brazil

ABSTRACT

Pulses (i.e. beans, lentils, and chickpeas) are rich in protein and non-digestible carbohydrates (e.g. soluble and insoluble fibre), that may beneficially impact intestinal and metabolic health. Pulses are rich in other nutritional components, including anti-inflammatory phenolic compounds, which are higher in dark-colored pulses (e.g dark red kidney beans) compared to light-colored pulses (e.g. white kidney beans). The objectives of this study were to determine if i) long-term consumption of diet supplemented with kidney beans would improve biomarkers of intestinal (microbial community structure and activity; intestinal barrier integrity) and metabolic health (serum biomarkers of energy homeostasis, ii) dark-colored beans would provide additional health benefits compared to light-colored beans. 5-week-old male C57Bl/6 mice were fed either a basal diet (BD; 20% casein, wt/wt), or isocaloric diets supplemented with 15% cooked white kidney bean (WK) or dark red kidney bean (DK) for 9 weeks (n=12/group). Consumption of diets supplemented with beans improved microbiota community structure and activity, as indicated by an increased abundance of short-chain fatty acid (SCFA) producing bacteria (Prevotella and S24-7) and intestinal SCFA concentrations, with DK diet inducing the greatest effects. Furthermore, biomarkers of colonic inflammation, barrier integrity, and metabolic health were beneficially impacted by kidney bean consumption. While kidney bean consumption leads to improvements in intestinal and metabolic health, the results were influenced by kidney bean variety. In conclusion, generalized recommendations to increase consumption of plant-based protein foods are supported by these findings, however, the magnitude of the health benefits may be improved by selecting darker colored bean varieties.

Deciphering the Role of GFPT1 in Congenital Myasthenic Syndrome

Holland, S[1,4], Gagnon, A[1], Spendiff, S[1], Lochmüller, H[1,2,3,4,5,6]

[1]Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada, [2]Division of Neurology, Department of Medicine, The Ottawa Hospital, Ottawa, Canada, [3]Brain and Mind Research Institute, University of Ottawa, Ottawa, Canada, [4]Department of Cellular Molecular Medicine, University of Ottawa, Ottawa, Canada, [5]Department of Neuropediatrics and Muscle Disorders, Medical Center – University of Freiburg, Faculty of Medicine, Freiburg, Germany, [6]Centro Nacional de Análsis Genómico (CNAG-CRG), Center for Genomic Regulation, Barcelona Institute of Science and Technology (BIST), Barcelona, Catalonia, Spain

ABSTRACT

Congenital myasthenic syndromes (CMS) are inherited neuromuscular disorders characterized by fatigable muscle weakness from impaired transmission at the neuromuscular junction (NMJ). ~35 causative genes have been identified which leads to impaired NMJ maintenance and function. A subset of five of these CMS causative gene mutations impact protein glycosylation through N- and O-linked glycosylation pathways. Glutamine-fructose-6-phosphate transaminase 1, GFPT1, functions as the rate limiting enzyme in the hexosamine biosynthetic pathway and yields precursors for N- and O-linked protein glycosylation. Mutations in GFPT1 have been reported, which result in reduced protein expression and decreased total glycosylation levels. We hypothesize that a functional impairment in GFPT1 causes a reduction in total protein glycosylation at the NMJ. To test this hypothesis, we aim to:

1)Develop model systems (in vitro and in vivo) to investigate the effects of mutations in GFPT1 on the NMJ

2) Determine the role of GFPT1 at the NMJ to elucidate the patho-mechanism of GFPT1-CMS

3) Investigate potential novel therapeutic options for CMS patients

To produce an in vitro cell model a 3rd generation lentivirus doxycycline-inducible GFPT1-miR30 knockdown expression vector was prepared in HEK293T, NSC-34, and C2C12 cells. These cells lines will be used to better characterize GFPT1 impairment both pre-synaptically and post-synaptically. Additionally, I have re-established our laboratory's skeletal muscle GFPT1 knockout mouse model, termed Gfpt1tm1d/tm1d. This murine model will be used to investigate novel therapeutic options for CMS. Currently, we are assessing pilot studies of treatment with galactose and a GFPT1 AVV9 genetic-based therapeutic.

Characterization of the Mutational Landscape of RbBP5 in Cancer

Karunakaran, G [1,2], Janna, A [1,2], Couture, JF [1,2]

[1]Department of Biochemistry, Microbiology and Immunology, University of Ottawa
[2] Faculty of Medicine, University of Ottawa

ABSTRACT

Lysine methyltransferase 2 (KMT2) is a family of enzymes associated with epigenetic regulation of cellular decisions such as hematopoiesis and neurogenesis. KMT2 interacts with protein subunits that regulate its histone H3 lysine 4 methyltransferase activity. Retinoblastoma Binding Protein 5 (RbBP5) is an important regulatory subunit known to be integral for KMT2 complex assembly and nucleosome binding. The Cancer Genome Atlas Database has reported 53 missense mutations of RbBP5 which have been observed in patients suffering from multiple forms of cancer. However, the functional impact of these mutations on KMT2 activity has yet to be established at the molecular and cellular level. We have identified that several mutations substitute evolutionary conserved residues located in functional domains of RbBP5. Identified mutations of human RbBP5 were located in the COMPASS structure and analyzed using PyMOL to predict whether these mutations will impact the functions of human RbBP5. Among the 53 reported mutations, 31 are well-conserved and located in regions associated with nucleosome binding or KMT2 subunit recruitment for complex assembly and stability. Due to the unknown function and poor conservation of the C-terminal wire, we suspect these mutations will not severely impact KMT2 activity explicitly. Notably, mutations of C233 and D262 may disrupt contacts with R236 and K266 respectively, which facilitate the interaction with DNA and thereby will likely affect DNA binding. Probing the mutational landscape of RbBP5 will give us insight on key residue mutations that alter epigenetic signaling and their significance in the progression of cancer.

Treatment of Sinusoidal Obstruction Syndrome with Defibrotide in Pediatric Cancer Patients Following Nontransplant-Associated Chemotherapy: A Case Report and Review of the Literature

Lawrence, MR [1], Johnston, D [1,2]

[1]Faculty of Medicine, University of Ottawa
[2]Children's Hospital of Eastern Ontario

ABSTRACT

Sinusoidal obstruction syndrome (SOS), formerly hepatic veno-occlusive disease (VOD), in pediatric cancer patients often presents as a complication of hematopoietic stem cell transplantation conditioning, and less commonly as an adverse event from nontransplant-associated chemotherapy. Therapy with defibrotide is well-described in the literature as the standard of care for transplant-associated SOS/VOD, but treatment of nontransplant-associated SOS/VOD is less clear. This report is of a 3-year-old female with relapsed Wilms' tumor and recurrent SOS/VOD during therapy, with successful use of defibrotide as treatment and prophylaxis with subsequent chemotherapy. We also present a literature review of pediatric cancer patients with nontransplant-associated SOS/VOD between 2009 and 2018 treated with defibrotide. Seventy-eight patients are included in this review, and 62 were reported to be in remission for the condition. This review supports early treatment with defibrotide, before progression to severe SOS/VOD and multi-organ dysfunction in patients with nontransplant-associated SOS/VOD.

Les Patients Impliqués dans L' éducation des Professionnels de la Santé: Une Revue de la Littérature

Burnier, I [1], Northrop, G [2], Fotsing, S [3], Khouani, Z [3]

[1]Faculté de médecine, Département de médecine familiale, Université d'Ottawa
[2]Faculté de médecine, Université d'Ottawa
[3]Affaires Francophones, Faculté de médecine, Université d'Ottawa

ABSTRACT

Problématique: Les termes employés pour décrire les patients vivant avec une maladie (patient réel) et engagés dans l'éducation des professionnels de santé sont source d'une confusion qui nuit à la mise en place de programme d'éducation centrée sur le patient ..

But: Notre objectif est d'extraire de la littérature anglophone des vingt dernières années les définitions données pour les termes suivants : (1) patient educator, (2) patient instructor, (3) patient mentor, (4) partner patient, (5) patient teacher, (6) Volunteer Patient et ceci dans le but de pouvoir identifier clairement les rôles des patients.

Méthodes: Les bases de données Medline, CINAHL, PsychInfo et Eric ont été consultées afin d'identifier des écrits traitant de « patient réel ». Suite à la lecture des titres, des résumés puis des textes intégraux, 41 articles ont été retenus pour analyse.

Résultats: la définition d'un « patient avec une condition médicale » est constante sauf pour patient instructor et patient teacher qui sont parfois définis comme des patients simulés. L'engagement en éducation et dans l'enseignement sont les caractéristiques les plus fréquentes sans toutefois définir ce que cela veut dire. La formation des patients n'apparait que pour patient educator, patient instructor et partner patient.

Conclusion: les définitions sont assez claires pour comprendre le rôle des patients mais manquent de précisions sur les notions d'engagement qui permettrait de bâtir une taxonomie. Cependant, en identifiant clairement les rôles de ces patients, nous pouvons leur offrir une formation adéquate et déterminer une terminologie adaptée.

Identifying the State of Social Accountability at the University of Ottawa, Faculty of Medicine Through an Internal Environmental Scan

Zhu, G [1,2], Lamontagne, S 1[,2], Fitzgerald, M [1], Kester, N [1], Campbell, C [3,4], Forgie, M [3,4], Hendry, P [5,6], Wiesenfeld, L [7,8], Kendall, C [1,2,9,10,11,12]

[1]C.T. Lamont Primary Health Care Research Centre, Bruyère Research Institute, [2]Department of Family Medicine, University of Ottawa, [3]Department of Medicine, University of Ottawa, [4]Undergraduate Medical Education Program, Faculty of Medicine, University of Ottawa, [5]Department of Surgery, University of Ottawa, [6]Continuing Professional Development, University of Ottawa, [7]Department of Emergency Medicine, University of Ottawa, [8]Postgraduate Medical Education, Faculty of Medicine, University of Ottawa, [9]ICES, Toronto, ON, [10] Li Ka Shing Knowledge Institute, St. Michael's Hospital, [11]Ottawa Hospital Research Institute, [12]Institut du Savoir Montfort

ABSTRACT

Background: The social accountability of medical schools is their obligation to address the priority health concerns of communities they serve, as identified together with governments, health care organizations, health professionals, and the public. Canadian faculties of medicine report regularly on their activities in this area, but it is unclear if communities are able to identify their needs in these processes.

Methods: We conducted a 10-week internal environmental scan of social accountability at the University of Ottawa Faculty of Medicine (FoM). We used available data sources to collect activities across domains of admissions, community outreach, curriculum, clinical service, professional affairs, and innovation and research. We analyzed data quantitatively by Faculty categories, values expressed, populations, and social obligation. We conducted thematic qualitative analysis of a small number of solicited project descriptions.

Results: Of 729 data items collected, 560 related to social accountability. Half of the items were classified in the Education category (281/560, 50.2%), with the vast majority falling under the curriculum domain (271/281, 96.4%). The values most frequently expressed were "quality" (293/560, 52.3%) and "partnership" (265/560, 47.3%), and the most frequently mentioned populations were "marginalized" (153/560, 27.3%), "Indigenous" (96/560, 17.1%) and "Francophone" (76/560, 13.6%). Only 17.1% (96/560) of all items were deemed socially accountable. In the qualitative analysis, partnership and maintaining relationships was again recognized as essential, as was a focus on priority health needs and populations.

Conclusion: Some FoM activities are clearly socially accountable. Other domains could benefit from a greater emphasis on engagement and identification of priority health needs.

