









PROGRAMME

CHAIR PERSON	PROFESSOR VALERIE SPEIRS
14:15 - 14:30	POSTER VIEWING START
14:30 - 14:35	INTRODUCTION BY PROF. RONA PATEY
14:35 - 14:55 14:35 - 14:45 14:45 - 14:55	INSPIRE INTERNATIONAL SCHOLARSHIP PRESENTATIONS MHARI MCGOWEN TIBERIU PANA
15:00 - 15:40 15:00 - 15:10 15:10 - 15:20 15:20 - 15:30 15:30 - 15:40	ASRS AND INSPIRE SCHOLARSHIP PRESENTATIONS RAMISHA BASHARAT ANNZELA D'COSTA ROSS LILLEY CHLOE HORSFALL
15:40 - 17:15	POSTER VIEWINGS AND REFRESHMENTS
17:15 - 17:45 17:15 - 17:25 17:25 - 17:35 17:35 - 17:45	ASRS & INSPIRE SCHOLARSHIP PRESENTATIONS JIE FEI LAU SAMANTHA GREEN SULEMAN RAHMAN SABIR
17:45 - 18:00	JUDGES DISCUSSION
18:00 - 18:15	ASRS PRIZES AND CLOSING REMARKS
18:15 - 19:00	REFRESHMENTS AND DRINK RECEPTION



ACKNOWLEDGEMENT

This abstract book contains an exciting collection of abstracts from wide range of research projects carried out by summer research scholarship students at the University of Aberdeen.

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Special thanks go to all students who submitted their work to share their research with the wider student community.



Prof. Phyo Kyaw Myint

INSPIRE Lead & Director of Clinical Academic Training and Development School of Medicine, Medical Sciences & Nutrition



MHAIRI MCGOWAN

Molecular mechanisms of Staphylococcus aureus resistance to a potential repurposed anti-bacterial compound

Background

Antimicrobial resistance (AMR) poses a major global health challenge. Treatment of *Staphylococcus aureus*, a potentially life-threatening human pathogen, is extremely difficult due to its resistance against most conventional antibiotics. It is therefore essential to establish alternative treatment options to combat this bacterium. Compound X, which is currently being developed as a potential anticancer drug, has been shown to have anti-bacterial properties against *S. aureus in vitro*, however the process by which it targets the bacteria is unknown. The aim of this research was therefore to gain insight into the molecular mechanisms of Compound X by identifying genes involved in its resistance.

Methods

This research was conducted in collaboration with the Medical Biotechnology Department of the University of Siena, Italy. The DNA of one wild type *S.aureus* strain and 3 mutant strains resistant to Compound X was extracted and purified using laboratory methods. State-of-the-art technology (GridION, Nanopore and Illumina) was then used to sequence the extracted DNA. The sequencing output was evaluated and filtered according to quality parameters using bioinformatic software. Further bioinformatic tools (Artemis, VarScan) and online databases were employed to assemble and annotate the genome in order to compare the *S.aureus* strains.

Progress to Date

Preliminary genomic analysis indicates that bacterial strains resistant to treatment with Compound X displayed a mutation in a gene associated with an efflux pump responsible for the removal of the environmental toxin, arsenic. Thus, it is hypothesised that this efflux pump may also remove Compound X from *S.aureus*, rendering it ineffective.

Expected Results

The potential anti-bacterial properties of Compound X may provide an alternative therapy to *S. aureus* infection. This project has generated preliminary evidence to indicate that Compound X resistance may be due to the presence of an arsenic efflux pump in the bacterial cell. Once genetic analysis is complete, future research should be aimed at establishing the efficacy of Compound X in a clinical setting.

Supervisors - Karolin Hijazi; Francesco Iannelli (Université di Siena)

Funded by - INSPIRE International Scholarship

TIBERIU PANA

Myocardial Regeneration in end-stage Heart Failure after Left Ventricular Unloading

Background

Murine studies have shown that decreased oxidative stress is associated with cell cycle re-entry and cell regeneration in the failing myocardium. The implantation of a Left Ventricular Assist Device (LVAD) may lead to a decrease in cardiomyocyte oxidative stress in humans by decreasing the mechanical work of the left ventricle, which relies on oxidative phosphorylation as a steady source of ATP. Therefore, we tested the hypothesis that LVAD implantation in patients with end-stage heart failure may be associated with myocardial regeneration in the long-term.

Methods

All patients aged 18-70 with end-stage dilated (DCM) or ischaemic cardiomyopathy (ICM) undergoing LVAD implantation between August 2016 and February 2018 at UT Southwestern Medical Center were invited to be enrolled in the study. Serial cardiac viability ¹8FDG-PET scans were performed at least 3 months after LVAD implantation and 6 monthly thereafter. Viable myocardium was defined as exhibiting ¹8FDG uptake of ≥50% of the maximum myocardial ¹8FDG uptake in the respective scan. The myocardial volumes were divided into 16 segments and the proportion of viable myocardium was compared between baseline and subsequent scans for each patient using a linear regression.

Results

A total of 5 patients were recruited into the study (1 ICM, 4 DCM). Two patients received a cardiac transplant within 12 months of LVAD implantation and underwent only 2 scans. The remaining patients underwent at least 3 scans. Only one patient exhibited a significant increase in viability between the baseline and the 6- month follow-up scan: percentage increase (95% confidence interval): 26.5 (13.4-39.6).

Conclusion

A modest increase in myocardial viability was seen in only 1 out of 5 patients over a follow-up of 6 months. Further studies on larger samples are required to determine whether clinically significant improvements in myocardial viability and function may be achieved after LVAD implantation.

Supervisors - Prof. Dana Dawson; Dr. Vlad Zaha (UT Southwestern Medical Center) **Funded by -** INSPIRE International Scholarship



RAMISHA BASHARAT

The role of specific Phosphoinositide 3-kinase (PI3K) isoforms in the proliferation and survival of head and neck cancer cell lines

Background

The PI3K/Akt pathway, which regulates cell growth and metabolism, is commonly mutated in head and neck cancer (HNC). Previous research has explored PI3K inhibition as a therapeutic target using pan-PI3K inhibitors. In T-cells, PI3K isoforms are shown to have differing roles in the regulation of immune cells, with inhibition of the PI3K- δ isoform being key in promoting anti-tumour immune responses. The role of specific PI3K isoforms in HNC has not been explored. This project aimed to investigate the effects of PI3K isoform inhibitors on the proliferation and viability of HNC cell lines.

Methods

Three HNC cell lines were used: Fadu, Cal27, and SCC154. These cell lines were cultured in the presence of isoform-specific PI3K inhibitors: Cal-101 (PI3K- δ inhibitor), A66 (PI3K- α inhibitor), TGX (PI3K- β inhibitor), pan- PI3K inhibitor GDC-0941 or the downstream pan-Akt inhibitor MK2206 for 48 hours. The inhibitors were used at concentrations previously optimized for T-cell inhibition. The cells were harvested and stained with Violet Cell Trace to evaluate proliferation. Viability was evaluated using 7AAD or DAPI staining. Flow cytometry data were collected using BD Fortessa. Data analysis was performed using Flow]o-10 software.

Results

The Violet Cell Trace assay showed no significant differences in proliferation between the isoform inhibitor treated cells and the control samples at the concentrations tested. No significant differences were observed in the proliferation of cells treated with the three PI3K isoform inhibitors or the pan-PI3K inhibitor. DAPI staining showed significant differences in viability between the pan-PI3K inhibitor GDC-0941 and control samples, but no differences were observed with the isoform specific inhibitors.

Conclusion

At the tested concentrations, the isoform-specific PI3K inhibitors showed no effect on proliferation or viability of the tested HNC cell lines. Further optimization of inhibitor concentrations and experimental conditions are required to understand the role of specific PI3K isoforms in these cell lines.

Supervisors - Dr. Rasha Abu Eid, Institute of Dentistry

Funded by - Future Leaders Award (CRANES), UoA Development Trust

ANNZELA D'COSTA

Recommendations regarding inter-pregnancy interval after miscarriage across international clinical practice guidelines: a systematic review

Background

The World Health Organisation recommends a six-month inter-pregnancy interval after miscarriage before conceiving again, based on one multicenter Latin-American observational study. Subsequent research instead proposes an inter-pregnancy interval below six months achieves better outcomes for mother and child. This systematic review intends to establish what clinical practice guidelines (CPGs) currently advise patients regarding when to conceive after miscarriage.

Methods

The following databases were searched for potential CPGs from May - August 2019: Google, Google Scholar, MEDLINE, EMBASE, PubMed. The search strategy included multiple search terms as no clear terminology is presently outlined. Potential CPGs from Google and Google Scholar were excluded at point of contact based on relevance and target user. Potential CPGs from MEDLINE, EMBASE and PubMed were screened for duplicates then excluded based on abstract for irrelevance and publication type. Remaining publications were excluded based on full-text analysis. The AGREE II tool was used to evaluate CPG quality.

Results

Fifteen CPGs from various international organisations were retrieved. Five CPGs provided no information on inter-pregnancy interval, the remaining CPGs provided varying recommendations: four recommended no delay, three recommended waiting at least six months and three recommended wait-times in between. NICE produced the highest rated CPG with a score of 84.2% and was the only CPG to achieve a score of >50% across six domains. CPGs recommending a delay of at least six months were chronologically created earliest (between 2005 – 2011) and had intermediate AGREE II scores. CPGs recommending no delay were all created between 2011 – 2019 and had the highest AGREE II scores overall

Conclusion

Despite the importance of advice regarding inter-pregnancy interval after miscarriage to clinicians and couples, CPGs differ greatly in the advice offered and is omitted entirely in some.

Supervisors - Dr. Sohinee Bhattacharya

Funded by - Aberdeen Summer Research Scholarship & Obstetrics Epidemiology Group

ROSS LILLEY

The Ageing Gut-Brain Project: exploring the role of the gut microbiota in dementia symptoms

Background

As our population ages, there is a continuing, inevitable increase in dementia-causing neurodegenerative diseases. The age-adjusted prevalence of dementia in Europeans over 65 is now 6.4%, with around 36 million people affected worldwide. Dementia is not limited to cognitive dysfunction: a majority (90%) of sufferers also experience 'Behavioural and Psychological Symptoms of Dementia (BPSD)'. These symptoms, which are detrimental to a patient's quality of life, include aggression, apathy, depression, mania, psychosis and agitation. Current management of these symptoms is conservative, has little benefit and may even increase mortality. A recent rise in research centred around the gut microbiota supports the presence of the microbiota-gut-brain axis. When the microbiota is modulated with nutritional interventions, it may improve BPSD.