Placental Abruption in an Eastern Ontario population: The Impact of Maternal Risk Factors and Placental Pathologies on Adverse Neonatal Outcomes

Mavedatnia, D [1], Tran, J [1], El Demellawy, D [1,2], Lawrence, S [1,2], Moretti, F [1,3], Oltean, I [2]

[1]Faculty of Medicine, University of Ottawa
[2]Children's Hospital of Eastern Ontario
[3]The Ottawa Hospital

ABSTRACT

Placental abruptions, defined as the separation of the placenta from the uterine wall prior to birth, is an obstetrical emergency with potential consequences of maternal and perinatal morbidity and mortality. The clinical and pathological indicators of placental abruptions and their relationship to adverse neonatal outcomes are poorly defined. In a population of pregnant women with placental abruptions, we aim to identify the maternal and placental risk factors, which may be associated with adverse neonatal outcomes. A retrospective chart review was conducted at the Children's Hospital of Eastern Ontario and The Ottawa Hospital. Patients with the clinical diagnosis of placental abruption from October 1st 2013 to April 30th 2020 were included. Clinical information such as maternal demographics, neonatal outcomes, and pathological findings were collected and analyzed using the Pearson correlation coefficient (r). The presence of retroplacental clots [r=0.12 (0.00, 0.24)], chorioamnionitis [r=0.27 (0.15, 0.38)] and PPROM [r=0.15 (0.03, 0.27)] were associated with neonatal death before discharge in premature and mature neonates. The presence of retroplacental clots were associated with cord pH < 7.0 or 7.1-7.16 [r= 0.26 (0.07, 0.43)] in mature neonates. Cannabis use during pregnancy was associated with the need for resuscitation [r = 0.26 (0.07, 0.44)] in mature neonates. In this population of pregnancies complicate by abruptions, placental pathologies and maternal habits (cannabis/drug use) can be predictors of adverse neonatal outcomes, independent of gestational age. Medical caregivers can use this information and examine patient's previous placental pathology and maternal behaviours to recommend optimal prevention and treatment strategies.

Évaluation de L'éducation Ciblée pour L'administration D'immunoglobulines Rh Pendant la Grossesse à L'aide de Questions à Choix Multiples: Une Analyse bayésienn

Hage, D [1], Pyra, K [2], McCudden, C [1,3,4], Padmore, R [1,3,4]

[1]Faculty of Medicine, University of Ottawa, [2]University of Calgary, Calgary, [3]The Ottawa Hospital, Ottawa, [4]Eastern Ontario Regional Laboratory Association, Ottawa

ABSTRACT

Introduction: Les immunoglobulines Rh (RhIG) administrées aux femmes Rh négatif pendant la grossesse lorsqu'elles portent un fœtus Rh positif préviennent la formation anti-D évitant la maladie hémolytique du fœtus et du nouveau-né. Une vérification rétrospective à L'Hôpital d'Ottawa (HO) a révélé un faible niveau (0,3%) d'évènements liés à la sécurité des patientes associés à l'administration de RhIG pendant la grossesse.

Objective: Ce projet est une intervention éducative sur l'administration du RhIG pendant la grossesse.

Méthodes: Des présentations ont été préparées en anglais et en français, examinant la théorie et la l'administration de RhIG pendant la grossesse et administrées à des professionnels de la santé à L'HO en anglais et à l'hôpital Montfort en français. Les présentations ont été précédées par un pré-test et l'efficacité de la présentation a été évaluée en posant les mêmes questions lors d'un post-test. Les questions ont été mises en correspondance avec les directives RhIG publiées. Les questions ont été validées et toute question ayant obtenu un score pré-test>80% était éliminée. Le groupe témoin était une présentation basée sur le curriculum de médecine/infirmier/technologie de laboratoire, avec les mêmes questions pré et post-test.

Résultats: Les résultats ont été examinés avec une probabilité proportionnelle basée sur une analyse bayésienne. La probabilité d'effet moyenne de l'intervention était de 4% (IC 95% -0,19-0,27%) pour le groupe témoin et de 30% (IC 95% 16%-43%) pour le groupe d'intervention éducative.

Conclusion: En utilisant l'analyse de probabilité proportionnelle bayésienne, notre intervention éducative a montré une meilleure connaissance de l'administration RhIG pendant la grossesse.

Newborn Hypoglycemia Screening: A Scoping Review

Musa, A [1], Horwitz, J [1], Mardiros, L [1], Hodgson, A [1], Welch, V [2], Saginur, M [3]

[1]University of Ottawa
[2]Bruyere Research Institute
[3]Montfort Research Institute

ABSTRACT

Background: The risk of neonatal hypoglycemia (NH) currently warrants repeated pre-feed bloodwork after birth in about a third of Canadian babies. Nonetheless, NH screening remains controversial.

Objective: The objectives of the scoping review are to summarize the scope of existing scientific literature that describes evidence about the defined benefits and harms of screening for then treating NH to the mother and newborn and to define gaps in the existing literature.

Methods: A MEDLINE and Embase search was done using MeSH terms for primary studies and guidelines relating to NH screening. Additional articles were gathered from the references of guidelines. After deduplication, 3149 articles were screened, 447 were eligible for full-text assessment, and 96 were included having 79 primary studies. Screening and data extraction were done independently by 2 parties and confirmed by a third party if necessary. The outcomes and themes were then grouped and summarized.

Results: There were 33 (41.8%) studies with a primary neurodevelopmental outcome, 32 (40.5%) primarily non-neurodevelopmental outcome, 1 (1.3%) primarily maternal outcome, and 13 (16.5%) that primarily evaluated both neurodevelopmental and non-neurodevelopmental outcome. There were 22 (22.9%) primary studies focused on overall neurodevelopmental status, 8 (10.1%) on NICU admission rates, 6 (7.6%) on comparisons of tools most suitable to measure for NH, and 9 (11.4%) on treatment options for NH and their cost.

Conclusion: Further primary studies are needed on the maternal perspective (1.3%), ophthalmologic outcome (3.8%), and consistent definitions for NH treatment threshold.

Evaluation of the Utility of Electrocochleography in Ambulatory Care Clinics

Kim, ST [1], Armstrong, S [2], Stacey, S [2], Lalonde-Couturier, S [2], Lacasse, C [2], Schramm, DR [1,3]

[1]Faculty of Medicine, University of Ottawa
[2]Department of Audiology, The Ottawa Hospital
[3]Department of Otolaryngology – Head and Neck Surgery, University of Ottawa

ABSTRACT

Objectives: Latest technological advances in cochlear implantation (CI) enable measurement of an electrocochleography (ECoG) signal intra-operatively in patients with residual hearing. Recently, it has been demonstrated that there is a strong correlation between ECoG thresholds and audiometric pure-tone thresholds in post-operative settings. These studies may suggest the clinical applicability of ECoG thresholds in Ambulatory Care settings. However, such an application has not been formally investigated. Our research aims to explore the novel use of ECoG for audiometric threshold measurement and its efficiency in an Ambulatory Care setting.

Methods: Adult unilateral CI patients with residual hearing were recruited based on the inclusion criteria. The post-operative audiometric pure-tone thresholds were measured in a soundproof booth and ECoG thresholds were measured using the Active Insertion Monitoring (AIM) System.

Results: Preliminary results in a subset of the study sample showed that there is a moderate correlation between audiometric and ECoG thresholds (r=0.67, p=0.0002). The AIM System tended to underestimate hearing in the lower frequencies (250 to 750Hz) and overestimate hearing in the higher frequencies (1000 to 4000Hz). The ECoG threshold measurement took substantially less time than the audiometric threshold measurement.

Conclusion: There is a moderate correlation between ECoG and audiometric thresholds in CI recipients with residual hearing. Furthermore, our preliminary results suggest that it is more time-efficient to use the ECoG threshold in an Audiology outpatient clinic. However, further refinements are needed in the AIM system to improve the correlation between audiometric and ECoG thresholds.

COVID-19 Public Health Information: Are We On The Same Page?

Treanor, L [1], Radonjic, A [1]

[1]Faculty of Medicine, University of Ottawa

ABSTRACT

Objective: In this study, we aimed to determine the reading level of the most popular websites that Canadians and Americans would come across when they searched for information on coronavirus disease 2019 (COVID-19).

Methods: Using three popular search engines, we entered the search term “coronavirus information” in five geographically representative virtual private network locations. Webpages were screened for inclusion from the first three pages of these search engines. Webpages were included if they pertained to information for the general public regarding COVID-19. As defined by the American Medical Association, an adequate readability for patient information is at (or below) a grade 7 reading level. Therefore, we categorized a general grade level of grade <7 to be “easy”, 7-10 as “moderate”, and >10 as “difficult”.

Results: Of 428 webpages included by screening, 371 were excluded (330 duplicates, 19 not for the general public, 11 not over 100 words, 11 news articles). The mean general grade level of the remaining 57 included webpages was 10.8 (standard deviation 1.9, range 7.3-15.6). By stratifying readability of sites with general grade level, 70% were considered ‘hard’, 30% were considered ‘intermediate’, and none were considered ‘easy’. None of the ten most popular webpages were at an adequate reading level.

Conclusion: In conclusion, the mean reading levels of the most popular public information websites far exceeded recommended levels. Government and health information websites should re-evaluate the readability of their webpages to ensure they provide information at an appropriate reading level for the general population.

Inflammatory Skin Disease Triggers: A Tool for Self-Management of Psoriasis and Atopic Dermatitis

Hanna, N [1], Finestone, H [2]

[1]University of Ottawa, Faculty of Medicine, Ottawa ON, Canada
[2]Bruyère Continuing Care, Ottawa Hospital Rehabilitation Centre, Ottawa ON, Canada

ABSTRACT

Psoriasis and atopic dermatitis are common inflammatory skin conditions, which have a prevalence of 2-3%, and 1-3% (up to 20% in children), respectively. Their clinical course is chronic, with remitting and relapsing periods of disease, known as flares. Flares can occur due to a variety of factors such as psychosocial stressors, weather or exposure to irritants. Many of these factors are modifiable, and as such, patients can benefit from counselling regarding these triggers. However, it has been identified that patients only retain a limited percentage of the information they receive during visits to the physician's office. The use of a question prompt sheet has been recognized as an effective tool in improving patients' recall during physician counselling. As such, we developed an interactive prompting tool to help patients recognize their unique trigger factors, and subsequently help them self-manage their inflammatory skin disease. This tool was adapted from The Pain Explanation and Treatment Diagram assessment form, which has been trialed with success in patients. The prompting questions are specific for either psoriatic disease or atopic dermatitis. Triggers outlined for psoriasis are grouped into the following categories: habits, stressors, diet, and environment. Triggers outlined for atopic dermatitis are grouped into the following categories: habits, stressors, irritants, and environment. The goal of this tool is to enhance patient education and facilitate patient-centred and holistic care. Additionally, this tool can help patients self-manage their chronic skin diseases during the pandemic, when access to physician care is limited.

No Mention or Recommendations of Complementary and Alternative Medicine Ovarian Cancer Guidelines: A Systematic Review

Lau, SKC [1], Ng, JY [2]

[1]Faculty of Medicine, University of Ottawa
[2]Department of Health Research Methods, Evidence, and Impact, Faculty of Health Sciences, McMaster University

ABSTRACT

Background: Ovarian cancer is the leading cause of morbidity and mortality among gynecological cancers; nearly 50% of those diagnosed use complementary and alternative medicine (CAM) in hope of improving their prognosis. However, improper use of CAM can result in a variety of harms. As healthcare providers generally have little to no training in CAM, they may consult clinical practice guidelines to guide the development of patient treatment plans. This study sought to identify the quantity and assessed the quality of CAM recommendations in ovarian cancer treatment and/or management guidelines.

Methods: MEDLINE, EMBASE, and CINAHL were systematically searched for ovarian cancer clinical practice guidelines; additionally the Guidelines International Network and the National Center for Complementary and Integrative Health websites. Had CAM recommendations been found, the guidelines would have been assessed with the Appraisal of Guidelines, Research and Evaluation (AGREE) II Instrument.

Results: Among the 356 unique search results, there were 13 eligible guidelines, none of which made mention or recommendations on CAM use in ovarian cancer.

Conclusions: The quality of CAM recommendations in ovarian cancer treatment could not be assessed and compared with overall guideline recommendations. Since a large proportion of ovarian cancer patients are CAM users and many healthcare providers rely on clinical practice guidelines, the lack of CAM recommendations in ovarian cancer represent a major knowledge gap. Future guidelines should consider incorporating evidence-based CAM recommendations given that clinicians require this information in order to inform important shared-decision making discussions regarding safe and effective CAM use with their patients.

Characteristics of patients managed by video-conferencing, teleconferencing or in-office visits in a community rheumatology practice during the early part of the COVID-19 pandemic

Misra, A [1], Bajaj, S [2,3,4], Ahluwalia, V [4], Papneja, T [4], Joshi, R [4]

[1]Faculty of Medicine, University of Ottawa, [2]Clinical Adjunct Professor, McMaster University, [3]Clinical Adjunct Professor, University of Toronto, [4]Division of Rheumatology, Department of Internal Medicine, William Osler Health System

ABSTRACT

Background: Because of the COVID-19 pandemic, physicians are using teleconferencing or video conferencing for patient evaluations. While teleconferencing and video conferencing may allow physicians to screen and manage patients without patients having to travel, it may present unique challenges. The current study was designed to compare patients seen by teleconferencing, video conferencing and in-person in a community rheumatology practice.

Methods: A retrospective chart review was conducted of 60 patients seen in a community rheumatology clinic of 4 rheumatologists between March-July 2020. The following characteristics were examined: age, sex, date of assessment and previous assessment, inflammatory versus non-inflammatory condition, new consult /follow-up, if English was their first language, and distance from the clinic. For patients who were brought into the office, we checked if they had intra-articular/muscular injections.

Results: Overall, 43/60 (71.7%) patients had inflammatory conditions. 18/20 (90.0%) of patients seen in person were follow-ups. In contrast, 12/20 (60.0%) of patients seen via video were follow-ups, and 15/20 (75.0%) of patients assessed via teleconference were follow-ups. 13/20 (65.0%) in-person were given injections. The average distance from the clinic for in-person, telephone, and video appointments were 14.8km, 21.6km, and 23.3km respectively. Eight patients had difficulties using videoconferencing.

Conclusions: The majority of patients were seen virtually since March 2020. Patients seen virtually lived, on average, further away than patients seen in office. Most patients who were seen in-person received injections. Technical difficulties were present in some appointments, leading to delays and to consults being done without visual aid.

Les Applications mHealth pour les Ayndromes Gériatriques : Une Revue de la Littérature

Riad, K [2], Bouchard-Lamothe, D [2], Fotsing, S [2], Joanisse, J [1]

[1]Department of Family Medicine, Hôpital Montfort, Ottawa, Ontario
[2]Faculty of Medicine, University of Ottawa

ABSTRACT

Introduction: Au Canada, il y a peu de gériatres et moins d'intérêt pour cette spécialité chez les étudiants en médecine, alors que les syndromes gériatriques sont associés à une morbidité et une mortalité accrues. Bien que des approches de gestion existent, les praticiens ne reconnaissent souvent pas ces syndromes ou n'utilisent pas les stratégies thérapeutiques disponibles. La littérature rapporte que les applications mHealth sont connues pour aider les praticiens dans l'amélioration des décisions cliniques, et de l'état de santé des patients.

Objectif: Identifier des applications, analyser les preuves de leur efficacité et déterminer les lacunes de la recherche sur les applications mHealth des syndromes gériatriques en français.

Méthodes: Une revue narrative de la littérature a été complétée. A partir de 2 bases de données (Medline et PubMed), ces mots-clés ont été utilisés : « elderly », « geriatric syndromes », « geriatrics », « mhealth », « application » et « decision making ». Des critères d'exclusion ont été appliqués : 1- la disponibilité, 2- la date, 3- la langue, et 4- la duplicité.

Résultats: 13 applications mHealth ont été jugées pertinentes pour mesurer leur efficacité. Medscape et Skyscape ont été déterminés comme les applications les plus complètes pour les informations générales en gériatrie. Peu d'application sont en français et aucune ne traitent de la gestion des syndromes gériatriques.

Conclusion: Il est impératif de développer une application mHealth pour les cliniciens francophones donnant rapidement accès à l'information concernant la gestion des syndromes gériatriques.

Online Patient Information for Hysterectomies: An Environmental Scan of Readability and Quality

Jain, M[1], Chkipov, P[1], Stacey, D[2], Posner, G[3,4], Bacal, V[3], Chen, I[3]

[1]University of Ottawa, Faculty of Medicine, Ottawa, ON, Canada, [2]Ottawa Hospital Research Institute, Ottawa, ON, Canada, [3]Department of Obstetrics and Gynecology, University of Ottawa, Ottawa, ON, Canada, [4]Department of Innovation in Medical Education, University of Ottawa, Ottawa, ON, Canada

ABSTRACT

Hysterectomy is a common gynaecological procedure. Accessible online patient information is highly important due to associated risks, lifestyle changes and treatment alternatives. The study aims to evaluate quality, comprehensiveness and readability of online patient information on hysterectomies. We evaluated websites that provided patient directed information on hysterectomies. The first 25 webpages on 5 search engines were included. Quality of websites was assessed by validated tools for online material (DISCERN and JAMA benchmark). We evaluated whether websites included information on alternatives (including minimally invasive approaches), risks, and benefits. Readability scores were calculated to assess the years of education needed to comprehend the material (FKLG, Gunning FOG, SMOG, FRES). Fifty websites were included. On average, websites were of good quality (52.5 +/- 10.5 of 80, DISCERN criteria; 2.6 +/- 1.3 of 4, JAMA criteria). The majority of websites described treatment alternatives (33/50, 66.0%) including minimally invasive options (21/50, 42.0%), and also described surgical risks (39/50, 78.0%) and benefits (49/50, 98.0%). However, website article readability corresponded to a grade 12 reading level (FKGL= 12.1 +/- 2.4) or reading levels of 11 or 15 years of education (SMOG= 11.3 +/- 1.8, Gunning FOG= 15.1 +/- 2.4) suggesting these websites are difficult to read for the general population (39.8 +/- 12.2 FRES). Online patient information on hysterectomy is of good quality and contains the majority of required information. However, the content is above the American Medical Association's recommended grade six reading level. Website authors should consider readability to make their content more accessible to patients.

Cochrane and Ageing: Are We Measuring the Right Things in Systematic Reviews Inclusive of Older Adults?

Janusz, N [1], Ghogomu, E [3], Dowling, S [2], Howe, T [4], Maxwell, L [1], Tugwell, P [1], Welch, V [3]

[1]Faculty of Medicine, University of Ottawa, [2]Faculty of Science, University of Ottawa, [3]Bruyère Research Institute, University of Ottawa, [4]Cochrane Global Ageing

ABSTRACT

Background: Musculoskeletal conditions are one of the main causes of disability among older adults, the burden of which is magnified with increasing age. Systematic reviews inclusive of older adults need to consider age-specific methods.

Objectives: To determine: (1) how Cochrane musculoskeletal reviews inclusive of older adults assess function; and (2) what methods are used to evaluate age-specific outcomes.

Methods: We included all Cochrane musculoskeletal reviews published after 2015 including participants over the age of 50 (n = 52). We extracted data on outcomes according to the International Classification of Functioning (ICF). We assessed the extent to which reviews 1) reported participants' age, 2) described age in the rationale, 3) performed subgroup analyses across age, 4) included age-specific summary of findings, or 5) described applicability of results based on age.

Results: The median age of participants was 54 (range 16-94). The most commonly assessed ICF domain was domestic life (90%), followed by mobility (89%), self-care (87%), interpersonal interactions and relationships (65%), community/social/civic life (64%), major life areas (31%), and communication (2%). Majority of reviews (73%) described participants' age, 54% considered age in the rationale, 54% planned a subgroup analysis across age, and 17% described applicability of results based on age. None of the reviews presented age disaggregated results.

Conclusions: Over two thirds of Cochrane musculoskeletal reviews evaluated the majority ICF functional domains. While most reviews described the age of participants, the limited consideration of age in analysis and interpretation of results is a barrier in judging their applicability to older adults.

Mobile Technology Assisted Mental Health Interventions Among Pregnant Women: Protocol for An Equity-focused Systematic Review

Saad, A [1,2], Magwood, O [2,3], Alkhateeb, Q [2,4], Hashmi, SS [5], Kassam, A [6,7,8], Pottie, K [1,2,9]

[1]School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, [2]C.T. Lamont Primary Healthcare Centre, Bruyère Research Institute, Ottawa, ON, [3]Interdisciplinary School of Health Sciences, University of Ottawa, Ottawa, ON, [4]Department of Internal Medicine, Schulich School of Medicine, London, ON, [5]School of Medicine, University of Ottawa, Ottawa, ON, [6]Department of Psychiatry, University of Ottawa, Ottawa, ON, [7]Pinecrest Queensway Community Health Centre, Ottawa, ON [8]Ottawa Newcomer Health Centre, Ottawa, ON, [9]Department of Family Medicine, University of Ottawa, Ottawa, ON

ABSTRACT

Context: Pregnant women experience psychological and emotional imbalances during and after their pregnancy which increase their risk of developing common mental health conditions. Mobile technology assisted mental health interventions may mitigate the barriers that pregnant women face when accessing mental healthcare.

Objectives: The objectives of this equity-focused systematic review are to a) examine the effectiveness of mobile technology-assisted mental health interventions among pregnant women and b) to explore the health equity impact of these interventions relating to pregnant women's age, socioeconomic status, race and ethnicity, social capital, and experience of intimate partner violence.

Dataset(s): We searched seven electronic bibliographic databases for relevant studies: MEDLINE, Embase, PsycINFO, Web of Science, CINAHL, PTSDPubs (PILOTS), and Cochrane CENTRAL. Population: Women who were pregnant regardless of the trimester, or who have given birth within the last 12 months regardless of the birth outcome.

Outcomes: Severity of psychological symptoms, psychological wellbeing and distress, changes in the occurrence of common mental health conditions, mental and pregnancy-related healthcare utilization.

Anticipated results: We anticipate to include a number of randomized and non-randomized controlled trials examining a myriad of applications focusing on the prevention and management of depression, anxiety, or stress symptoms. Results will be critically appraised and findings will be assessed for certainty. Equity-focused subgroup analyses will be undertaken.

Relevance: Our findings will inform the response to the mental health global crisis of the COVID-19 pandemic and will inform healthcare providers on whether technology carries the potential to ensure the continuity of mental health care.