Methods

To determine differences between the gut microbiota profiles of three cohorts, short chain fatty acid (SCFA) analysis and DNA sequencing were carried out. The three cohorts were: Alzheimer's Disease (AD) patients with no diagnosis of BPSD, AD patients with BPSD and a healthy control group, all as residents in a care home environment. Each participant provided two faecal samples for analysis in order to determine the within-subject variation. Ethical approval was obtained from the Scotland A REC and written, informed consent from residents or relatives was obtained.

Results

SCFA analysis to date has revealed relatively low within-subject variability of % SCFA profiles. Average percentages of acetate, propionate, butyrate, lactate, succinate in sample 1 were: 67, 19, 11, 0, 2%

respectively, compared to 68, 18, 12, 0, 1% in sample 2. In comparison, there was large between-subject variability, ranging from 4-10% (expressed as a SD of SCFA%). The SCFA patterns also differ from healthy adults.

Conclusion

Any differences in the abundance and diversity of the gut microbiota of participant groups will be revealed with completion of SCFA analysis and DNA sequencing to inform future intervention studies.

Supervisors - Prof. Alexandra Johnstone; Dr. Karen Scott; Prof. Phyo K Myint; Dr. Roy Soiza **Funded by -** INSPIRE Interdisciplinary Scholarship Scheme, Tenovus Scotland

ROSS LILLEY

Probiotic, prebiotic and synbiotic supplementation for the treatment of cognitive, behavioural and psychological symptoms in neurodegenerative diseases

Background

Dementia and its associated cognitive and 'Behavioural and Psychological Symptoms' (BPSD) have a significant impact on both patient and caregiver quality of life. Current treatments for dementia-causing neurodegenerative diseases offer only conservative management and some, like antipsychotics, increase mortality. With the growing prevalence of dementia (now affecting 6.4% of Europeans over 65), a new, safe way to manage these conditions is gravely needed. A recent boom in research supports the presence of the gut-brain axis. Modulating the gut microbiota with supplements such as prebiotics, probiotics and synbiotics may help improve dementia symptoms via this pathway.

Methods

A systematic review is being carried out to determine the effect of probiotics, prebiotics and synbiotics on the cognitive, behavioural and psychological symptoms of adults with dementia. MEDLINE, Embase, PsycINFO, CAB abstracts and Cochrane Databases were searched up to July 2019. Three reviewers independently screened titles and abstracts in order to isolate eligible randomised control trials or observational studies with a suitable control group. Shortlisting and data extraction were carried out independently by three researchers.

Progress to Date

The search of databases produced 4268 titles, of which 18 were selected for full-text review. Six randomised control trials involving a total of 381 participants (mean age 63.6, 74% female) met all inclusion criteria. Data extraction has been carried out on these studies using a tool for consistency. Next, a risk of bias assessment will be carried out using The Cochrane Collaboration risk of bias tool. Should meta-analysis be possible; effect sizes between similar outcomes will be determined.

Expected Outcome

As the evidence-base is small, it is currently not possible to speculate on outcomes. The authors intend to publish this systematic review in a scientific journal.

Supervisors - Prof. Phyo K Myint; Dr. Roy Soiza; Prof. Alexandra Johnstone; Dr. Karen Scott **Funded by -** INSPIRE Interdisciplinary Scholarship Scheme

CHLOE HORSFALL

The effectiveness of digital prep-analysis technology in teaching dental clinical skills: A Systematic Review of the Literature

Background

The future dental workforce is currently being trained to take care of all our oral needs, past, present and future. Undergraduate students are educated using mostly conventional methods of teaching. However, today some university courses on clinical skills, such as crown preparation, are taught using various technology-based preparation analysis systems. They offer more interactive and accessible ways for students to learn and assess their progress. The aim of this systematic review of published literature was to compare the effectiveness of digital technology-based systems with conventional teaching methods in clinical skills teaching.

Methods

A systematic search of PubMed, MEDLINE, Scopus and the Cochrane library using the search terms 'dental education', 'teaching', 'tooth preparation', 'clinical skills', 'digital', 'computer' was completed. Exclusion criteria included Non-English publications and review articles. Inclusion criteria were studies conducted in undergraduate dentistry institutions, and articles that compared digital preparation analysis tools with conventional methods of teaching.

Results

From an initial total of 72 articles, 16 studies were included in this qualitative analysis. They all used single cohort and site participants. Small sample size was a limitation of all the studies. Prep-analysis systems quantitatively showed evidence of providing numeric feedback accurately. It also allowed for assessments to be completed without the bias of subjectivity. The studies analysed lacked quality to confirm the advantage of technology-based systems over conventional teaching.

Conclusion

In spite of the ability to avoid subjectivity, interestingly none of the studies reviewed showed a significant difference between conventional and digital technology-based teaching methods. Further quality research is needed to confirm the merits of using technology-based systems in teaching clinical skills.

Supervisors - Dr. George Cherukara **Funded by** - Aberdeen Dental Institute Summer Scholarship Fund

MARIKKA BEECROFT

Predicting the colposcopy workload in Scotland

Background

Since the introduction of HPV immunisation in 2008, uptake in Scotland has been 90%. Falling rates of high grade dyskaryosis and all grades of CIN have been reported in younger women with fewer colposcopies. The launch in March 2020 in Scotland of HPV primary screening will increase colposcopy referrals based on recent reports from the pilot sites in England. The impact of the move to 5 yearly screening and mRNA HPV test may also impact on colposcopy workload. Understanding the possible effect of such changes, allows Scottish colposcopists to plan for workload and service delivery.

Methods

NCCIAS reports on the number of referrals and number of cases of CIN were retrieved to identify trends in the number of new colposcopy visits and cases of CIN since 2007. Recent literature reporting on impact of vaccination and primary HPV screening was reviewed and used to generate assumptions to predict workload. These were applied to each age cohorts for the next 5 years. Non-SCCRS referrals were not considered.

Results

From 2007, a mean of 9800 women were referred via SCCRS to colposcopy and peaked in 2009 possibly due to the 'Jade Goodie effect'. In women under 30, new referrals decreased by 42% from 4752 in 2008 to 2738 in 2018. In women over 30 there was an increase from 4511 to 5744 from 2007 to 2018. Predicted numbers from 2020-2022, based on current literature, suggests the largest increase in colposcopy referrals are women aged 30-49 where 418-1513 more cases than 2018. However, in 2025 all age groups saw decreases in numbers as HPV screening enters the second round of screening.

Conclusion

Understanding future workload in light of new strategies to reduce cervical cancer is essential for Scottish colposcopists to provide continuing services especially if we anticipate fluctuating referrals rates.

Supervisors - Prof. Margaret Cruickshank **Funded by -** Aberdeen Centre for Women's Health Research

NISHU CHHANTYAL

Can dental student learning be enhanced using peer assessment? A review of the literature

Background

Peer assessment is an arrangement for learners to consider and specify the level, value, or quality of a product or performance of other equal status learners. The use of formative peer view can help students plan their learning. Feedback from peers can be available with greater immediacy and be equally valid and reliable to that of a teacher. In Dental Education, the value of peer assessment is recognised but it is only used anecdotally, evidence is needed to illustrate its benefit. The aim of this study is to investigate the Dental Education Literature surrounding peer assessment.

Methods

Systematic search of MEDLINE, PubMed, CINAHL and Scopus, using the search terms: 'Dental Education', 'Peer', 'Peer assisted', 'Clinical Skills', 'Teaching', 'Learning' and 'Assessment'. Inclusion criteria: papers after 2000, undergraduate dental or hygiene therapy students, where a comparison is made between one's own and peer assessment or that of faculty assessment, in the English language. Exclusion criteria: postgraduate students and no evaluation of a skill or project by a peer.

Results

Twenty papers were selected for analysis. Five looked at preclinical skills, four at clinical skills, six at communication skills and five examined a range of other dental competencies. Fifteen studies looked at student perceptions, 13 having positive feedback. Negative perceptions included concern over friendship, and it may not benefit learning. Several studies highlighted that training is required to maximise learner benefit. Nine papers had faculty grading, five established fair agreement between peer and faculty assessment. Almost all studies concluded peer assessment increased student confidence and enhanced learning.

Conclusion

Peer assessment is positively perceived. Further studies are needed to provide evidence of learner benefit in the development of clinical and non-clinical competencies.

Supervisors - Jane Smith

Funded by - Aberdeen Dental Institute Summer Scholarship Fund

SEOK JUN JEONG

Development and validation of FUTURE bladder diary by comparing current FUTURE bladder diary to patient specific baseline questionnaire

Background

Urinary bladder diaries are clinically used to assess one's lower urinary tract symptoms (LUTS) and to diagnose the type of urinary incontinence. However, the Female Urgency, Trial of Urodynamics as Routine Evaluation (FUTURE) bladder diary has not been validated. Hence, the aim of this research is to validate and to establish a FUTURE urinary diary by comparing current FUTURE diary to specific patient-reported questions from the baseline questionnaire.

Methods

Eligible female patients aged ≥18 from 61 hospitals across the UK were randomised to the FUTURE study. They were asked to complete a baseline questionnaire and a 3-day bladder diary prior to randomisation. 870 patients are currently recruited out of a target of 1096 patients. From the bladder diary, the following variables were derived; Day time frequency, night time frequency, Grade of urgency (mild, moderate, severe), Frequency of incontinence episodes, and number of pads used (severity of incontinence). These variables will be compared to the participant reported urgency perception scale and four ICIQ LUTS questions from the FUTURE baseline questionnaire. This data is already entered on the FUTURE database. Categorical data (Grade of urgency and Severity of incontinence) will be analysed using chi-squared tests. Numerical data (Day time frequency, Night time frequency and Frequency of incontinence episodes) will be analysed at participant level using parametric tests (ie. paired t-test) or non-parametric tests (ie. Wilcoxon test) depending on the distribution of the data.

Progress to Date

Over 1000 days of bladder diary data has been collected from 363 patients. Once 500 patients' bladder dairies are entered, data analysis will begin.

Expected Outcome

Concordance between bladder diary and participant reported questions may indicate that bladder diaries capture the same data as the questionnaire and are therefore no longer clinically required.

Supervisors - Prof. Abdel-Fattah; Suzanne Breeman; David Cooper

Funded by - Aberdeen Summer Research Scholarship

DIANA PITUC

Patient and staff perceptions of short procedural sedation with Propofol for orthopaedic procedures in the Emergency Department: a qualitative study

Background

Propofol is a sedative agent that is rapid and predictable in both onset and offset and so is widely used in the Emergency Department to facilitate the reduction of fractures or dislocations. While Propofol sedation is commonly adopted and clinically safe, little is known about the patient and staff perceptions of the practice. A better understanding of these aspects could lead to improved patient care, enhanced patient-clinician communication and inform training.

Methods

A qualitative study involving both audio-recorded semi-structured patient interviews and ED staff focus groups. Adult patients were interviewed one hour after their sedation episode by single trained study team member. Audio recordings were anonymised, transcribed verbatim and entered on to a bespoke database. Thematic analysis of all transcripts was undertaken using a general inductive method and themes and codes were developed until data saturation was reached. ED focus groups recordings were also transcribed and triangulated to the outcomes of the patient interviews. All transcripts and analyses were checked for trustworthiness and authentication of their analysis by at least two study team members.

Results

Data saturation was reached after 16 patient interviews. Analysis of the interview transcripts demonstrated that overall, patients were satisfied with the experience of Propofol sedation and with the information received. The central themes were fear of the unknown and expressed relief that the procedure was comfortable. Key themes included trust in the medical team, efficacy of pain management prior to sedation and quality of the information delivered to patients. Focus group discussion around the patient interview outcomes led to ideas that need further explored such as the need for patient pain relief prior to the procedure and a more effective triage to help identify priority patients.

Conclusion

The interview transcripts will be further analysed to gain a better understanding of patients' and staff perception of Propofol sedation in the ED to help identify any areas of future improvement.

Supervisors - Jamie Cooper **Funded by -** NHSG ED Endowment Fund

ABDEL RAHMAN OSMAN

A retrospective audit on long term overall survival in woman under 40 with primary breast cancer

Background

Approximately 2200 woman under 40 are diagnosed with breast cancer annually in the United Kingdom, representing only 4% of the disease burden. Prognostic tools have been poorly studied and validated in this sub cohort of patients. This retrospective audit seeks to look locally at the pathology, treatments and overall survival in this sub cohort of patients.

Methods

377 women diagnosed with breast cancer before the age of 40, between 1991 and 2006 at NHS Grampian were included in this audit. Data collection included age at diagnosis, treatment received (chemotherapy, endocrine treatments, radiotherapy and surgery), pathology (tumour size, grade, node positivity receptors and response to near-adjuvant treatments if given) and survival data.

Progress to Date

Mortality data was compiled for 280 patients (10-year survival of 74.3%,). Initial survival data analysis has shown that patients treated more recently have lower mortality. Data on pathology and treatment will be collected at a later date, hence completing the first phase of this project.

Expected Outcome

This audit will show the local treatment protocols, pathology and survival data, allowing comparison with the national average. Data availability will determine if there is sufficient material for a research project application to validate different prognostic tools for this understudied sub-cohort of patients.

Supervisors - Mr. Yazan Masannat

Funded by - NHSG Breast Cancer Research Endowment Fund

ANDREW WALL

Variation in Scottish Hospitals in the provision of acute care of the elderly services: Findings from the Scottish Care of Older People (SCoOP) survey

Background

The Scottish Care of Older People (SCoOP) national audit aims to improve care standards for older persons (aged > 65 years) across Scotland. In this comprehensive geriatric assessment survey, we examined whether differences exist in the provision of specialist services for older adults and consultant geriatrician availability in 28 hospitals from the 14 Scottish Health Boards.

Methods

Previous scoping surveys (Donaldson et al.) were utilised to inform the design of our comprehensive geriatric assessment survey which was distributed to consultant geriatricians nominated by the BGS Scotland Council for each hospital. We report here a summary score for services derived from occupational therapists (OT) and Physiotherapists (PT) availability for acute reviews; composition and availability of a comprehensive geriatric assessment (CGA) team; multidisciplinary team (MDT) composition and availability; and composition of specialists available and consultant availability for acute reviews. Higher scores reflect greater service availability for acute patient review.

Results

Median national service provision score was 3.13 (Range 0.12-8.23), the geriatrician consultant acute availability was 7.10 and (Range 0-21.9), the comprehensive geriatric assessment median score was 0.10 (Range 0-0.67). Specialist acute input median score was 0.36 (Range 0-1), MDT median score 5.41 (Range 0-14.59) PT median score 1.21 (Range: 0-2.75), OT median score 2.34 (Range 0-6.36), and number of specialist staff median 5.38 (Range 0-17.8).

Conclusion

Survey results highlights a mismatch in service provisions and variability between hospitals particularly for staff availability for acute input. Whilst, this is not a definitive score, our results serve as evidence for the need for further research as to the reasons and outcomes of these discrepancies.

Supervisors - Dr. Adrian Wood; Dr. Marc Locherty **Funded by -** Department of Medicine for the Elderly "Gwyn Seymour" Scholarship

GEORGIOS KOUNIDAS

A pilot study of nutritional status in patients with Huntington's disease

Background

Huntington's disease (HD) is an autosomal dominant disorder of (generally) adult onset. Weight loss is well documented as a clinical feature of all stages of HD. However, its metabolic basis is poorly understood and appetite has not been formally studied in patients with the condition. Current guidelines for HD treatment are based on research on people with other causes of weight loss. To improve clinical management of HD patients our long term goal is to examine the mechanisms of weight loss in an HD cohort. This studentship was focused on developing a protocol and applying for research permissions for a pilot study to determine which measures are feasible for use in patients manifesting clinical features of HD, and which are most helpful in detecting clinically meaningful assessment of nutrition status.

Methods

In this pilot study, 20 patients in HD stage 2 and 3 will be recruited. Ten will have reported at least 5% weight loss in a 12-month period, and ten will be weight stable. Patients will undergo clinical and non- clinical interventions on several aspects of nutrition and appetite.

Progress to Date

The protocol of the study, informed consent forms, participant information sheets, invitation letters and GP letters were developed by Georgios Kounidas. These were submitted to Research Governance for sponsorship approval on 25th September 2019. Provisional sponsorship approval was granted on the 15th October 2019. An application will be made to the Research Ethics Committee for the December meeting. We aim to recruit our first patient by February 2020.

Expected Outcome

This study will pilot the tools to inform the development of clinical trials protocols. We will measure the proportion of HD patients who can complete each nutritional measure, and will determine which are most helpful in detecting clinically meaningful changes in nutrition status.

Supervisors - Prof. Zosia Miedzybrodzka & Prof. Alex Johnstone **Funded by -** Aberdeen Summer Research Scholarship

KATHERINE GRAVES-MORRIS

The prognostic value of anticholinergic burden measures in relation to mortality in older individuals: a systematic review

Background

It has been suggested that greater anticholinergic burden (ACB) from medications increases the risk of mortality in older individuals, yet significance and strength of this association varies between studies. Multiple measures exist to quantify ACB, however no evidence yet exists comparing individual measures in relation to the outcome of mortality. Therefore, the aim of this systematic review is to assess the prognostic utility of ACB-specific measures on mortality in older individuals.

Methods

The following PROSPERO-registered systematic review was conducted in accordance with PRISMA guidelines. A literature search was conducted in MEDLINE (Ovid), EMBASE (Ovid), PsycINFO (Ovid) and CINAHL (EBSCO) from 2006-2018. Observational studies assessing the association between ACB and mortality which utilised ≥ 1 ACB measure, involving exclusively individuals aged ≥ 65 years, were included. Data were analysed narratively, using meta-analysis techniques where appropriate.

Results

Twenty published studies including 18 cohorts and 498,056 older individuals assessed this association and were eligible to be included. Eight anticholinergic-specific measures were identified, of which the most frequent were the ACBS (Anticholinergic Cognitive Burden Scale; 9 studies) and the ARS (Anticholinergic Risk Scale; 8 studies). Meta-analysis for the ACBS indicated small but significant effect sizes when stratified into anticholinergic exposure levels (Low ACB: HR 1.39 (95%CI 1.1-1.75) / OR 1.53 (95%CI 1.34-1.75); High ACB: HR 1.47 (95%CI 1.19-1.81) / OR 1.37 (95%CI 1.12-1.68)). Meta-analysis for the ARS comparatively indicated smaller effect sizes, partly exhibiting no effect (Low ACB: HR 1.15 (95%CI 1.08-1.22) / OR 1.07 (95%CI 0.68-1.68); High ACB: HR 1.14 (95%CI 1.06-1.22) / OR 0.81(95%CI 0.3-2.16)).

Conclusion

There was a modest association between several anticholinergic risk measures and mortality, with the most evidence for ACBS. However, studies directly comparing different measures were lacking. Identifying the ACB measure with the highest prognostic utility would require direct comparisons of multiple, previously- validated ACB measures in large-scale cohorts.

Supervisors - Dr. Carrie Stewart; Dr. Roy Soiza; Prof. Phyo K Myint **Funded by -** Aberdeen Summer Research Scholarship; Institute of Applied Health Sciences

JASMINE LUANGBORIBOON

The paperless classroom: Developing OSPE assessments for rapid evaluation and feedback

Background

In 2014, the Objective Structure Practical Examination (OSPE) assessment was introduced to Intercalating and Honours medical sciences students to assess their communication and laboratory science skills. Six stations, each assessing a mixture of different practical, theoretical, communications and problem-solving skills, were developed. During the assessment, students move round and are given 10 minutes to complete each station. With hundreds of students in the course, there is a heavy workload on the examiners.

This project aims to minimize variation in marking between examiners and optimize quality and speed of feedback to students by developing a paperless OSPE assessment using the university's virtual learning environment (Blackboard Ultra).

Methods

In 2018, Blackboard introduced "Ultra", which describes the transformation of the user interface and workflows in Blackboard Learn. With help from the eLearning team, a trial test course was developed. The six OSPE stations were altered to fit the capability of Blackboard Ultra.

Results

No relevant results were obtained. Due to the degree of the success from this project and the lack of student volunteers, a trial run was not conducted.

Conclusion

The current Blackboard Ultra could not be used to create an assessment that suits the needs of the OSPE examination. With only 7 question types available, OSPE stations have to be modified. This leads to a decrease in the difficulty of the examination. However, Blackboard Ultra is a continually developing product and many functions will be made available in the future.

Supervisors - Dr. Derek Scott; Dr. James Hislop; Prof. Alison Jenkinson **Funded by -** INSPIRE Scheme

TSE YI HONG BENJAMIN

Updated Systematic Review of Mortality in Parkinson's Disease

Background

Parkinson's disease (PD) is a neurological disorder that leads to both motor and non-motor symptoms which is both progressive and incurable. Age plays an important role in PD with mean age of onset of about 70 years old. The incidence of PD is about 18/100 000 in the UK and is expected to rise. An accurate understanding of the mortality of this condition is important for appropriate information provision to those affected by the disease, for health service planning and for clinical trial design. We aimed to update a previous systematic review of mortality in Parkinson's disease, published in 2014.

Methods

We searched Embase, Medline and CINAHL for papers relating to mortality in Parkinson's disease. We included inception studies of idiopathic Parkinson's disease with long-term follow-up, published after 12 October 2012. We excluded studies that were restricted to a specific subgroup of Parkinson's disease or, studies of other forms of parkinsonism. All titles and abstract were screened by a single author and the data on study methods, measures of mortality and prognostic factors for mortality were extracted independently by two authors. Quality was assessed using the QUIPS tool.

Progress to Date

2555 references were identified by the search strategy following de-duplication. After screening of titles, abstracts, and full text where appropriate, 10 were included. Data from the 10 papers were extracted and quality assessment was performed.