Modernizing Preclerkship Medical Education: The Flipped Classroom

Kundapur, D [1], Tran, C [1,2]

[1]University of Ottawa Faculty of Medicine
[2]The Ottawa Hospital, Department of Medicine

ABSTRACT

Background: "Flipped-classroom" (FC) refers to a blended learning model where students access preparatory educational materials (typically online videos or modules) prior to attending traditional lectures or small-group sessions. By allowing students to familiarize themselves with lower-order concepts on their own, live teaching sessions can focus on high-order principles such as clinical reasoning in the case of medical school. This pilot project aims to enhance learning experiences for medical students at the University of Ottawa during their Endocrinology block. Methods: Literature review of 23 articles identified important constructs to consider when implementing FC, including: student engagement, knowledge acquisition, teacher-student interaction, and learner attitudes. Using these themes, a needs-assessment survey was designed and distributed to preclerkship medical students to explore student preferences for FC.

Results: We collected a total of 154 responses (46% response rate). Over 90% of respondents prioritized small-group sessions for videos whereas less than 50% placed priority on lectures. Videos regarding basic physiology and case-based clinical reasoning were preferred. Given this information, we produced 11 videos using a note-taking software and mapped the content to curricular objectives, focusing on physiology and/or clinical reasoning depending on the video.

Next Steps: The videos will be accompanied by pre-video and post-video comprehension quizzes for immediate feedback as well as a end-of-block survey to assess student perceptions and learner experiences. If the videos are found to have a positive effect on student learning, the FC approach may be extended to include blocks outside of Endocrinology.

SPIN in Randomized Controlled Trials in Obstetrics and Gynecology: A Systematic Review

Chow, R [1], Huang, E [1], Fu, S [1], Kim, E [1], Li, S [2], Tulandi, T [3], Cobey, K [4], Bacal, V [4], Chen, I [4]

[1]University of Ottawa, Faculty of Medicine, 451 Smyth Road, Ottawa, ON K1N 6N5, Canada, [2]McMaster University, Faculty of Health Sciences, 1280 Main St W, Hamilton, ON L8S 4L8, Canada, [3]Department of Obstetrics & Gynecology, McGill University Health Centre 1001 Decarie Blvd, Montreal, QC, H4A 3J1, Canada, [4]Ottawa Hospital Research Institute, 501 Smyth Road, Ottawa, ON K1H 8L6, Canada

ABSTRACT

Background: The universal standard for determining the efficacy or safety of an intervention generally consists of the implementation of a randomized clinical trial (RCT). RCTs require a high level of methodological rigour to generate valid and reliable evidence to inform effective healthcare policymaking. Therefore, impartial and unbiased language must be used when reporting a study to avoid consciously or subconsciously altering the reader's impression of the results. The primary aim of this systematic review was to evaluate RCTs in the field of obstetrics and gynecology and appraise them for type, extent, and level of SPIN. The secondary aim is to determine whether different study characteristics are associated with higher levels of SPIN.

Methods: A comprehensive search of Medline from January 1, 2019 to present was completed. Articles were retrieved from the top five high impact obstetrics and gynecology journals. Cochrane Risk of Bias Tool (RoB2) and a SPIN assessment was used to evaluate the risk of bias.

Results: As observed by the Cochrane Risk of Bias assessment, RCTs generally do not have bias arising from randomization or missing data. Thus, many RCT's in the field of OB/GYN seem to be internally valid. However, there seems to be themes of selective reporting which influence the paper's overall risk of bias. SPIN is present in over half of the included studies and is mostly found in the conclusions of the main-text.

Conclusion: Healthcare professionals intending to apply the results of RCTs in the field of obstetrics and gynecology should critically appraise the literature.

Efficacité des Interventions Ciblant le Travail D'équipe Interprofessionnelles pour Améliorer le Bien-être au Travail en Soins Périopératoires: Une Revue Systématique

Turcotte, M [1], Etherington, N [2], Mansour, F [1], Zahrai, A [1], Rowe, J [1], Kaur, M [1], Duong, A [3], Talbot, Z [5], Mohamed, J [1], Boet, S [1,2,6]

[1]Faculty of Medicine, University of Ottawa, [2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, [3]Faculty of Medicine, University of Ottawa, [4]Faculty of Health Sciences, University of Ottawa, [5]Faculty of Science, University of Ottawa, [6]Francophone Affairs, Faculty of Medicine, University of Ottawa

ABSTRACT

Le bien-être au travail des professionnels de santé (PDS) contribuent à la prestation de soins de haute qualité et de la sécurité des patients, surtout dans le cadre chirurgical où les risques sont particulièrement élevés. Parmi les facteurs influençant le bien-être, la qualité du travail d'équipe est l'un des prédicteurs les plus importants. Cependant, l'effet des interventions ciblant le travail en équipe sur le bien-être des PDS n'a pas encore été rigoureusement synthétisé pour l'environnement périopératoire. Cette revue systématique vise à analyser la littérature pour évaluer l'efficacité des interventions ciblant le travail d'équipe interprofessionnel sur le bien-être au travail chez les professionnels en soins périopératoires. Des recherches documentaires ont été effectuées dans MEDLINE, EMBASE, CINAHL, Web of Science et PsycINFO jusqu'au 4 février 2020. Les études qui investiguaient des interventions de travail d'équipe interprofessionnelle pendant la période périopératoire ont été incluses. Les critères d'intérêt comprenaient: l'épuisement professionnel, l'absentéisme, l'engagement, la satisfaction, et le stress lié au travail. L'admissibilité a été évaluée en double par deux paires d'examinateurs indépendants, les désaccords ayant été résolus par consensus. Nous fournirons un résumé narratif des résultats décrivant les interventions de travail d'équipe périopératoire et leurs impacts globaux et par catégories sur le bien-être professionnel des PDS. Nous identifierons les lacunes dans la littérature qui pourraient nécessiter des recherches supplémentaires. Notre but est de proposer un ensemble normalisé de stratégies de travail en équipe pouvant être appliquées pendant la période périopératoire pour améliorer le bien-être professionnel ainsi que les résultats pour les patients.

Incisions and Decisions: The History of Vasectomy

Song, Y [1], Lamb, S [2]

[1]Faculty of Medicine, University of Ottawa
[2]Jason A. Hannah Chair in History of Medicine, Faculty of Medicine, University of Ottawa

ABSTRACT

Background: Modern day discourse regarding reproductive choice often revolves around women and female bodies. At the same time, the study of male contraceptive options—namely, vasectomy—is needed to invoke a greater understanding of Western society's changing attitudes toward sterilization and other contraceptive choices, and how reproductive decisions have been made between families and healthcare providers in the bedroom and beyond. In the 19th and 20th centuries, vasectomy was medicalized, and transformed from a procedure used to control institutionalized citizens by way of eugenics, to an elective office procedure available to male patients with comparatively greater privilege and autonomy. This research identifies critical social, cultural, technological, and intellectual factors that influenced this transformation.

Methods: Online databases were mined for historical sources such as medical and scientific journal articles, legal discussions, magazine and newspaper articles, and secondary sources that would give insight into changing attitudes and practices regarding vasectomy both within and beyond the medical community.

Results and Conclusions: For vasectomy to be accepted into common medical practice, perspective had to change such that both physician and male patient were situated as favourable—and in some cases, heroic—agents of change. Clinical interpretations of vasectomy-seeking and vasectomized patients changed too, from pathologized to privileged, respectively. Legal ambiguity of the procedure was evident in the years surrounding the decriminalization of birth control, causing confusion and frustration for physicians. Further research is needed to compare the ways in which marginalized individuals, such as Indigenous and racialized people, interacted with evolving contraceptive options.

PRIME-IPD: A Systematic Method to Prepare Individual Participant Data for Systematic Reviews and Meta-Analyses

Dewidar, O [1,2], Riddle, A [1], Ghogomu, E [1], Hossain, A [2,3], Arora, P [4], Bhutta, ZA [5,6], Black, RE [7], Cousens, S [8], Gaffey, MF [6], Mathew, C [1], Trawin, J [9], Tugwell, P [10,11,12], Welch V [1 2], Wells GA [1,2,3]

[1]Bruyère Research Institute, University of Ottawa, 85 Primrose Ave, Ottawa, Ontario, K1R 6M1, Canada, [2]School of Epidemiology and Public Health, University of Ottawa, 600 Peter Morand Crescent, Ottawa, Ontario, K1G 5Z3, Canada, [3]Department of Medicine (Cardiology), The University of Ottawa Heart Institute and University of Ottawa, 40 Ruskin Street, Ottawa, Ontario, K1Y 4W7, Canada, [4]Dalla Lana School of Public Health, University of Toronto, 155 College St Room 500, Toronto, Ontario M5T 3M7, Canada, [5]Centre for Global Child Health, Hospital for Sick Children, 555 University Ave, Toronto, Ontario, M5G 1X8, Canada, [6]Center of Excellence in Women and Child Health, Aga Khan University, Karachi, Karachi City, Sindh, Pakistan, [7]Department of International Health, Johns Hopkins School of Hygiene and Public Health, 615 N Wolfe St Suite E8527, Baltimore, Maryland, 21205, United States, [8]Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine (LSHTM), Keppel Street, London, WC1E 7HT, UK, [9]Women's Health Research Institute, 4500 Oak St, Vancouver, British Columbia, V6H 2N9, Canada, [10]Clinical Epidemiology Program, Ottawa Hospital Research Institute, 501 Smyth Rd, Ottawa, Ontario K1H 8L6, Canada, [11]Department of Medicine, University of Ottawa Faculty of Medicine, Roger Guindon Hall, 451 Smyth Rd #2044, Ottawa, Ontario, K1H 8M5, Canada

ABSTRACT

Background: Individual participant data (IPD) meta-analysis (MA) is considered the gold standard for systematic reviews. However, investigators face multiple obstacles while preparing IPD for MA, including differences in data collection methods and outcome variables, and incomplete data dictionaries, which impact the efficiency in preparing IPD for MA. The purpose of this tool is to describe a systematic approach to preparing IPD for MA.

Methods: We explored guidance from the relevant literature including Cochrane Handbook, Get Real-IPD working group, and Cochrane Multiple Interventions group. Through consultation with the advisory board for an IPD-MA and systematic review, we iteratively developed a five-step approach to preparing IPD.

Results: Our approach is composed of: Processing, Replication, Imputation, and Merging and Estimation (PRIME). The processing step verifies that the variables of interest are available in the original datasets and standardizes the variables of interests across the datasets. The replication step verifies that the processed dataset is consistent with the analyzed dataset in the published papers, using standardized differences. The imputation step involves an algorithm for how to handle datasets with missing values including multiple imputation. The merging step proposes combining all datasets after dealing with missing data. The estimation step involves calculating new variables required for analysis, such as categorical variables for gradations of intensity or severity of outcome variables.

Conclusion: The PRIME-IPD methodology can guide researchers in the process of preparing data for IPD-MA. This guidance needs to be evaluated by application to other systematic reviews and meta-analyses.