Expected Outcome

Synthesis of data and meta-analysis of absolute measures of survival and ratios of mortality between Parkinson's disease and controls are ongoing. We will use meta-regression to explore heterogeneity. Results from this systematic review will be combined with studies identified in the previous systematic review.

Supervisors - Dr. Angus Macleod **Funded by -** Chief Scientist Office

JESUS PERDOMO LAMPIGNANO

Developing a workforce and service questionnaire: A Scottish breast service national survey

Background

In 2018, Cancer Research UK detailed the increasing need for early-stage diagnosis of common cancers, including breast cancer. This report highlighted shortages in the diagnostic workforce in Scotland and the need for a workforce audit to form the base of future efforts to meet demand. In this project, we aim to produce a cross-sectional survey instrument that provides a detailed profile of the breast service and of the different specialties needed to provide this service across Scotland.

Methods

The survey instrument was designed to collate information about breast services in Scotland and the differences between screening and symptomatic services. It was developed with the guidance of clinical academics in breast surgery and survey methods, as well as by following the Best Practice Guidelines from the Association of Breast Surgery, the recommendations of the NHS Breast Cancer Screening Programme, and the latest quality standard guidelines on breast cancer care from the National Institute for Health and Care Excellence. Furthermore, in response to previous studies reporting differences in breast cancer management of older patients, we have included questions to examine differences in the delivery of these services in older women (>70 years) as part of the Scottish Care of Older People National Audit.

Progress to Date

The final version of the survey instrument comprises 94 questions covering 3 key areas: Workforce and Available Services, Assessment Process & Equipment, and Multidisciplinary Team Meetings. With this comprehensive survey, we hope to answer a number of research questions to achieve stated aims.

Expected Results

We hope to develop an audit report detailing the breast cancer service organisation in Scotland as well as highlighting any differences among centres to reduce unwanted variations in service provision. In the future, we plan to link patient diagnostic and outcome data to the knowledge gathered using this survey instrument to identify service level factors that may be linked to best outcomes for benchmarking purpose.

Supervisors - Mr. Yazan Masannat & Prof. Phyo K. Myint **Funded by -** NHS Grampian Breast Surgery Department

JONATHAN QUINN

Thrombolytic treatment for Acute Ischemic Stroke and renal dysfunction: A United States-wide analysis

Objectives

To determine if the safety of thrombolysis treatment in acute ischemic stroke (AIS) varies with the patients' level of renal dysfunction.

Methods

A representative sample of 3,951,368 cases of AIS (drawn from 819,318 admissions) from the Nationwide Inpatient Sample in the USA from 2005-2014 were analysed. They were categorised into 3 mutually exclusive groups based on the level of renal dysfunction: normal kidney function, chronic kidney disease (CKD) without end-stage renal disease (ESRD) and ESRD. Outcome measures (mortality, length-of-stay (LoS) and disability on discharge) were compared between groups using multivariable logistic regressions, adjusting for age, sex, race, region, teaching hospital status, stroke severity and 10 major cardiovascular co-morbidities including previous cardiovascular disease.

Results

The cohort's mean age (\square SD) was 71.1±14.4 years (52.84% women). After adjustment, thrombolysis treatment was associated with increased odds of all outcome measures (p<0.005 for all associations) compared to no thrombolysis treatment. For in-hospital mortality, this increase was not significantly different between those with no renal disease and those with ESRD (OR 1.42, 99% confidence interval (Cl) 1.38-1.46 versus OR 1.22, 99% CI 1.03-1.45) compared to those not receiving thrombolysis, and was significantly higher in those with chronic kidney disease (OR 1.62, 99% CI 1.52-1.74) compared to those not receiving thrombolysis. Across all levels of renal dysfunction, thrombolysis was associated with increased odds of LoS \ge 4 days (OR between 1.39 and 1.58) and moderate-to-severe disability on discharge (OR between 1.21 and 1.23), compared to no thrombolysis treatment. These increases however were not significantly different between levels of renal dysfunction.

Conclusion

Compared to patients with no renal disease, thrombolysis was not associated with increases in mortality in ESRD but was associated with a significant increase in mortality in patients with CKD but no ESRD. Thrombolysis should not be withheld based solely on the presence of ESRD.

Supervisors - Prof. Phyo K Myint & Tiberiu Pana

Funded by - NHSG Department of Medicine for the Elderly "Leslie Wilson Scholarship"

SAMYAK VERMA

Feasibility of collecting patient reported outcomes measures in older adults undergoing emergency abdominal surgery (general and vascular) as recommended by Royal College of Surgeons

Background

As the older population increases in size, emergency abdominal surgery will become more common due to increasing co-morbidities and frailty. The elderly population have a higher risk of mortality from surgery and higher postoperative complications than the young, which will impact their quality of life. The current hospital measures do not record long-term health of patients who live with the surgery. Surgery should be provided with the intent to improve quality of life and decrease dependence after admission. We investigated the feasibility of collecting patient reported outcome measures (PROM) data on elderly patients undergoing emergency surgery and if these surgeries had a beneficial change on patient's quality of life.

Methods

Elderly patients (above 65) having emergency abdominal surgery were recruited from general and vascular surgical wards in Aberdeen Royal Infirmary over a period of 3 weeks to take part in PROM questionnaires (5Q-5D-5L and ICECAP-0). Frailty while at hospital was collected using CSHA frailty score and physical activity using WHO performance status. These patients will be followed up after 6 months to recollect PROM data for comparison.

Progress to Date

32 patients were approached of which 30 patients (94%) accepted to take part while 2 patients (6%) rejected to take part due to pain before and after surgery. Of the recruited 16 (53%) patients were aged over 65 years with average age 74 years, but 2 patients were unable to complete the questionnaire due to lack of understanding of the questions. Feasibility was affected by the urgency of surgery, therefore health status prior to surgery could not be consistently measured and most data was collected postoperatively. None of the 16 patients rejected being followed up after 6 months.

Expected Outcome

Patients are likely to show positive improvement in PROM index score after 6 months with hospital frailty correlating strongly.

Supervisors - Dr. Roy Soiza & Dr. Eilidh Bruce **Funded by -** NHS Grampian Vascular Surgery Department

IZABELA WOJSLAW

Silver diamine fluoride use in children with dental problems: A literature review

Background

Silver diamine fluoride (SDF) is an easy to use topical agent, approved in the UK for treatment of hypersensitivity which is increasingly been used for caries treatment and prevention in children. The aim of this review was to assess existing scientific evidence on uses and limitations of SDE in children.

Methods

A literature search was conducted using the keywords "silver diamine fluoride" or "silver diammine fluoride" in four databases: Ovid (Medline), Elsevier (Science Direct), PubMed and Cochrane. A total of 574 publication were identified. Duplicates were removed and titles and abstracts were screened. Fifteen full text articles were included in the review.

Results

Recent umbrella review summarising information from 7 systematic reviews concluded that SDF was effective in arresting coronal caries in the primary dentition while insufficient evidence was found to draw conclusions on the use of SDF for prevention in primary teeth and prevention and arrest in permanent teeth in children. For the treatment of hypersensitivity three studies concluded that SDF is a good desensitiser. In terms of impact of SDF on bonding of different dental materials, one systematic review of 11 in-vitro studies showed strong evidence that SDF does not influence GIC bonding but may influence resin bonding. None of the studies reported any adverse systemic effects of SDF. Three studies concluded that that parental acceptance is usually low due to irreversible staining. Two, low-quality, unpublished studies suggest that SDF may be a good desensitiser and remineralising agent of MIH teeth.

Conclusion

SDF is a significantly non-invasive, easy-to use product which has the potential to be SDF is a significantly non-invasive, easy-to use product which has the potential to be used more widely, in the treatment of dental diseases in children. It is suggested that future research should investigate the potential of treating MIH in children using silver diamine fluoride.

Supervisors - Dr. Malcolm Stewart

Funded by - Aberdeen Summer Research Scholarship

JIE FEI LAU

Induction of IL-10 production by recombinant soluble CTLA-4

Background

Cytotoxic T-lymphocyte associated antigen 4 (CTLA-4) is an immunosuppressive receptor that acts as an important target for immunotherapy. The soluble form of CTLA-4 (sCTLA-4) is a genetic variant that has immunosuppressive properties. Previous work identified that adding natural sCTLA-4 to peripheral blood mononuclear cells (PBMCs) after antigen stimulation induced the secretion of IL-10, an anti-inflammatory cytokine. The aim of this project was to determine if the same observation could be detected using recombinant sCTLA-4

Methods

Peripheral blood mononuclear cells (PBMCs) were isolated from blood samples provided by healthy volunteer donors with ethical permission. Recombinant sCTLA-4 was added to the PBMCs in the presence or absence of purified protein derivative (PPD) and in the presence or absence of 73B1, a monoclonal antibody that targets it. An enzyme-linked immunosorbent assay (ELISA) was performed to measure the concentration of IL-10 secretion

Results

Addition of recombinant sCTLA-4 to the PBMCs after antigen stimulation using PPD generally increased the concentration of IL-10 secretion as compared to the PBMCs that were not stimulated with PPD. Blocking the recombinant sCTLA-4 with 73B1 after stimulating the PBMCs with PPD induced less secretion of IL-10 as compared to not blocking the recombinant sCTLA-4. Another observation is that the higher the concentration of recombinant sCTLA-4 added to the PBMCs, the lower the concentration of IL-10 secretion, which differs from the results from previous work whereby the relative IL-10 increase was proportional to the concentration of natural sCTLA-4 added.

Conclusion

Preliminary results suggest that adding recombinant sCTLA-4 after antigen stimulation does not induce IL-10 secretion. The results also suggest that natural and recombinant sCTLA-4 may vary in their immunosuppressive properties.

Supervisors - Dr. Frank J Ward & Dr. Rasha Abu-Eid **Funded by -** CRANES - Cancer Research Aberdeen and North East Scotland

SAMANTHA GREEN

The frequency, predictors, and outcomes of delirium in Parkinson's disease and atypical parkinsonism

Background

Delirium is common in the elderly and is associated with poor outcomes. Its frequency and prognosis in Parkinson's disease (PD) are unclear.

Methods

We studied delirium in the PINE study, a prospective, community based incidence cohort of parkinsonism. Retrospective case note review identified the first hospital episode of delirium after parkinsonism diagnosis using a definition based on DSM-V criteria. We used multivariable Cox regression to study predictors of delirium and a Cox regression model (in PD only) with time-varying covariates to investigate the influence of delirium on dementia

Results

294 patients (93% of PINE cohort) were included in the analysis. Of those, 187 had PD (mean age 72.9yrs, 39% female) and 107 had atypical parkinsonism (mean age = 78.1yrs, 36% female). 150 patients developed delirium (PD=96, atypical parkinsonism=54). Median time from diagnosis to delirium was 8.4 years in PD and 3.9 years in atypical parkinsonism. PD was associated with lower hazards of delirium than atypical parkinsonism (HR=0.37, 95%CI 0.21-0.66). Age was associated with delirium in PD (HR=1.77, 95%CI 1.05- 3.02) but not in atypical parkinsonism (HR=1.23, 95%CI 0.77-1.99). Baseline MMSE (HR=0.95, 95%CI 0.91- 0.99) but not gender, baseline UPDRS, or Charlson score predicted delirium. Median time from delirium to death (in all with delirium) was 1.9 years and from delirium to dementia (in non-demented PD) was 2.7 years. Hazards of dementia in PD were increased six-fold after delirium (HR 6.2, 95%CI 3.6-10.7).

Conclusion

Delirium is common in parkinsonism, particularly in atypical syndromes. Its outcomes are poor with high risk of dementia.

Supervisors - Dr. Angus Macleod

Funded by - Chief Scientist Office; NHS Education for Scotland

SULEMAN RAHMAN SABIR

A Comparative Evaluation of Anti-Porphyromonas gingivalis Serum IgA and Salivary IgA2 Antibody Levels in Myocardial Infarction Participants and Healthy Controls

Background

A range of epidemiological studies have indicated a potential link between periodontal disease and atherosclerosis. Specifically, the systemic effects of oral bacteria on influencing pro-atherogenic processes has gained significant attention. Of these, the gram-negative bacillus – *Porphyromonas gingivalis* (*P. gingivalis*) – has been shown to influence various pro-atherogenic processes, including the expression of virulence factors, promoting endothelial invasion and influencing immune responses. Furthermore, cross-reactivity between atherogenic antigens – such as oxidised low-density lipoprotein (Ox-LDL) and IgA antibodies against *P. gingivalis* has been indicated. We aimed to compare serum IgA and salivary IgA2 antibody titres against *P. gingivalis* in myocardial infarction (MI) and control participants. Furthermore, we aimed to correlate these titres with troponin levels – a marker of MI.

Methods

Anti-*P. gingivalis* serum IgA and salivary IgA2 titres were determined by direct enzyme linked immunosorbent assay (ELISA) in participants having suffered an MI and those having not suffered a MI. A periodontal examination was used to quantify the prevalence of periodontal disease in both groups. Results are expressed as mean ± standard deviation of optical density. Intergroup analysis of statistical significance was performed using a student's t-test analysis. Spearman's correlation analyses between anti-*P. gingivalis* antibody titres, troponin and percentage inflamed periodontal surface area was conducted. P<0.05 was considered statistically significant.

Results

Periodontal examination revealed a higher prevalence of periodontal disease in MI participants than control participants (16-vs-56). Participants suffering a MI did not display elevated anti-*P. gingivalis* serum IgA antibody titres (0.59-vs-0.64 optical density (OD)). Anti-*P. gingivalis* salivary IgA2 antibody levels were, however, significantly increased in MI participants (0.98-vs-1.65 OD, P<0.0001). No correlation between antibody titres and troponin or percentage area of gum affected could be determined.

Conclusion

Together, these pre-liminary investigations suggest that anti-*P. gingivalis* salivary IgA2 antibodies may be of potential significance in participants suffering MI.

Supervisors - Dr. Karolin Hijazi **Funded by -** NHSG Vascular Department



REKHA GURUNG

Quantifying the fungal burden in a mouse model of disseminated Emergomyces africanus

Background

Emergomyces africanus is a new fungal pathogen endemic in sub-Saharan Africa and first described in patients with advanced AIDS/HIV in South Africa. *E. africanus* belongs to a cluster of emerging dimorphic fungal pathogens that can infect humans and is the first new dimorphic fungal pathogen to be reported in over 50 years. *E. africanus* causes disseminated disease in individuals with compromised immune function and is fatal if untreated, yet little is known about this pathogen. Therefore, the aim of this project was to implement quantitative-PCR into the established model with the overarching goal of understanding the host immune response to *E. africanus* and dissecting the pathogenesis during disease.

Methods

Using an established mouse model of disseminated *E. africanus* disease, we infected C57BL/6 wild type and RAG1-deficient immunocompromised mice via intratracheal instillation with 10³ yeast cells. The mice were euthanized at 1-week-post-infection to determine disease parameters and dissemination to other organs. Lung, spleen, liver and kidney homogenates were cultured on BHI media at 37°C to determine the presence of yeast cells (CFU). Statistical differences were determined using GraphPad Prism 5. Photomicrographs were taken of GMS silver, H&E and PAS stained lung sections to be evaluated by a pathologist (Prof. Dhiren Govender).

Results

We established that lung infection with *E. africanus* caused disseminated disease especially to spleen and liver in wild type mice. This was exacerbated in RAG1-deficient mice, shown by increased CFUs in culture. We used a conventional PCR assay to confirm the presence of *E. africanus* DNA in the samples. We successfully established the qPCR assay for *E. africanus* organisms alone.

Conclusion

Our preliminary data demonstrates that infection with *E. africanus* causes disseminated disease in wild type mice and that this is exacerbated in immunocompromised animals. Future work will involve the final optimization of the qPCR assay for mouse tissue and further dissecting the host immune components that contribute to disease resolution.

Supervisors - Dr. Claire Hoving & Prof. Adilia Warris **Funded by** - Medical Research Council Centre for Medical Mycology

CHRISTOPHER THOROUGHGOOD

Inhibition of Candida morphogenesis, biofilms and virulence by the EntV bacteriocin

Background

C. albicans is a fungal pathogen that is responsible for a number of hospital-acquired infections every year. Treatment of *C. albicans* infections is difficult due to the low number of antifungal therapies available and the limited mode of actions they target. It is a dimorphic organism growing either as yeasts or the filamentous hyphal forms. The ability for *C. albicans* to switch between yeast and hyphal cells gives the cells an advantage as hyphal *C. albicans* can escape macrophages.

The bacteria *Enterococcus faecalis* is also an opportunistic pathogen that resides in the gastrointestinal tract. It has been demonstrated that *E. faecalis* expresses a unique protein (EntV) that shows antimicrobial activity against *C. albicans*. EntV is a bacteriocin that inhibits yeast-hypha morphogenesis and is a potent inhibitor of biofilm formation in *C. albicans*. We investigate the mechanism by which EntV blocks biofilm formation in *C. albicans*.

Methods

Synthetic peptides of the EntV protein were synthesised and tested in a range of experiments. The activity of the EntV peptide and its variants were tested in biofilm assays against *C. albicans*. The biofilm mass was determined using cell viability assays. Interactions of the EntV peptide was also tested against various components of the *C. albicans* cell wall using SDS-PAGE pull down assays.

Results

EntV and variants of the protein inhibited biofilm growth against *C. albcians*. EntV appears to bind to oligosaccharide polymers with different affinities as determined by the SDS-PAGE pull down assays. EntV showed interactions with both whole cell wall preparations of both *C. albicans* (Mannan, Glucan and Chitin) and *E. faecalis* (Peptidoglycan).

Conclusion

Results confirm that EntV inhibits biofilm formation. It appears that EntV may have an affinity for sugar polymers and its mode of action of hyphal inhibition is possible due to its interaction with the *C. albicans* cell wall.

Supervisors - Prof. Michael Lorenz & Prof. Danielle Garsin **Funded by** - Medical Research Council Centre for Medical Mycology



ANDRA MARIA CIUTAC

The role of inflammation in takotsubo cardiomyopathy

Background

Takotsubo cardiomyopathy is an increasingly recognised form of acute heart failure, which has been linked to a wide variety of emotional and physical triggers. The eponym of "takotsubo" refers to an octopus trap used by Japanese fishermen and alludes to the typical shape of the left ventricle in this syndrome, consisting of a dyskinetic apex and relatively hyperkinetic base. The pathophysiological mechanisms of the disease remain incompletely understood, however, recently inflammation has been shown to play a pivotal role.

Methods

The review summarises the most notable findings of myocardial inflammation, demonstrated from biopsies and cardiac magnetic resonance imaging. Further on, systemic inflammation was considered in the background of the cardiomyopathy. Acute phase proteins, cytokines, monocyte phenotyping and matrix metalloprotienases were given particular attention.

Results

In the acute stage macrophage infiltration appears to represent the substrate for myocardial oedema, together defining the local myocardial inflammation. This appears to evolve into a low grade systemic chronic inflammation which could explain the protracted clinical progress of these patients and raises hope for finding a specific takotsubo cardiac biomarker.

Conclusion

Current advancements reveal more dilemmas concerning the pathological processes underlying takotsubo. It is clear that inflammation is an integral part of the disease, but the cause-effect relationship remains unknown. It could be that the inflammation in this disease is a secondary phenomenon, perhaps precipitated by autonomic imbalance/ overdrive or micro-vascular abnormalities, or conversely the inflammatory process being causative in the course of takotsubo, driving the microcirculatory abnormalities through a mechanical, compressing effect of oedema for example.

Supervisors - Prof. Dana Dawson **Funded by -** INSPIRE National Scholarship

RORY MACIVER

Advances in Head and Neck Immunotherapy - Characterization of CTLA-4 expression in head and neck cancer cell lines

Background

The incidence of head and neck cancer (HNC) in UK is on the rise with the highest rates reported in Scotland. Despite advances in HNC treatment, the mortality rate is high, which is mainly attributed to late diagnosis. Therefore, understanding the pathogenesis of HNC, especially the interaction with the immune system is essential for predicting disease progression, and developing new therapies. Cancer immunotherapy has made great strides in the management of different types of cancer including HNC through targeting and boosting anti-tumour immunity and checkpoint inhibitor antibodies, which target PD-1 and CTLA-4 have been approved for HNC treatment. Current anti-CTLA-4 antibodies can bind the full-length receptor isoform and an alternatively spliced form, called soluble CTLA-4 (sCTLA-4). Developing specific antibodies that can bind either of these forms can inform the development of more specific and highly effective therapies. To achieve this, studying the expression of the two isoforms in different cancer types is essential. The aim of this project was to study the expression of both forms of CTLA-4 in HNC cell lines.

Methods

HPV-positive and HPV-negative HNC cell lines were cultured, fixed and stained. Confocal microscopy was used to analyse patterns of CTLA-4 receptor and sCTLA-4 expression in these cells.

Results

Both CTLA-4 and sCTLA-4 are expressed in HPV+ and HPV- HNC cell lines. Preliminary data suggest that HPV+ and HPV- HNC cell lines show different patterns of expression of CTLA-4 and sCTLA-4. Interestingly, our preliminary data show a higher expression level of sCTLA-4 than previously assumed.

Conclusion

Our preliminary data suggest that sCTLA-4 has a significant role in HNC tumour microenvironment and is therefore a good target for specific anti-sCTLA-4 therapies. These data are promising in the search for new and improved immune therapies for HNC.