Developing Patient-Centred Strategies to Optimize the Management of Vasomotor Symptoms in Patients with Early Breast Cancer: Interim Analysis of Patient Surveys

Cole, K [1], Clemons, M [2], Larocque, G [3], Vandermeer, L [4], Hutton, B [5], Piper, A [6], Pond, G [7], MacDonald, F [3], McGee, S [1]

[1]Department of Medicine, Division of Medical Oncology, The Ottawa Hospital and University of Ottawa, [2]Department of Medicine, Division of Clinical Epidemiology, The Ottawa Hospital and University of Ottawa, [3]The Ottawa Hospital Cancer Centre, [4]Cancer Therapeutics Program, The Ottawa Hospital Research Institute, [5]Clinical Epidemiology Program, The Ottawa Hospital Research Institute, [6]University of Ottawa Health Services, [7]Department of Medicine, Division of Medical Oncology, McMaster University

ABSTRACT

Systemic treatments for early breast cancer (EBC) commonly result in vasomotor side effects including hot flashes and night sweats. These symptoms can negatively impact patient quality of life and treatment adherence. Moreover, there is a lack of evidence regarding patient centred strategies for the management of hot flashes in this population. Between June 4 and August 15, 2020, 103 women who experienced hot flashes during treatment for EBC at The Ottawa Hospital participated in an electronic or paper survey. The primary objective of this study is to determine a patient derived definition of optimal control of hot flashes. An interim analysis of 25% of the final sample size (n=400) is presented. The average age of respondents was 55 years old (range 34-78), with a reported average of five hot flashes per day. Forty seven percent of respondents rated their level of distress from hot flashes as moderate to severe. Reported levels of distress were correlated with the number of hot flashes per day ($p < 0.001$, $R2$ 0.169). The most commonly reported symptoms of concern were vasomotor symptoms, and disturbed sleep. The majority of respondents indicated that they would consider a treatment effective if it controlled nocturnal symptoms (n = 59). While a minority of patients reported receiving treatment for their hot flashes (n = 21), 71% of patients were interested in pursuing an intervention to manage their symptoms. This data will help inform the design of future pragmatic clinical trials to improve the management of vasomotor symptoms in EBC patients.

End of Life Care of Patients with Hematologic Malignancy treated at The Ottawa Hospital

Aw, M [1], Christou, G [2]

[1]Faculty of Medicine, University of Ottawa
[2]Division of Hematology, The Ottawa Hospital

ABSTRACT

Background: Hematologic cancers are a leading cause of cancer deaths. While most patients wish to die at home, most do not for several reasons including uneven palliative care access, rapid clinical deterioration and more aggressive treatment at end of life. To date, there has been no analysis of end of life care of patients with hematologic malignancy at The Ottawa Hospital.

Methods: We analyzed retrospective data on adult patients with a hematologic malignancy treated at TOH and who died between 01/01/2016 – 01/05/2019. Patient data from the last 3 months of life was collected from medical charts and The Ottawa Hospital Data Warehouse.

Results: 377 patients died during the study period, of which, 243 died at TOH hospital (lymphoma:89; leukemia:114; myeloma:40); 106 patients died at home or hospice (lymphoma:42; leukemia:40; myeloma:24); and 28 others died at non-TOH hospitals (lymphoma:9; leukemia:13; myeloma:6). The sex, proportion of patients receiving chemotherapy, supportive treatment and palliative care consults were comparable between those who died in hospital and those who died at home or in palliation. In contrast, those who died in hospital were generally younger ($p=0.001$); and were more likely to die unexpectedly ($p<0.0001$) and from something other than their blood cancer ($p<0.0001$); received more transfusions ($p<0.0001$); had more and longer ICU ($p<0.0001$) and inpatient admissions ($p<0.0001$) in the last 3 months of life.

Conclusion: The majority of hematologic malignancy patients die in hospital and despite representing primarily expected deaths, they still receive aggressive care. Multivariate analysis will be conducted to elucidate predictors of in-hospital deaths.

Predicting Permanent vs. Transient Hypothyroidism in Children with Confirmed Congenital Hypothyroidism Identified Through Newborn Screening Ontario (NSO)

Yokubynas, N [1], Marr, A [2], Tang, K [2], Chakraborty, P [2,3], Lawrence, S [2]

[1]University of Ottawa, Faculty of Medicine
[2]Children's Hospital of Eastern Ontario
[3]Newborn Screening Ontario

ABSTRACT

Background: Congenital Hypothyroidism (CH) is characterized by thyroid hormone deficiency at birth, which can lead to permanent neurological and cognitive impairment. Over time, the incidence of CH has increased appreciably, commonly correlated with increased detection of transient forms of the condition. Unfortunately, transient CH (TCH) remains poorly defined during the first few years of life. Consequently, management is paralleled with permanent CH (PCH), which includes mandatory L-thyroxine supplementation for 3 years, at which point a trial-off therapy may be considered. This delay in differentiation results in unnecessary medicalization for those with TCH. Therefore, this study aims to identify predictive markers for TCH and establish a predictive tool for its earlier differentiation from PCH.

Methods: We conducted a retrospective chart review of patients identified with CH through Newborn Screening Ontario between 2006 and 2014 (N = 846). Potential predictive markers analyzed include: GA, BW, screening TSH, diagnostic TSH and T4, thyroid location, maternal thyroid disease during pregnancy, family history of thyroid disease, and follow-up TSH, FT4 and L-thyroxine dose/kg at 6 months, 1, 2 and 3 years of age. Children with a successful trial-off therapy at 3 years of age were classified as TCH.

Results: Overall, 506 cases (58.4%) were included: 348(69.5%) had PCH, 105(21%) had TCH and 48(7.5%) were indeterminate. Here, we will review the descriptive differences between PCH vs. TCH. Ongoing research is working towards developing a predictive tool for earlier differentiation of TCH, ultimately avoiding excess medicalization and healthcare costs in these patients.

Venous Thromboembolism Among Acute Leukemia Patients Treated at the Ottawa Hospital (TOH)

Chatterjee, A [1], Sabloff, M [2]

[1]University of Ottawa Faculty of Medicine
[2]Ottawa Hospital Department of Hematology

ABSTRACT

Background: Malignancy-associated venous thromboembolism (VTE) is well described in the literature. Risk factors in this population include type of underlying malignancy, active chemotherapy, and central venous catheters. Despite this, there remains a paucity of data regarding leukemia-associated VTE in the adult population. Furthermore, treatment of VTE in patients with acute leukemia is based on expert opinion without standardization. We aim to describe the incidence and characteristics of VTE in patients with acute leukemia at our center, including the VTE treatments received.

Methods: The Medical records of 440 patients treated at the Ottawa Hospital (TOH) for acute leukemia with intensive therapy between January 2007 to September 2015, were reviewed, retrospectively. Basic demographic and outcome data was extracted. Thrombocytopenia was defined as a platelet count less than 50 x 109/L. The patients were divided in three cohorts. Those diagnosed with VTE within 30 days of diagnosis of AL; those diagnosed between 30 and 90 days and >90 days from the time of diagnosis of AL.

Results: The cumulative incidence of VTE was 9%. Most patients developed VTEs in the upper extremities and 53% of cases were associated with catheter. The recurrence beyond 30 days of cancer-associated VTE was 33%. Three cases of non-fatal bleeding were observed. Platelet transfusion was recommended to 19% of patients. Platelets adjusted anticoagulants was offered to majority of patients. Low molecular weight heparin was the most common anticoagulant used by clinicians. The median survival was lowest in those that developed VTE in the first 30 days of leukemia.

Predictors of Adherence to Positive Airway Pressure (PAP) therapy: A Retrospective Longitudinal Observational Study

Villa, J [1], Dales, R [1], Kendzerska, T [1,2]

[1]Faculty of Medicine, University of Ottawa
[2]Ottawa Hospital Research Institute

ABSTRACT

Purpose: Despite being the treatment of choice for clinically-significant Obstructive Sleep Apnea (OSA), adherence to Positive Airway Pressure (PAP) therapy is poor. We conducted a retrospective longitudinal observational study to evaluate the association between selected factors and PAP adherence.

Methods: We considered all consented individuals diagnosed with OSA who purchased a PAP device from a registered Assistive Device Program Vendor (Ottawa, Ontario) between 2011 and 2017, and who had data available on PAP adherence measured objectively as PAP use for at least 4 hours on at least 70% of days on treatment. We used logistic regression to address our research objective.

Results: 11,634 of 12,014 considered individuals (96.8%) were included in our analysis: median age of 53 years, 59% men, median BMI of 31 kg/m2, median apnea-hypopnea index of 21 events per hour, and median minimum nocturnal O2 saturation (SaO2 min) of 85% prior to treatment initiation. 61.5% (7,147/11,614) of these participants were adherent to PAP treatment over a median PAP usage period of 330 days.
Increased BMI (OR [odds ratio] per SD [standard deviation] of 1.16; 1.05-1.29), older age (OR per SD of 1.16; 1.06-1.27), and lower SaO2 min (OR per SD of 0.89; 0.80-0.99) were associated with increased odds of PAP treatment adherence controlling for type of PAP treatment, sex, and respiratory disturbance index.

Conclusion: There are easily obtainable factors which predict adherence to PAP therapy. Physicians should utilize these factors to identify which patients may need more encouragement or resources in order to remain adherent to treatment.

Receptiveness to Participating in Cannabis Research in Pregnancy: A Survey Study at The Ottawa Hospital

Bombay, K [1], Murphy, MSQ [1], Denize, KM [1], Cantin, C [2,3], McGee, A [4], Rennicks-White, R [1], Wen, SW [1,5,6], Walker, M [1,5,6,7,8], Corsi, D [1,6,8,9]

[1]OMNI Research Group, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada, [2]Champlain Maternal Newborn Regional Program, Ottawa, Canada, [3]Ottawa Hospital Research Institute, Ottawa, Canada, [4]Department of Midwifery, The Ottawa Hospital, Ottawa, Canada, [5]Department of Obstetrics and Gynecology, University of Ottawa, Ottawa, Canada, [6]School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada, [7]Department of Obstetrics, Gynecology & Newborn Care, The Ottawa Hospital, Ottawa, Canada, [8]BORN Ontario, Children's Hospital of Eastern Ontario, Ottawa, Canada, [9]CHEO Research Institute, Ottawa, Canada

ABSTRACT

Background: Hematologic cancers are a leading cause of cancer deaths. While most patients wish to die at home, most do not for several reasons including uneven palliative care access, rapid clinical deterioration and more aggressive treatment at end of life. To date, there has been no analysis of end of life care of patients with hematologic malignancy at The Ottawa Hospital.

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Conclusion: The majority of hematologic malignancy patients die in hospital and despite representing primarily expected deaths, they still receive aggressive care. Multivariate analysis will be conducted to elucidate predictors of in-hospital deaths.

Judgement Day: Exploring the Long-Term Implications of an Unsuccessful or Disappointing Canadian Residency Matching Service (CaRMS) Match

Mian, O [1], Wood, T [2], Scowcroft, K [2], Halman, S [3], Taylor, T [4,5], LaDonna, K [2]

[1]Faculty of Medicine, University of Ottawa, [2]Department of Innovation in Medical Education, Faculty of Medicine, University of Ottawa, [3]Division of General Internal Medicine, The Ottawa Hospital – General Campus, [4]Centre for Education Research & Innovation, Western University, [5]Department of Obstetrics & Gynaecology, Western University

ABSTRACT

Background: "Match day" is the day in which medical students discover which residency program they will be attending upon graduation. Ideally, all students would match but in 2019, 372 Canadian medical students did not match to their preferred program and some did not match at all. The consequences of a disappointing match are wide ranging and potentially long-lasting, yet we know little about how this experience impacts student well-being across their careers.

Objective: To understand the long-term impact of a disappointing match and identify strategies to better support individuals during CaRMS and its aftermath.

Methods: To date, 4 of 20 residents have participated in semi-structured interviews. All had experienced a disappointing match. Preliminary themes were identified during the initial coding stage of Constructivist grounded theory.

Results: Although match results were initially upsetting, participants described feeling satisfied with their alternate career path. Additional training, family support, and having "an optimistic perspective" were reported as being integral. However, some experienced lingering embarrassment, worrying they'd be perceived as less competent if faculty supervisors or peers knew about their match outcome. Participants speculated that the emotional repercussions of an unsuccessful match might have been avoided if they had been coached to make strategic decisions by considering multiple paths for success.

Conclusion: While additional data collection and analysis will generate a richer understanding, these findings uncover the long-term effects of a disappointing match, both revealing an under-explored dimension of factors impacting well-being for physicians and physicians-in-training and providing a starting point for strategizing match-related supports.

Outcomes from the First Year of Ottawa Inner City Health's Managed Opioid Program (MOP)

Seliga, R [1], Harris, M [2,3], Turnbull, J [4,5]

[1]Faculty of Medicine, University of Ottawa, [2]Grayken Centre for Addiction, Boston Medical Centre, [3]Department of Medicine Boston University, McGill University, [4]The Ottawa Hospital, [5]Ottawa Inner City Health

ABSTRACT

Background: Persons' experiencing homelessness, with severe opioid use disorder refractory to oral opioid agonist therapy, and frequent overdoses were eligible for Ottawa's Managed Opioid Program (MOP), where they were prescribed injectable hydromorphone and either long-acting oral hydromorphone or slow release oral morphine in a residential setting.

Objective: To describe changes in persistent non-prescribed opioid use and intravenous drug use (IVDU)-related complications, and secondarily to describe physical and mental health service connection, and social and personal development milestones.

Methods: Participants enrolled and retained for 12 months between August 2017-2018 (n=20) were included in this retrospective cohort study. Data were collected via chart review at enrolment and longitudinally every three months for the study-period. Non-prescribed opioid use, IVDU complications (skin and soft tissue infections, bacteremia, and sequelae), overdose, health service connection, and personal/social progress milestones (connecting with family, starting school/work/volunteering) were defined by events noted in clinical team charting. Descriptive statistics were used to summarize findings.

Results: After one year in the program, 45% of participants abstained from using non-prescribed opioids in the last three months. Between 25-35% of participants experienced IVDU-related complications per three month period, 100% of which were rapidly identified and treated. Fifty-five percent reported no overdoses throughout the year. All participants were connected with physical and mental health services. Fifty percent reconnected with family, and 40% engaged in school, work, or volunteering.

Conclusions: MOP participants had a marked reduction in non-prescribed opioid use and overdose events, and many achieved significant personal development milestones.

An Assessment of the Efficacy of Searching in Biomedical Databases Beyond MEDLINE in Identifying Randomized Controlled Trials on Hyperbaric Oxygen Therapy for Systematic Reviews

Boet, S [1,2], Burns, J [2], Khan, H [2,3], Etherington, N [2], Ahmed, R [4], Begunova, L [5], Calderon, LM [6], Campbell, C [4], Mansour, F [6], Maximous, R [6], Rowe, J [6], Said, H [6], Davis, AS [7]

[1]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, [2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, [3]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, [4]Department of Health Sciences, Faculty of Health Sciences, Carleton University, [5]Department of Psychological and Brain Sciences, Dartmouth College, [6]Faculty of Medicine, University of Ottawa, [7]Learning Services, The Ottawa Hospital

ABSTRACT

Background: As the research field of hyperbaric oxygen therapy (HBOT) continues to grow, it is necessary to determine best practices for conducting comprehensive literature searches. Using more than one database is generally recommended but may not always be necessary for some fields. This study aimed to determine the added value of searching additional databases beyond Medline when conducting a literature search of HBOT randomized controlled trials (RCTs).

Methods: RCTs in the HBOT field were identified via a scoping review following the PRISMA-ScR checklist. Medline and Embase (via OVID), CENTRAL, and CINAHL were searched without date or language restrictions. Screening and data extraction were conducted in duplicate by two independent reviewers. Included RCTs involved human subjects, clinical or simulated settings, and at least one HBOT, offered either on its own or in combination with other treatments. The comparator was defined as no HBOT or a different protocol of HBOT.

Results: The literature search identified 2429 different citations, of which 476 RCTs were eligible for inclusion. About 67.2% of the included studies were uniquely identified by Medline, 8.6% by EMBASE, 6.5% by Cochrane, and 14.1% by CINAHL. Only one study was identified by a combination of two databases that did not contain Medline. The Medline search strategy had the highest relative recall (70.6%), was the most sensitive (70.6%) and precise (35.9%), requiring only about 3 papers to be screened to find one relevant paper (NNR=2.8).

Conclusions: Searching Medline alone is not adequate for HBOT systematic reviews..

MedExpo: A Medical Education Outreach Program

Hughes-Visentin, A [1], Kundapur, D [1]; Kandiah, T [1], Ramnanan, C [2]

[1]Faculty of Medicine, University of Ottawa.
[2]Faculty of Medicine, Department of Innovation in Medical Education, University of Ottawa, Ottawa, Ontario, Canada

ABSTRACT

Medical School Exposed (MedExpo) is an outreach program that aims to provide valuable teaching experience to medical students while engaging high school learners in interactive medical school-relevant activities such as cadaveric anatomy laboratory sessions, clinical use of point-of-care ultrasound (PoCUS), and the assessment of vital signs. To address whether the activities in MedExpo effectively results in long-term knowledge retention, we surveyed high school participants at different time points to assess their understanding of the major topics discussed (anatomy, PoCUS, and vital signs). 218 high school students (from 7 different high school visits) participated in MedExpo and completed identical quizzes pre-session (n=218), post-session (n=218), and three months post-session (n=116). Average post-session quiz scores (82%) were significantly higher than average pre-session survey scores (58%) ($p<0.001$), and post-session quiz scores were 30%, 18%, and 25% higher for individual PoCUS, anatomy, and vital sign components, respectively, as well ($p<0.001$). While this increase in knowledge did wane when assessed three months post-session, quiz scores at this relatively long-term time point still remained significantly elevated relative to pre-session quiz performance, in all three areas ($p<0.01$). Our findings indicate that MedExpo can positively impact high school student knowledge well beyond the outreach sessions themselves, resulting in long-term retention. This suggests that incorporating formative assessments in science outreach programs may be valuable to participants. As MedExpo continues to grow, further study is warranted to determine whether differences in teaching approach (student-centered vs. didactic) can further impact students' long-term knowledge retention.

Un Guide à L'injection Intra-Articulaire Glèno-Humérale Guidée Par Ultrasons (IAGHGU)

Ragusa, M [1], Youssef, N [2], Fotsing, S [2], Jalali, A

[1]Faculty of Medicine, University of Ottawa
[2]Faculty of Medicine, Department of Innovation in Medical Education (DIME), University of Ottawa

ABSTRACT

Objectifs: L'échographie est un outil indispensable à la pratique médicale d'autant pour le diagnostic, les procédures et le traitement des pathologies. Cette technologie est accessible, portable, non invasive, peu coûteuse, non irradiante. Les étudiants en médecine manquent souvent de formation en ultrasons et les procédures guidées par ultrasons. Les facultés de médecine n'ont pas de composante curriculaire portant sur les procédures échoguidées dont l'injection intra-articulaire. Le but de ce projet de recherche est d'explorer l'efficacité, les indications et les techniques d'injection intra-articulaire gleno-humérale guidée par ultrasons (IAGHGU).

Méthode: Une revue narrative de la littérature fut complétée en juin 2020 en cherchant dans les bases de données PubMed, Education source et ProQuest ainsi que la littérature grise. Les mots clés ont été regroupés en thèmes: education medicale; articulation de l'épaule; injection échoguidée et lignes directrices.

Résultats: Les IGHGU sont sécuritaires et plus efficaces que la technique guidée par repère anatomique, respectivement 93% versus 30-70%. Les indications incluent l'arthrose, l'arthrite rhumatoïde, la capsulite adhésive et le syndrome de la coiffe des rotateurs (intra-articulaire). Les techniques d'apprentissage consistent de sessions didactiques et de sessions pratiques utilisant des modèles animal, cadavérique ou synthétique humain. Il existe 2 techniques et approches aux IGHGU. Les techniques en trainée de la sonde et en battement de la sonde font allusion au placement relatif de l'aiguille et la sonde d'ultrason. Les approches antérieures et postérieures se réfèrent au site d'injection. L'approche postérieure avec technique en trainée de la sonde est préférée.

Conclusion: Cette revue de la littérature à permis de regrouper l'information importante concernant les IGHGU. Une version préliminaire d'un livret guide sur les IGHGU a été créé afin de faciliter l'apprentissage des étudiants en médecine. Les prochaines étapes consistent à publier et disséminer ce livret aux étudiants en médecine ainsi qu'à évaluer l'utilité du livret pour l'enseignement des IGHGU à travers une étude de modèle classe inversées.

The Impact of Physician Sex/Gender on Operative Collaboration and Patient Outcomes in Cardiac Surgery: A Systematic Literature Review

Etherington, N [1,2], Deng, M [3,5], Boet, S [1,2,3], Johnston, A [4], Mansour, F [2], Said, H [3], Zheng, K [3,5], Sun, L [5,6]

[1]Clinical Epidemiology Program, The Ottawa Hospital Research Institute, [2]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, [3]Faculty of Medicine, University of Ottawa, [4]Cardiovascular Research Methods Centre, University of Ottawa Heart Institute, [5]Division of Cardiac Anesthesiology, Department of Anesthesiology and Pain Medicine, University of Ottawa Heart Institute, [6]School of Epidemiology and Public Health, University of Ottawa

ABSTRACT

Purpose: Evidence suggests that physician sex and gender influence processes of care and outcomes in non-cardiac medical and surgical care, as well as in primary cardiac care. The purpose of this systematic review is to identify peer-reviewed studies that investigate the implications of physician sex/gender in cardiac surgery.

Methods: Quantitative studies of any design involving patients undergoing a cardiac surgical procedure with anaesthetic care, and specifically assessed differences in processes of care or clinical patient outcomes by anaesthesiologist and/or surgeon sex or gender. Searches were conducted in PsycINFO, Embase, and Medline from inception to September 6th, 2018.

Results: 2095 publications were eligible for inclusion. Two English quantitative articles indirectly assessing the impact of physician sex or gender in cardiothoracic surgery were included in our systematic review. A recent retrospective cohort study of 25 cardiac and non-cardiac surgical procedures performed in Ontario, Canada suggests that patients treated by female surgeons compared to male surgeons had a lower 30-day mortality. Conversely, an observational study in the United States collected data from 20 types of surgeries, including five common cardiac procedures, and concluded that postoperative death during hospital admission or within 30 days post-operation was comparable between male and female surgeons.

Conclusion: The limited data surrounding the impact of physician sex and/or gender on the outcomes of cardiac surgery inhibits drawing a robust conclusion at this time. This systematic review identified a knowledge gap and our findings highlight the need for primary research to determine how these factors may influence cardiac operative practice.

Élaboration D'une Capsule Éducative sur les Soins de Longue Surée pour Résidents et Étudiants en Médecine

Lavigne, V [1], Joanisse, J [1,2,3]

[1]Faculté de médecine, Université d'Ottawa
[2]Institut du Savoir Montfort
[3]Hôpital Montfort

ABSTRACT

Introduction: L'espérance de vie au Canada augmente régulièrement, et avec la croissance de la population âgée vient l'inévitable besoin d'un plus grand nombre de soignants et de soins de santé adaptés aux personnes âgées. Cependant, il semble y avoir un manque de ressources en français, ainsi qu'une lacune dans le cursus médical en ce qui concerne ce qui est enseigné aux étudiants sur les soins de longue durée (SLD). Ce projet vise à découvrir quel type d'informations pourrait être inclus dans une capsule éducative destinée aux étudiants et aux résidents qui se rendent en milieu résidentiel ou en SLD.