Supervisors - Prof. John Gibson; Dr. Rasha Abu-Eid; Dr. Frank Ward **Funded by -** INSPIRE National Scholarship



DOMINIKA BOLDOVJAKOVA

Development a benign colorectal database of IBD

Background

Inflammatory bowel disease (IBD) are chronic conditions with the highest incidence in Scotland. In recent decades IBD has experienced rapid increase in both incidence and prevalence. The standard method of treatment includes both medical therapies and surgical resection of the bowel. In 2015 Scottish Medicine Consortium approved use of biologics as a routine treatment for these conditions for the first time. Whether increased prescribing of biologics has any effect on rates of surgical management and post-operative recovery of the IBD patients is not yet fully understood.

Methods

A colectomy database was created for IBD patients within NHS Grampian. Clinical notes of patients who underwent subtotal colectomies in Aberdeen Royal Infirmary were retrospectively analysed and relevant data was extracted. The data set contains information about demographics of the patients (age, gender, BMI), diagnosis (ulcerative colitis/ Crohn's disease and the date), past medical history (comorbidities, previous hospital admissions and abdominal surgeries), medical therapy (steroids, immunosuppressants and biologics), surgical management (date and type, urgency, length of procedure and blood loss, post- operative complications, length of post-operative hospital stay and post-operative treatment pathway). Bowel resection for non IBD diagnoses (such as cancer) and small bowel resections were excluded from this study. The study was registered with the clinical effectiveness department of NHS Grampian and performed in accordance with their instructions.

Progress to Date

Data from 189 IBD patients that have undergone colectomy in the time period from 2009-2011 and 2014- April 2019 was collected. The collected data will be analysed to answer following questions: Has the introduction of biologics had any effects on the rate of colectomies, post-operative infective and non-infective complications, length of stay, length of time from diagnosis to surgery and rates of emergency surgeries vs elective.

Expected Outcome

Whether increased biologic prescribing has affected colectomy rates in patients with inflammatory bowel condition is poorly described. The preliminary data analysis does not show any obvious trends in the reduction of number of surgeries nor increased number of infective complications. Full statistical analysis is required to make a definitive conclusion.

Supervisors - Mr. George Ramsay

Funded by - Innes Will Endowed Scholarship

PANAYIOTIS TANOS

SHARP risk score: A predictor of poor outcomes in adults admitted for emergency general surgery

Background

Post-operative complications following emergency abdominal surgery can be associated with significant morbidity and mortality. Despite numerous prognostic factors associated with poor surgical outcomes; there is a lack of data describing the emergency surgical population and a simple index for predicting outcomes based on admission data. Our aim is to create a simple to use point-of-care risk scale that predicts adults at an increased risk of poor outcomes in acute surgical setting.

Methods

We used data from an international multi-centre prospective cohort study of participating in the Older Persons Surgical Outcomes Collaboration (www.OPSC.eu). The effect of selected characteristics on 90-day mortality was examined using fully adjusted multivariable models. For our secondary outcome we aimed to test whether these characteristics could be combined to predict poor outcomes in adults undergoing emergency general surgery. Subsequently, the impact of incremental increase in derived SHARP score on outcomes was assessed.

Results

The cohort consisted of 419 adult patients (men 48.7%; median (range) 52 (16-94) years) consecutively admitted to 5 emergency general surgical units across the United Kingdom, during 2013 and 2014 audit periods. In fully adjusted models according to gender, frailty and C-Reactive protein; each SHARP characteristic (having age greater or equal to Sixty-five (4.32(95%CI 1.42-13.11); p<0.010), Hypalbuminaemia (4.60(95%CI 1.39-15.30); p<0.013), Anaemia (3.33(95%CI 1.148-9.70); p<0.027), Renal Insufficiency (4.55(95%CI 1.61-12.87); p<0.001), Polypharmacy (3.53(95%CI 2.20-5.68); p<0.001) was significantly associated with 90-day mortality and increased hospital length of stay. Every point increase in SHARP score was associated with higher odds of mortality in adults who underwent emergency general surgery.

Conclusion

SHARP risk score provides clinicians with an easy method of calculating the risk of poor outcomes based on point-of-care information in patients undergoing emergency general surgery. This information may be used to improve management plans and aid clinicians in delivering more person-centred care.

Supervisors - Prof. Phyo Myint; Andrew Ablett **Funded by -** Innes Will Endowed Scholarship

BETHANY MCLOUGHLIN

Intramedullary Nails for Tibial Shaft Fractures – An evaluation of the Suprapatellar Approach in the Aberdeen Orthopaedic Unit between 2016-2019

Background

The current gold standard for operative treatment of tibial fractures is intramedullary nailing (IMN). Traditional approaches use a hyperflexed knee position, which leads to increased force exerted on the proximal fracture by the quadriceps. This results in poorer fracture and IMN alignment, plus increased post- operative knee pain. A semi-extended knee position, as used in the suprapatellar (SP) approach, neutralises the quadriceps, maintaining fracture alignment. The SP approach is reported to offer improved post-operative fracture alignment and knee function. This project aims to evaluate the popularity of the SP approach in the Aberdeen Orthopaedic unit and radiologically compare IMN approaches.

Methods

All tibial fractures treated with IMN between 2016 – 19 in the Aberdeen Orthopaedic unit were identified. The approach used was gathered from the Op note. Each fracture was classified according to the AO Tibial Fracture Classification. X-rays were excluded if the degree of radiological rotation distorted anatomical relationships. Radiological analysis is still ongoing. IMN placement on the lateral X-ray is being measured via anterior (ACN) and posterior distance to the nail centre (PCN), nail depth and angle between mid-nail and tibia. For the AP measurements, the medial distance replaces ACN and lateral distance replaces PCN.

Progress to Date

158 fractures were identified. 37.3% were excluded, primarily due to unsuitable post-operative X-rays. 28.2% of the remaining 99 had no approach recorded or inaccessible records. 12.9% of cases used the SP approach. 4.04% of these used the SP approach in conjunction with another approach. The most popular approach was the medial parapatellar, used in 54.5% of cases.

Expected Outcome

The SP approach offers clear advantages in the literature yet wasn't the most popular. The clinical reasoning behind this should be explored. Subsequent radiological analysis aims to compare post-operative fracture and IMN alignment to identify which approach is the most beneficial for fractures with angular deformity and translation.

Supervisors - Prof. Alan Johnstone

Funded by - Innes Will Endowed Scholarship

JEREMY WONG

Exacerbation of Adjacent Segment Disease due to Mismatch of Pelvic incidence and Lumbar Lordosis after Lumbar Spinal Fusion

Background

Pelvic incidence-lumbar lordosis (PI-LL) mismatch has recently been acknowledged to be a risk factor for adjacent segment disease (ASD) following lumbar fusion surgery. However, the extent of such influence on the pathogenesis of ASD is still unknown. Due to the rapidly increasing volume of spinal fusion to accommodate the aging population, there is a dire need for understanding of the risk of postoperative complications following lumbar spinal fusion. Moreover, as patients who have higher post-operative PI-LL mismatch have less favorable functional outcomes and are prone to future revision surgeries, it is imperative to lay the framework for early intervention and future diagnostic application in patients at risk of ASD.

Methods

The target population will be adult patients who have undergone elective lumbar fusion surgery in Aberdeen, Scotland starting from 2006. Patients with diagnosis of ASD who underwent or are scheduled for revision surgery will be divided into three classifications based on patients' respective post-lumbar fusion and pre- revision surgery pelvic incidence and lumbar lordosis mismatch: type A (ΔPI-LL ≤10°), type B (ΔPI-LL 11° - 14°) and type C (ΔPI-LL ≥15°). The mean days between lumbar fusion surgery and revision surgery will be compared across all three groups. Primary objective will be analysed by ANOVA to and followed up by t-tests. Significant results will be followed up by Post-Hoc analysis. All statistical calculations will be determined by SPSS.

Results

Research Ethics Committee of the Health Research Authority has reviewed and approved the research project. Local Caldicott approval has been obtained.

Conclusion

Project is currently ongoing.

Supervisors - Mr. Santosh Baliga **Funded by -** Innes Will Endowed Scholarship

RAFSAN CHOWDHURY

A Review of Grommet and T-tube insertion operations carried out in Aberdeen Royal Infirmary under the care of Miss Maini

Background

The Eustachian tube is a narrow tube joining the middle ear to the back of the nose and equalises middle ear pressure. It can become blocked or dysfunctional, where common symptoms include hearing loss, aural fullness, otalgia and dizziness. Eustachian Tube Dysfunction is common in the age range of 1-8 years. Less commonly, adults can have ETD, resulting in hearing loss, middle ear effusion, otalgia, inability to pop ears and pain on flying. Where medical treatments including steroids and decongestants fail, ventilation tubes may be surgically implanted. Aim: To determine the efficacy of grommet and T-tube insertion operations in improving symptoms in adult patients with Eustachian Tube Dysfunction.

Methods

Anonymised clinic data from 232 NHS Grampian patients who underwent ventilation tube insertions between 2014-2019 was received. Clinic letters for the 40 patients aged 16 and over was retrospectively reviewed. The date of surgery and date of recurrence of symptoms was noted. The number of months of symptom benefit for each patient was calculated. Complications from the grommet or t-tube, as well as if the case was revision or new was recorded.

Results

40 (17.2%) of the patients were adults. From this, 19 patients (47.5%) had undergone T-tube insertion; the remaining 21 patients(52.2%) underwent grommet insertions. 17(42.5%) patients were male, and 23(57.5%) patients were female. From the grommet patients, 7(33.3%) of patients were revisions, and 14(66.7%) were new. For T-tube patients, 16(83.3%) of the cases were revisions, and 3(16.7%) were new. 15 out of the 40 patients (37.5%) were non-smokers, and 25 patients (62.5%) were smokers/ex-smokers.

Conclusion

The mean duration of benefit from grommets was 17.1 months and 31.8 months for T-tubes. No relation was found between the patient BMI and the duration of symptomatic improvement. Some of the most common co-morbidities in the patient cohort included allergic rhinitis, otitis media, asthma, dermatitis and eczema.

Supervisors - Ms. Sangeeta Maini Kapur **Funded by -** Innes Will Endowed Scholarship

NICOLE SIME

Diet Matters: Talking to Patients about Food- A Workshop for Medical Students

Background

The medical school curriculum underwent criticism last year due to the lack of teaching of lifestyle interventions. Lifestyle interventions are first line treatment for cardiovascular disease and type 2 diabetes- two of the leading causes of morbidity and mortality in Scotland. Medical students and doctors have expressed a lack of confidence in giving lifestyle advice and dietician referrals are reserved for patients most at risk of sequela from metabolic disease. This project produced a workshop for medical students detailing basic nutrition and dietary guidelines for Scotland and strategies of relaying that information to patients.

Methods

A review of the literature regarding nutrition teaching in medical schools was carried out and a reflection about nutrition teaching in the current curriculum was written. Learning outcomes were devised based on the current dietary recommendations for Scotland. Advice on interacting with patients about lifestyle interventions and diet was incorporated. The workshop utilises different mediums for knowledge exchange- lecture format, video interviews, interactive sections, quiz sections and a clinical skills section. Students will work in groups of 5 to facilitate discussion. Outcomes of the workshop will be measured through evaluation forms to determine if the learning outcomes were met.

Results

An interactive and engaging workshop and workbook was created entitled "Diet Matters: Talking to Patients about Food". An evaluation of the workshop will take place to determine whether the workshop attained the learning outcomes and whether students enjoyed and found the content useful.

Conclusion

By attending the workshop students will be able to identify patients who could be at risk of obesity and associated metabolic disease, understand current diet recommendations and be able to start a conversation with patients about food and weight.

Supervisors - Prof. Alex Johnstone **Funded by -** Innes Will Endowed Scholarship

LIAM LENNOX

Parkinson Disease and cognitive decline: analysis of the English Longitudinal Study of Ageing

Objective

We aimed to compare cognition over long-term follow-up in people with Parkinson disease (PD) against those without.

Methods

A nested case-control study was based on waves 1 (2002-2003) to 8 (2016-2017) of the English Longitudinal Study of Ageing (ELSA), a population based prospective cohort with biennial follow-up. Cases were defined as ELSA participants who received a diagnosis of PD at any point until the end of follow-up and were matched by age, sex and total number of co-morbidities with 6 controls drawn from the same cohort. Multi-level linear regression analysis was used to analyse the change in cognition over time (global, orientation, memory and executive function). The analysis was adjusted for smoking, cardiovascular disease, diabetes, stroke and psychiatric disorders.

Results

A total of 735 participants (105 cases, 630 controls) were followed up for a median of 8 years (0 to 14 years follow-up). After adjustments, PD was significantly associated with an increased rate of decline in global cognitive Z-scores (-0.32779 SD/year, 95% CI -0.64099, -0.01459) and executive function Z-scores (-0.37732 SD/year, 95% CI -0.69093, -0.06372). It was not significantly associated with memory Z-scores (-0.25250 SD/year, 95% CI -0.56905, 0.06405) or orientation Z-scores (-0.03185 SD/year, 95% CI -0.42376, 0.36006). Beyond 6 years the decline in cognition in the PD group became more rapid than in the non-PD group (PD global Z-score at 6 years, -0.27541 SDs, 95% CI -0.49445, -0.05637, no PD global Z-score at 6 years - 0.11944 SDs, 95% CI -0.21429, -0.02460, PD global Z-score at 14 years -0.74777 SDs, 95% CI -0.96779, - 0.52776, no PD global Z-score at 14 years -0.1789274 SDs, 95% CI -0.30276, -0.05510).

Conclusion

PD was associated with a significant decline in global cognitive function, as well as executive function and memory over the long term follow up (after 8, 12 and 14 years respectively).

Supervisors - Dr. Isobel Sleeman; Tiberiu Pana; Jesus Perdomo-Lampignano **Funded by -** Innes Will Endowed Scholarship

BILAL BENZAHIA

Assessing the viability of novel electrode materials for supporting sensory neuron growth

Background

Indwelling electrodes are used increasingly for neural stimulation, but existing electrodes have limitations. Metals create damaging heat, free radicals and pH changes and the mechanical mismatch of rigid electrodes with soft neural tissues is damaging. We tested the ability of flexible materials coated with a thin (12 nm), transparent Pt layer to support neuron growth. Materials were Cycloolefinic polymer (COP) with and without a platinum (Pt) layer and Polyimide coated with Pt (PI+Pt), Polydimethylsiloxane coated with Pt (PDMS+Pt) (all prepared at Instituto de Microelectronica de Barcelona by Nieves Casañ-Pastor). Tissue culture plastic and glass coverslips were positive controls.

Methods

Dissociated dorsal root ganglia neurons from postnatal day 3 or 4 (P3 or P4) rats were grown in Epilife medium with S7 supplement. All surfaces were pre-coated with fibronectin and collagen. Neurite outgrowth was assessed from β -III tubulin immunofluorescence and propidium iodide nuclear staining of cells fixed after 3 days in vitro. Neuron morphology was categorised as: no neurites (<1 cell diameter), simple (1-2 neurites >1 cell diameter) or complex (neurites >2 cell diameters, branches). Values are the percentage of total neurons.

Results

All materials supported attachment and survival of neurons at least as well as glass and plastic. P3 and P4 neuron complexity was highest (~ 85% each) on tissue culture plastic, followed by glass (58% for P3: 36% for P4) and PDMS+Pt (42% for P4). About 23% of P3 neurons on COP had complex morphologies regardless of the Pt layer. Simpler morphologies were most common on COP: about half were simple, whether without Pt (53%; P4) or with Pt (48%; P3). Although PI supported cell attachment and survival nearly all had no neurites, regardless of Pt coating.

Conclusion

The data indicate that PDMS and COP are promising materials to test using sensory neurons and electrical stimulation. Conversely, PI was not promising.

Supervisors - Dr. Ann M Rajnicek **Funded by -** Innes Will Endowed Scholarship

IOANNIS GEORGIOU

Intra-operative pituitary identification: Is Tissue "Firmness" A Reliable Indicator?

Background

Accurate differentiation of adenoma from normal pituitary tissue is critical during transsphenoidal surgery for pituitary tumours. Reliably differentiating the two allows maximal resection while minimising postoperative pituitary dysfunction. Traditionally, a means of differentiation has been using the "firmness" of the tissue, where normal pituitary tissue and adenoma are considered "firm" and "soft" respectively. This study aims to determine the efficacy of this technique in the differentiation of normal and abnormal pituitary using the pathology reports of intraoperative tissue samples and comparing these to their intraoperative characteristics.

Methods

A review of the medical records, from April 2004 to September 2018, at the Department of Neurosurgery was conducted to identify all cases of sellar tumour resection for which histology samples were labelled as "firm". The samples were compared to the pathology reports to confirm whether they were normal or abnormal pituitary. An analysis was conducted using SPSS to find whether excision of firm samples that were normal pituitary had any associations with intra-operative CSF leakage, hospital stay and postoperative complications.

Results

44 patients had tissue samples labelled "firm". 19 (43.2%) were normal pituitary and 25 (56.8%) were pathological. Using firm tissues to identify normal from abnormal pituitary yielded the following; sensitivity= 0.432, specificity=0.045, positive predictive value =0.232 and negative predictive value=0.107. No associations were drawn between normal pituitary excision and intraoperative CSF leakage (p=0.368, CI=95%), hospital stay (p=0.385, Median=9(6), CI=95%) or postoperative complications (p=0.653, CI=95%).

Conclusion

The retrospective study suggests that firm tissue from pituitary abnormalities is not an accurate for differentiating pathological from normal pituitary tissue. Therefore, it is important to utilise other methods for differentiation during transsphenoidal tumour resections, potentially including the use of intraoperative pathological examination with frozen section. Further larger, prospective studies would be meaningful to more rigorously determine the accuracy— of this technique.

Supervisors - Mr. Mahmood Kamel **Funded by -** Flora Gow Murray Endowed Scholarship



SOPHIE BARRACK

Remote and Rural Medicine: A journey through cases

Background

This Teaching Development award was designed to give undergraduate medical students experience of educational research and curriculum development. The aim of this project was to develop cases exemplifying how common clinical problems can be effectively treated in a remote and rural to supplement the online library of cased based learning. These cases aimed to aid revision and increase exposure of University of Aberdeen 4th and 5th year medical students to the demographics and clinical picture of remote and rural medicine in NHS Highland. They also demonstrate the ability to deliver high quality, evidence-based healthcare in a remote and rural setting – but emphasise patients may follow a different pathway compared to urban-based patients with the same condition.

Methods

Research was conducted using NHS Highland Guidelines, NICE Guidelines and BMJ Best Practice online resources as well as contributions from consultant specialists in Raigmore Hospital, Inverness and Caithness General Hospital, Wick. Rural GPs and ambulance crews were also interviewed for their insight and knowledge. Structured PowerPoint slides were created comprising: remote and rural demographic data; a presenting complaint; symptoms and signs; diagnosis (gold standard from NICE guidelines vs remote and rural management) and treatment/follow up with consideration of transport implications and the use of NHS Near Me. Cases contained a mixture of interactive questions, learning points and links to further learning materials. Completed PowerPoints were fact-checked by a consultant specialising in the area of the case topic, before being sent to MediCal to be formatted for publication on MyMBChB.

Results

3 PowerPoint presentations - 1 medical (myocardial infarction), 1 surgical (lower GI carcinoma and palliative care) and 1 trauma (catastrophic haemorrhage) - were produced, each focussed on increasing knowledge and awareness of how to manage common scenarios in a remote and rural environment.

Conclusion

Medical education is an important aspect of medical research and remote and rural medicine is an important field which provides quality, evidence-based healthcare.

Supervisors - Prof. John Duncan; Dr. Danielle Jeffreys; Dr. Kevin Deans; Dr. Owen Dempsey **Funded by -** NHS Highland



MAIRI CAMERON

Clinical factors associated with poor response to first line treatment in oral lichen planus

Background

Previous studies have demonstrated significant treatment failure in oral lichen planus (OLP). Efficacy of topical steroids (first line medication for OLP) has been reported as low as 30%. There has been little research into which factors play a role in poor response to treatment. We asked whether smoking, alcohol consumption, poor oral hygiene or haematinic deficiencies could predict a poor response to treatment with the view to improving patient outcomes by tailoring individuals' treatments.

Methods

A retrospective review of OLP patients' records was carried out to determine whether there was a relationship between certain clinical characteristics and poor response to topical steroids. Data were collected on smoking status, alcohol consumption, liver function, and B12, folate and ferritin levels.

Results

Sixty-two patients eligible for the study attended our centre in January 2016 and between June 2018 and June 2019. Treatment failure occurred in 23 - 42% of this population. Binary logistic regression showed that increasing age was associated with improved treatment response (p = 0.015, OR = 1.080, CI = 1.015 – 1.149). Although not a significant finding, the Kruskal-Wallis test showed patients who consumed more alcohol tended to have poorer response to treatment (p = 0.097; alcohol groupings = 0-5, 5-14, >14 units/week, mean rank = 21.2, 30.1, 31.6 respectively).

Conclusion

Treatment failure is an issue in OLP and, based on the results of our small sample, there may be a link between this and increased alcohol consumption. In contrast, increasing age appears to be associated with better outcomes. Further data collection is required to support these findings and perhaps elucidate other factors at play.