Méthods: Revue de la littérature actuelle et révision des objectifs d'apprentissages des programmes d'études liés aux soins aux personnes âgées. Des entretiens téléphoniques ont été menés avec les précepteurs et des questionnaires en lignes pour étudiants, résidents et précepteurs ont été distribués. Une capsule éducative sera éventuellement créée avec les informations recueillies.

Résultants: Nos données suggèrent que les étudiants et les résidents pourraient bénéficier d'une formation complémentaire en SLD. Notamment sur les rôles et les responsabilités des médecins, la prise en charge des patients ainsi que les différents membres de l'équipe de soins dans ces milieux, parmi bien d'autres.

Conclusion: Une capsule éducative pourrait permettre de mieux préparer les étudiants à des stages dans ces milieux, ainsi que de les aider à envisager une carrière incluant cette population. En outre, cette formation supplémentaire pourrait soutenir davantage les précepteurs et les encourager à recevoir des apprenants dans des milieux résidentiels ou SLD.

Effet de la COVID-19 sur L'expérience Académique et Personnelle des Résidents

Pitre, L [1], Pomerleau, M [1], Cipro, M [2]

[1]Département de médecine familiale, Hôpital Montfort
[2]Faculté de médecine, Université d'Ottawa

ABSTRACT

Contexte: La pandémie engendrée par le SARS-CoV-2 est une expérience déstabilisante pour les étudiants en médecine et les médecins-résidents. Elle trouble surtout le déroulement de leur formation en milieu hospitalier. Ce projet vise à identifier l'effet d'épidémies et de pandémies antérieures sur la vie académique et personnelle des résidents et à élaborer des solutions d'encadrement de ces derniers.

Méthodes: Les bases de données EducationSource, MedLine et PsychInfo ont été consultées afin d'identifier les articles qui expliquent l'effet du SARS-CoV-1 (2002), du SARS-CoV-2 (en cours) ou du A/H1N1 (2009) sur les apprenants en médecine. Des 94 manuscrits générés, 15 ont été retenus et révisés qualitativement.

Résultats: Au niveau académique, les apprenants considèrent leur éducation compromise, notamment par les délais encourus dans le déroulement des rotations et des examens ainsi que par la suspension des activités académiques et des chirurgies électives. Sur le plan personnel, il ressort que leur santé mentale est altérée par l'anxiété associée à cette perturbation académique et à la distanciation sociale imposée, par la peur liée au risque d'infection de proches, et par la prévalence d'épuisement professionnel et de dépression enflée par le fardeau de travail hissé. Des pistes de solutions allant de l'accès continu à des soins de santé mentale et au suivi rigoureux des résidents quant à leur bien-être global pourraient améliorer leur expérience.

Conclusion: Il serait intéressant d'apprécier l'effet de la COVID-19 sur la vie académique et personnelle des résidents de l'Hôpital Montfort. Un sondage à cet effet est en cours.

Trends in Neurosurgery: Increased Academic Qualifications and Increased Female Representation

Malvea, A [1], Yan, C [1], Nguyen, L [1], Beaudry-Richard, A [1], Tsai, E [2]

[1]Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
[2]Division of Neurosurgery, Department of Surgery, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada

ABSTRACT

Introduction: Rapid growth and advancements in neurosurgery warrant exploration of current demographics and trends in career outcomes. This study serves to investigate said trends for the purpose of informing hopeful medical students and residents of the qualifications required for a career as a neurosurgeon.

Methods: A list of currently practicing neurosurgeons in Canada was created by using active membership status in provincial colleges and status on faculty webpages. Information on certification year, additional degrees, fellowship training, leadership positions, teaching positions was collected using publicly available information and surgeon confirmation.

Results: Two-hundred and ninety-six neurosurgeons are currently practicing in Canada (F=32, M=264). Today, 46% of neurosurgeons have at least one additional (61% - Master's, 45% - PhD). In each 5-year certification period between 1970 and 1989 15 - 25% of neurosurgeons had at least one additional degree and 0 - 62% had obtained fellowship training. Between 2000 and 2019, 50 – 67% had an additional degree and 77 – 89% had obtained fellowship training. Overall, the most common fellowship training is spine surgery (26% of fellowship trainees pursued spine surgery). The most common fellowship training(s) among females were paediatrics and cerebrovascular neurosurgery with 29 % of female fellowship trainees pursuing each of the fellowships. Among males, spine surgery was pursued by 28% of male fellowship trainees.

Conclusions: There appears to be a trend towards obtaining additional degrees and fellowships overtime. Gender based trends may also exist, statistical significance is yet to be elicited - however, the number of female neurosurgeons is increasing over time.

Adult Skills Development and Training

Welch, V [1], Mathew, C [1], Manhaes Marins, L [2], Ghogomu, E [1], Dowling, S [1], Abdisalam, S [1], Madani, M [1], Murphy, E [1], Kebedom, K [1], Ogborogu, J [1], Gallagher-Mackay, K [2]

[1]Bruyère Research Institute
[2]Future Skills Centre - Centre de Compétences futures

ABSTRACT

Background: Human capital is an important component for economic development. In the current global pandemic of COVID-19, unemployment is a problem now more than ever. The UN has suggested that skills development may be a part of policy response to COVID-19.

Objective: The objective was to identify primary studies and systematic reviews on adult skills development and training in high income countries.

Methods: We searched 12 electronic social science databases (e.g. EconLit, PsycINFO) from 2000 up to March 15, 2020. We screened in duplicate for inclusion and coded according to an interventions and outcomes framework developed with stakeholders. We appraised the quality of systematic reviews using AMSTAR2.

Results: The search yielded 11,069 records, of which 413 primary studies and 64 systematic reviews were included. The most commonly assessed skills development approach was career pathway guidance (60%), such as resume support and job search assistance for those who are unemployed followed by training in specific technical skills (59%), social-emotional skills training (50%) and work experience (44%). Less commonly assessed skills were provision of wraparound support (36%), financial incentives (34%), and training in digital skills (10%). In terms of outcomes, the most commonly assessed were employment (83%) and earnings (38%), followed by individual well-being and skills gains (22%). Few studies assessed civic engagement (2%), or employer outcomes such as hire satisfaction (0.2%) and retention (0.4%).

Conclusions: This evidence and gap map can help decision-makers find evidence on skills development and training quickly to inform decisions and research investments within a post-COVID-19 context.

Dealing with Missing Data in Medical Research – The Impact of Multiple Imputation

Malek, J [1], Warnet, C [1], Dahrouge S [1]

[1]Bruyere Research Institute

ABSTRACT

Background: Studies that rely on surveys or existing data (e.g. EMR) commonly have missing information. Cases with missing data are automatically removed in multi-variate analyses. We provide an example of the use of Multiple Imputation (MI) to complete missing data. MI creates multiple records with "plausible" values for missing data. We report on the impact of imputing data on results.

Methods: We analyzed survey data from a randomized controlled trial of 326 patients comparing two navigation services (Access to Resources in the Community (ARC) and Ontario 211) in helping individuals access community resources. While only 3.3% of the data was missing, 39.6% of the cases had at least one piece of missing data. The variable with most (14%) missing data was "race." We used SPSS to create 14 multiple imputed datasets. We regressed the original and imputed data on the study outcome (Access: having accessed at least one community resource) and compared the odds ratio (OR) to assess whether the imputation changed the estimated effect size of the variable.

Results: The relative difference in the ORs (OR imputed/OR non-imputed) was negligible (<0.5%) for (Missing data) occupation (0.9%), having depression (5.5%), and living alone (6%); modest (2 %-7%) for education level (0.6%), marital status (7.1%), and Financial situation (8.3%); high (21%) for race (14%).

Conclusions: MI is required to avoid bias resulting from excluding cases with missing data. However, the potential impact of the uncertainty in the imputed data can be meaningful and can reduce the confidence in the result interpretation.

Investiagting the Role of EnaH In Melanoma Cell Invasion

Mourcos, C [1], Copeland, S [2], Copeland, J [1,2]

[1]Translational and Molecular Medicine, University of Ottawa
[2]Department of Cellular and Molecular Medicine, University of Ottawa

ABSTRACT

Background: Urinary tract injuries are severe complications of hysterectomy. Our objective is to determine the risk factors associated with urologic injury in women undergoing hysterectomy for benign indication.

Methods: A retrospective cohort study (2011-2017) was conducted using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). Women without urologic injury were compared to women with injury, and multivariate logistic regression models were constructed to control for patient demographics and intraoperative variables.

Results: Among 213,980 women who underwent hysterectomy for benign indication, the rate of urologic injury rate was low (0.6%). The majority of injuries involved the bladder (86.2%); 13.8% involved the ureters. Younger age, lower BMI and abdominal hysterectomy were associated with increased injury. Patients who underwent total hysterectomy had increased odds of urologic injury compared to subtotal (adjusted OR 1.54, 95%CI [1.23-1.93]). Patients with Class III obesity had decreased odds of injury compared with patients of normal weight (AOR 0.70, 95%CI [0.55-0.89]). An interaction was observed between surgical approach and indication for hysterectomy. Abdominal compared to laparoscopic approach was associated with urologic injury for women with endometriosis (AOR 3.67, 95%CI [2.35-5.72]), pelvic pain (AOR 4.36, 95%CI [2.06-9.26]), menstrual disorders (AOR 5.71, 95%CI [2.15-15.2]), and fibroids (AOR 2.17, 95%CI [1.59-2.96]). Vaginal compared to laparoscopic approach was associated with increased odds of injury for women with endometriosis (AOR 2.25, 95%CI [1.16-4.40]), menstrual disorders (AOR 14.4, 95%CI [2.28-91.6]), and pain (AOR 54.99, 95%CI [1.24-20.1]). Iatrogenic urologic injury was associated with increased healthcare utilization.

Conclusion: While the risk of urologic injury during hysterectomy for benign indication is low, the risk is dependent on certain patient disease factors and surgical approach.

Histoire de L'éducation Médicale en Français à L'Université d'Ottawa

Mélodie Vermette[1], Susan Lamb[2]

[1]Faculté de Médecine, Université d'Ottawa, Ottawa, ON, K1H 8M5, [2]Chaire Jason A. Hannah, de l'histoire de la médecine, Faculté de Médecine, Université d'Ottawa

ABSTRACT

Contexte: Au cours des dernières décennies, la formation médicale dans le monde s'est largement déroulée en anglais, y compris dans des pays où ce n'est pas la langue de la majorité. La Faculté de médecine de l'Université d'Ottawa fait exception à cette règle, car ce n'est qu'en 1999 qu'elle a ajouté un volet français à son programme d'anglais déjà établi. Cet ajout a été largement rendu possible par la création du BAF1 et du CNFS2, tous deux ayant pour objectif d'améliorer l'accès aux services de santé en français pour les francophones en milieu minoritaire. L'importance de cette filière a été mise en évidence lors du SOS Montfort, ainsi que les luttes que de nombreux francophones vivant en milieu minoritaire ont à essayer d'accéder aux services de santé en français. Le CNFS a contribué à régler ce problème en réservant des places aux étudiants francophones issus de la minorité française dans le but qu'ils retournent exercer dans ces communautés.