Supervisors - Prof. John Gibson & Dr. Karolin Hijazi **Funded by -** Medical Research Scotland

EMMA KRZOSKA

Applying Raman Spectroscopy to Assist Breast Cancer Stratification

Background

Breast cancer is the most common cause of cancer mortality in the UK, affecting 1 in 8 women. Although survival outcomes have improved, there is an ongoing need to develop reliable diagnostic and prognostic tools, capable of detecting pre-cancerous changes and predicting recurrence. In recent years, the application of Raman spectroscopy in the analysis of biological samples has been of increasing interest. This form of vibrational spectroscopy can generate a unique biochemical fingerprint capable of distinguishing normal and malignant cells or tissues by comparing amide, lipid and carotenoid profiles. There is currently no standardised protocol for tissue and cell line Raman analysis. For clinical application of Raman, a standardised protocol must be developed.

Methods

Two malignant cell lines (MCF-7 and T47D) and one non-malignant cell line (HB2) were seeded onto glass coverslips at cell densities of 10,000 or 100,000 and illuminated using a 785nm laser. Anonymised FFPE breast cancer tissue sections were de-waxed using standard laboratory procedures and analysed using the same cell line instrument parameters. As an alternative sample preparation, an anonymised paraffin embedded tissue block was scanned in two regions; directly onto cut tissue surface and onto plain paraffin wax.

Progress to Date

No biological information could be obtained for all samples involving glass substrates due to prominent peak between 1000cm⁻¹ and 2000cm⁻¹. The presence of glass causes significant photoluminescence and could not be used in future analysis. Raman peaks corresponding only to paraffin wax were observed in both regions of the cell block.

Expected Outcome

Preliminary results indicate glass substrates interfere with Raman analysis of translucent biological materials. An alternative substrate such as stainless steel could be used to avoid future interference. The presence of paraffin wax in samples also contributes to spectra therefore effective de-waxing protocols must be developed.

Supervisors - Prof. Valerie Speirs **Funded by -** Friends of Anchor

ZAHRA PASDAR

Predicting the risk of cardiovascular disease in women with a history of hypertensive disorders of pregnancy: Development of a prediction model using pooled data from the Aberdeen Study of Cardiovascular Health in Women (ASCHW) and EPIC – Norfolk prospective cohorts

Background

Whilst international guidelines recognise hypertensive disorders of pregnancy (HDP) as a major risk factor for cardiovascular disease (CVD), there is a paucity of recommendations for how to identify those with greatest risk. We aimed to develop a prediction model in women with prior HDP.

Methods

Eligible women were identified from the Aberdeen Study of Cardiovascular Health in Women (ASCHW) and European Prospective Investigation into Cancer (EPIC)-Norfolk cohorts and were followed for incident CVD through record linkage using ICD 9/10 in both cohorts. Of 4,186 women with prior HDP, 3,468 attended clinic assessment. Missing data were handled using multiple imputation. We examined the prospective relationship between HDP and incident CVD by performing three univariate and multivariate logistic regression analyses on: lifestyle questionnaire variables, questionnaire and clinic assessment variables and plasma cardiovascular biomarkers. The final model consisted of statistically significant predictors (p- value<0.05) from multivariate analyses. Model performance was assessed by discrimination and calibration.

Results

Predictors for CVD in women with HDP in the final model were age over 49 years, no university education, high BMI, total cholesterol, triglyceride and plasma fibrinogen; usage of aspirin and lipid lowering medications; hypertension, family history of CVD, repeated HDP exposure and the cohort population. Risk factors conferring the greatest odds (≥2-fold) of CVD included: age beyond 49 years, hypertension, aspirin users, morbidly obese BMI and the EPIC-Norfolk population. Median AUC was 0.82 and calibration ranged from <0.001 to 0.003 in imputed datasets.

Conclusion

We propose a highly predictive risk model which suggests that women with prior HDP should be followed up from 49 years of age. Biomarkers including triglyceride and fibrinogen should be monitored, particularly if women have hypertension, high BMI, family history of CVD or repeated HDP exposure. Further external validation work is recommended to confirm the clinical utility of the proposed risk model.

Supervisors - Dr. David T Gamble; Dr. Sohinee Bhattacharya; Prof. Phyo K Myint **Funded by -** Medical Research Scotland

WERONIKA SZLACHETKA

Development and internal validation of a prediction score for 10year ischaemic stroke mortality

Aims

To develop a user-friendly clinical nomogram that can predict post-ischaemic stroke mortality over 10 years.

Methods

We extracted data for 10,366 patients who had their first-ever ischaemic stroke from the Norfolk and Norwich Stroke and TIA Register. A Cox model was used to predict the chance of 10-year post-discharge mortality. The predictors included were age, sex, the Oxfordshire Community Stroke Project classification, estimated glomerular filtration rate (eGFR), pre-admission modified Rankin Score, admission blood data (haemoglobin, sodium, white blood cell count) and comorbidities (atrial fibrillation, coronary heart disease, heart failure, cancer, hypertension, chronic obstructive pulmonary disease, liver disease and peripheral vascular disease). The model was internally validated using the optimism-adjusted c-statistic obtained by bootstrapping. It was subsequently converted into a nomogram for clinical use.

Results

Mean age was 77.8 years (standard deviation 12.1 years), 52% (5,481) female. Most strokes were classified as partial anterior circulation syndromes (36.21%). Predictors of 10-year mortality were total anterior circulation stroke [hazard ratio (HR) (95% confidence intervals (CI)) 2.77 (2.53,3.03)], eGFR lower than 15 [1.92 (1.48- 2.48)], 1-year increment in age [1.04(1.04-1.05)], liver disease [1.54(1.23-1.93)], peripheral vascular disease 1.44(1.26-1.63), cancers 1.36(1.26-1.47), heart failure 1.24(1.12-1.34), higher pre-admission Rankin Score 1.21(1.18-1.23), atrial fibrillation 1.18(1.11-1.26), coronary heart disease 1.09(1.02-1.17) and chronic obstructive pulmonary disease 1.13(1.02-1.25). Hypertension was found to have a protective effect [0.77 (0.72-0.82)]. Optimism-adjusted c-statistic was 0.76.

Conclusion

A simple mortality score identifies the patients who will have a poor prognosis over 10 years and allows clinicians to plan their management accordingly. It uses patient data available on admission and may be calculated by all clinicians on an easy to use nomogram. Although the model discriminated well between patients at low and high risk, external validation is required to assess generalisability of the score.

Supervisors - Dr. David McLernon & Prof. Phyo K Myint **Funded by -** Medical Research Scotland

MARCIN SZOSTOK

Hormone Receptor Phosphorylation Patterns In Male Breast Cancer

Background

Breast cancer (BC) is the most common cancer in the UK. The disease is much more prevalent in females but males can also be affected, with the incidence of male BC slowly increasing. A growing body of evidence shows that male BC is molecularly different to female BC. This is of clinical relevance due to similarities in current treatments used for both male and female patients. BC expresses molecular markers such as oestrogen receptors (ER), progesterone receptors, HER-2 and androgen receptors (AR). Presence or absence of these may affect patient outcome. The understanding and significance of phosphorylation status of ER and AR expression is currently lacking. Phosphorylation signifies an active receptor. The aim of this project was to analyse commonly phosphorylated ERα (S104, S118, S167, S294) and AR (S81, S210/213) in male BC tissue sections using immunohistochemistry (IHC).

Methods

Following ethical approval (06/Q1205/156), IHC was performed on male BC tissue microarrays (TMAs) for AR phosphorylated at ser-81 (AR-81) and ser-210/213 (AR-210/213) using standard procedures. QuPath Image analysis software was used to assess positivity of the stained TMAs. Analysed images originated from two sources: IHC performed in previous years (ERQ S104, S118, S167, S294) and IHC performed during the time of this project (AR-81, AR-210/213).

Progress to Date

IHC and image analysis have been fully completed. Mean Allred and H-score for each of the male BC samples were extracted and analysis of these scores is ongoing. In future, these scores could enable a cut-off point to be determined for the positivity of the biomarkers. This will assist in determining whether a relationship between these biomarkers and overall and relapse-free survival exist, using univariate and multivariate predictor models.

Expected Outcome

Patterns of expression of phosphorylated $ER\alpha$ and AR receptors could influence patient survival outcomes.

Supervisors - Prof. Valerie Speirs **Funded by -** The Pathological Society

CATRIONA YOUNG

Duration of second stage of labour and maternal and offspring outcomes at Aberdeen Maternity Hospital 2000-2016

Background

The second stage of labour starts with full dilatation of the cervix and ends when the baby is born. A systematic review in 2006 studied an association between prolonged second stage of labour and adverse maternal and offspring outcomes. It could not reach clinical conclusions due to the limited quality of primary studies. This project has been able to address many of those limitations due to use of a unique dataset. It has also evaluated the impact of longer second stage durations due to a protocol change in Aberdeen which allowed second stage to extend an hour beyond national guidelines.

Methods

Data on 51,689 women delivering in Aberdeen Maternity hospital between 2000 and 2016 was utilised. The cohort was split into nulliparous and multiparous women. The duration of second stage of labour was recoded to: less than 3 hours, 3 to 4, 4 to 5, 5 to 6 and more than 6 hours. Baseline characteristics and outcomes across these durations were studied using <3 hours as the reference group. Univariate and multivariate analyses were performed: linear regression for continuous outcomes (requiring log transformation), binary logistic regression for binary outcomes and multinomial regression for categorical outcomes.

Results

Duration of second stage of labour was associated with adverse maternal but not offspring outcomes in both cohorts. The risk of 3rd/4th degree tears increased by 302.5% (RR 3.025 95% CI) by 4 to 5 hours. The same trend existed for postpartum haemorrhage (PPH), for example vaginal delivery PPH's risk is 57.9% greater at 3 to 4 hours (RR 1.579 95% CI 1.164-2.141). There was an association also found with a raising number of forceps, episiotomies and a drop in caesarean sections.

Conclusion

Prolonged second stage of labour is associated with adverse maternal outcomes including 3rd/4th degree tears, postpartum haemorrhage but lowers the chance of emergency caesarean birth. No association was found with offspring outcomes.

Supervisors - Dr. Mairead Black **Funded by -** Medical Research Scotland

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FURTHER YOUR ACADEMIC INTEREST

Below is a selection of useful organisations and websites to help further your interest in academic medicine as a student.

Aberdeen Student Society for Academic Medicine (ASSAM)

"The Aberdeen Student Society for Academic Medicine (ASSAM) was established in 2012 with the hope to encourage undergraduate interest in medical research. Even though their primary aim is to inspire medical students to pursue a career in academia, they also try to highlight the importance of basic research skills and critical appraisal in normal clinical practice. "

www.assam.nsamr.org | assam@nsamr.ac.uk | Facebook: AberdeenASSAM

Aberdeen Clinical Academic Training (ACAT)

Training programmes and support for postgraduate clinicians in Aberdeen. www.abdn.ac.uk/smmsn/acat