Méthodes: Des bases de données en ligne et des documents partagés ont été utilisés pour le contexte historique de l'enseignement de l'Université d'Ottawa, du CNFS, du BAF et de la langue de la minorité. Celles-ci comprenaient des revues scientifiques et des articles de journaux, des annuaires, des rapports et des enquêtes, ainsi que des sources primaires et secondaires.

Conclusions: Les défis qu'ont éprouvés la communauté franco-ontarienne ont permis au développement d'un programme de médecine complètement français à l'Université d'Ottawa.

Conception d'une Application Médicale Sur L'imagerie Cardiaque en Contexte Pédagogique et Clinique : Phase 1

Saint-Georges, Z [1,2], Gobeil Odai, K [1], Viltakis, R [1], Fisher, S [1], Tuominen, L [2], Denis-Leblanc, M [1,3], Chamoun, C [3], Hafez, N [3], Fotsing, S [1,3], Nicole, M [1,3]

[1]Faculté de médecine, Université d'Ottawa, [2]L'institut de recherche en santé mental du Royal, [3]Institut du Savoir Montfort

ABSTRACT

Contexte: Les avancées technologiques en imagerie cardiaque ont révolutionné le diagnostic ainsi que la gestion des pathologies cardiaques et exigent continuellement une plus grande expertise de la part des étudiants en médecine et des médecins. Conséquemment, plusieurs ressources anglophones sont aujourd'hui disponibles, tandis qu'il y a un manque de ressources francophones. L'objectif de la phase 1 de ce projet était de faire la recension des usages actuels d'imageries cardiaques, dans le but de bâtir un manuel exhaustif sur l'usage de l'imagerie en cardiologie qui servira de fondation à la création d'une application médicale.

Méthodologie: Revue narrative des usages d'imageries en cardiologie et synthèse thématique pour chaque modalité d'imagerie selon chaque condition médicale cardiaque commune. Préalablement, les plus récents livres spécialisés d'imagerie cardiaques ont été consultés, ensuite, des recherches quasi-systématiques ont été faite sur PubMed suivant des mots clés suggérés par un groupe d'experts médecins spécialistes en cardiologie.

Résultats: La synthèse thématique résultante rapporte que l'échocardiographie, la radiographie et la tomodensitométrie, l'imagerie nucléaire et la résonance magnétique jouent un rôle indispensable en cardiologie. Un manuel a été rédigé en réconciliant l'ensemble des thèmes émergeant de notre analyse.

Conclusion: L'analyse thématique démontre une grande complexité d'utilisation de l'imagerie en cardiologie et cette dernière justifie la conception d'une application médicale ciblant les étudiants et médecins francophones. Le manuel est en cours de révision par le groupe d'experts et devrait servir de base à la conception d'une application mobile médicale dans la prochaine étape de ce projet.

Quels Sont les Facteurs Influençant la Rétention des Gradués du Programme de Médecine Familiale Comme Hospitalistes à L'Hôpital Montfort?

Pomerleau, M [1], Taki, J [2]

[1]Médecine familiale, Hôpital Montfort, Ottawa, Ontario, Canada
[2]Faculté de médecine, Université d'Ottawa, Ottawa, Ontario, Canada

ABSTRACT

Contexte: L'intérêt pour la médecine hospitalière est remarquable à l'Hôpital Montfort. Nous cherchons à identifier les facteurs influençant le choix de pratiquer la médecine hospitalière et de comprendre si leurs expériences lors de la résidence a un impact sur leur choix de carrière. Une revue systématique de littérature a été conduite.

Méthodes: Les bases de données Medline (Ovid) et PubMed ont été utilisées. 20 résultats ont été obtenus et 11 articles ont été analysés.

Résultats: Parmi les étudiants gradués qui ont continué leur travail en médecine familiale, ces derniers ont identifié que le fait qu'ils voulaient rendre service aux autres, qu'ils désiraient offrir des soins exhaustifs à leurs patients et qu'ils pouvaient travailler en petite communauté représentaient quelques raisons pour justifier leur décision de demeurer en médecine familiale (3). 49% des résidents en médecine interne qui ont répondu à un sondage ont noté que la présence de défis et le large éventail de cas cliniques qui se présentaient aux soins aigus généraux sont des éléments qui les captivent envers la médecine hospitalière (2). 97% des 98 résidents ont identifié les possibilités de jouer un rôle en éducation et 94% des 98 étaient en accord que les hospitalistes en pédiatrie étaient mieux rémunérés que les médecins en soins primaires (1).

Conclusions: Nous planifions vérifier les intérêts motivant les hospitalistes ainsi que les résidents en médecine familiale de Montfort à pratiquer la médecine hospitalière. La cueillette des données via deux sondages est en cours pour ces populations.

Nombre de mots: 245

Validation and Pilot Testing of an Asthma Knowledge Questionnaire for Children & Caregivers

Kotrri, E [1]; Thipse, M [2]; Higginson, A [3]; Radhakrishnan, D [4,5]

[1]Faculty of Medicine, University of Ottawa, [2]Children's Hospital of Eastern Ontario (CHEO), [3]Children's Hospital of Eastern Ontario (CHEO), [4]Children's Hospital of Eastern Ontario (CHEO), [5]Department of Pediatrics, University of Ottawa

ABSTRACT

Background: Previous questionnaires that have been developed to measure asthma knowledge among children with asthma and their caregivers are outdated and/or have not been well validated.

Objective: We aimed to develop, validate and pilot test a new tool for measuring asthma knowledge of caregivers of children with asthma, and adolescents with asthma.

Methods: We used 3 previously validated asthma knowledge questionnaires to develop our tool, which was assessed for face validity by our study team and asthma experts. Our next steps are to further test the questionnaire for its face validity and reliability among a group of asthma patients/caregivers, then to measure responsiveness, or change in asthma knowledge in a pilot group of patients/caregivers before and after attending a CHEO asthma education session.

Results: The response rate for face validity testing was 100% among 8 asthma experts (2 nurses/asthma educators, 5 respirologists, 1 pediatrician). Responses of asthma experts were used to modify the tool and to ensure consistency of responses for all questions. An electronic version of the modified questionnaire has been successfully created and currently consists of 24 asthma knowledge questions, with additional sections on demographic information and asthma severity. For the subsequent stages of questionnaire validation, 20 patients/families representing a range of age groups have been identified for pilot testing.

Discussion: Once validated, this tool will help identify knowledge gaps in patients/caregivers admitted to CHEO for asthma exacerbations, and aid us in improving asthma management by addressing those gaps through our education interventions.

Side by Side: Evaluation and Improvement of a Peer Support Program for Medical Students

Shore, I [1], Haykal, K [1]

[1]Faculty of Medicine, University of Ottawa

ABSTRACT

Introduction: Burnout and mental illness are increasingly being recognized as challenges in medicine. Numerous studies have shown that medical students have higher rates of depression and suicidal ideation compared to the general population, and that mental health deteriorates over the course of medical school. Side by Side is a peer support program that was created at the Faculty of Medicine of the University of Ottawa. The goal of this program is to provide accessible and non-judgemental social support to medical students, delivered by peers with specialized training. The pilot year of the project ran from September 2019 to June 2020. The goal of this project was to assess the utilization of the program over the pilot year.

Methods: Peer support interactions were logged by Peer Supporters in an anonymized database, which was used to evaluate the nature and quantity of interactions.

Results: 34 Peer Supporters completed 303 interactions, with 25% being focused on mental health (n=76), 23% (n=69) being focused on academic concerns, and 29% (n=89) being proactive interactions where a peer supporter reached out to a peer to check in. Self-reported quality of interactions was 4.8/5. Approximately 49% (n=147) of interactions were in person, while 51% (n=156) were by phone or online messenger. Peer Supporters initiated 60% (n=159) of the interactions.

Conclusions: Peer Supporters provided support on multiple topics, including mental health and academic problems. Interactions were evenly distributed between in-person and online mediums, and interactions were more frequently initiated by a Peer Supporter than by students.

Facteurs Académiques et Non-Académiques Prédicteurs de la Performance en Résidence: Une Recension des Écrits

Bloomfield, S [1], Pomerleau, M [2], Haykal, K-H [1]

[1]Faculté de médecine, Université d'Ottawa
[2]Département de médecine familiale, Hôpital Montfort

ABSTRACT

Contexte: Certains résidents en médecine familiale dans le programme d'Ottawa ont démontré des défis de performance. Il serait intéressant d'effectuer une mise à jour des connaissances sur les facteurs prédicteurs de la performance afin d'identifier et d'appuyer les apprenants ayant besoin de plus de support.

Objectif: identifier les facteurs académiques et non-académiques qui pourraient prédire la performance au niveau de la résidence.

Méthodes: La base de données Pubmed a été utilisé afin d'identifier des articles pertinents publiés entre janvier 1975 à Juillet 2020. Les articles (53) retenus traitaient des facteurs prédicteurs de la performance en médecine et en résidence. Les mots clés utilisés étaient « résidence », « étude rétrospective », « performance académique », « compétence clinique » et « remédiation ». Le titre et le résumé de tous les résultats ont été examinés, ainsi que les références pour d'autres articles appropriés. Les articles complets ont ensuite été récupérés pour un examen plus approfondi si nécessaire.

Résultats: Parmi les facteurs académiques, les notes à l'admission en médecine peuvent prédire la performance aux examens en médecine, les notes durant les études en médecine peuvent prédire la performance aux examens en résidence et la performance aux ÉCOS peuvent prédire la performance clinique ultérieure. Pour ce qui est des facteurs non-académiques, un manque de professionnalisme lors des études médicales semble prédire un manque de professionnalisme en résidence.

Conclusion: Ces trouvailles suggèrent que certains facteurs académiques et non-académiques sont prédicteurs de la performance future en résidence.

Will My Patients Access the Community Resources I Recommend?

Sethuraman,S [1], Dahrouge, S [2]

[1]Faculty of Medicine, University of Ottawa
[2]Bruyere Research Institute

ABSTRACT

Introduction: Patients commonly face barriers (e.g. financial, literacy, motivation) accessing health enabling resources (HERs) recommended to them (e.g. diabetes education, smoking cessation). We used data from a study comparing two patient navigation services (1. Access to Resources in the Community (ARC): a face to face service embedded in primary care, and 2. Ontario 211: a web-based and telephone service) to identify the patient factors associated with access to HER when receiving navigation support.

Methods: Retrospective analytical study using baseline (patient profile) and 3 months post-intervention (Outcome: Access to > 1 HER) survey data for 326 patients. We performed bivariate and multivariate logistic regressions of patient factors on access to a HER (dependent variable).

Results: In bivariate analyses, factors associated with HER access (P<0.10) were (Odds Ratio, (95% Confidence Interval)): greater network support: 3.3 (1.1-10.1); university education*: 2.0(1.2-3.3), prior access to HERs *: 1.6 (1.0-2.6); French (+/- English) at home*: 2.2 (1.3-3.6); more needs for HERs*: 1.19(1.03-1.34); Living in Ottawa(vs Sudbury): 2.0 (1.2-3.5). P>0.10 for: Age, sex, immigration status, medical complexity, marital status, caregiving responsibilities, occupation.

In the multivariate analysis, starred (*) factors remained significant. When stratified by arm, only university education differed meaningfully between arms (211: 3.0 (1.4-6.4) – ARC: 1.7 (0.8-3.3)).

Conclusion: Several patient factors may influence an individual's ability to benefit from navigation services. Low education was strongly associated with poor access, but less so in the ARC arm, suggesting that the face to face navigation services embedded in primary care might mitigate the effect of that factor.