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Best undergraduate poster prize winner

Global Epidemiological Surveillance – where does RSV fit in?

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The World Health Organisation (WHO) sets global standards for disease surveillance and coordinates multiple global surveillance networks. Respiratory Syncytial Virus (RSV) causes significant healthcare burden and mortality in young children, with the majority of disease occurring in low income countries (1). Many of these nations are eligible for financial support from donors such as the Global Alliance for Vaccine and Immunization (GAVI). There are 65 vaccines currently in development; two are in Phase III clinical trials (2). With vaccines potentially available in the near future, there is an increasing need for capturing baseline epidemiological data upon RSV. However, there are no existing global standards for RSV surveillance. The WHO Invasive Bacterial Vaccine Preventable Disease (IB-VPD) network currently collects case-based surveillance data on a variety of pathogens, including those causing acute lower respiratory tract infections (ALRI). It has been proposed that the IB-VPD network may be leveraged to host RSV-surveillance through capture of RSV-associated ALRI cases. The aim of this project was to examine how the existing IB-VPD surveillance network may be leveraged to host RSV surveillance.

Patients and methods A systems analysis using 2015-2016 case-based surveillance data from 52942 cases captured by the IB-VPD network. Cases were classified as a 'Pneumonia', 'Severe Pneumonia' or 'Sepsis', using the case-based data and the Integrated Management of Childhood Illness case definitions. The clinical features used to compose the case definitions were analysed for data completion and missing data. A hand-search of current literature upon RSV surveillance was undertaken to identify key data and surveillance gaps that exist in the IB-VPD network. Data analysis was performed on R.

Results 14 countries undertook surveillance; 4 countries were eligible for targeted support by the GAVI. Through literature searches 'Chest wall in-drawing' and 'Sepsis' features were identified as key clinical features of severe RSV-associated ALRI and mortality. Completion ranged from 56% (Lethargy) to 87% (Severe malnutrition). Literature searches highlighted several data gaps within the IB-VPD network. PCR on Nasopharyngeal swabs (NPS), the gold standard of RSV infection diagnosis and serotyping, is not currently performed within the system. Apnoea and hypoxaemia are not collected within the network and have been identified as important markers of severe disease and mortality.

Conclusions The IB-VPD network requires greater representation of low income and resource poor nations within RSV surveillance to reflect the global distribution of RSV-associated healthcare burden. Additional capacities are required within the IB-VPD network to improve data collection of important existing and newly identified clinical features of severe RSV-associated ALRI and mortality and for the diagnosis and serotyping of RSV.

References

- 1 Shi T, McAllister DA, O'Brien KL et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *The Lancet*. 2017 Jul 7.

- 2 Giersing BK, Vekemans J, Nava S et al. WHO Product Development for Vaccines Advisory Committee. Report from the World Health Organization's third Product Development for Vaccines Advisory Committee (PDVAC) meeting, Geneva, 8–10th June 2016. Vaccine. 2017 Mar 3.

Best postgraduate poster prize winner

Effect of IV lidocaine on the resumption of gut function after colorectal surgery: a meta-analysis

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Introduction Resumption of normal gut function is a critical determinant of recovery after colorectal surgery. This study aims to evaluate whether IV lidocaine, an increasingly popular analgesic technique, accelerates return of gastrointestinal function after colorectal resection.

Methods A meta-analysis of randomised control trials was conducted comparing IV lidocaine as part of a multimodal analgesic regimen versus i) placebo and ii) epidural in patients undergoing colorectal resection. The primary outcome was time to first bowel movement. Secondary outcomes included other determinants of gut function, pain scores and opioid requirements.

Results Four hundred and ninety patients from ten RCTs were included. Time to first bowel movement was decreased and resumption of diet was accelerated with use of IV lidocaine compared to placebo when included in a multimodal analgesic regimen [8 studies, 353 patients, weighted mean difference -9.14 hours, 95% confidence interval -17.52 to -0.77, $p=0.03$]. Incidence of ileus, time to passage of first flatus, length of stay and numerical pain scores were reduced with IV lidocaine compared with placebo in subgroup analysis. No significant differences were demonstrated in indices of return of GI function in subgroup analysis comparing IV lidocaine and epidural analgesia. Epidural was associated with significantly lower pain scores compared with IV lidocaine.

Conclusions This meta-analysis is the first to look primarily at the resumption of gut function, an important marker of recovery, after colorectal resection in patients treated with IV lidocaine peri-operatively. Addition of IV lidocaine significantly promotes resumption of gut function compared to groups receiving systemic multimodal analgesia without lidocaine. IV lidocaine was not more effective than epidural analgesia in facilitating recovery of gut function. Further studies are warranted, specifically to evaluate the duration of IV lidocaine treatment.

Best undergraduate oral presentation winner

Immune extracellular vesicles as novel quantitative biomarkers of acute renal transplant rejection?

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Introduction Acute renal transplant rejection affects 10% of patients within their first year post-transplant¹. It is vital that rejection is diagnosed and treated to prevent graft failure¹. Renal biopsy is

the current 'gold-standard' diagnostic test for acute rejection². However, biopsy carries high risk of haemorrhage, detects *established* damage so cannot facilitate *preventative* intervention, and its invasive nature means it cannot be performed at sufficient frequency to enable clinical monitoring³. There is thus urgent need for a non-invasive biomarker to allow prediction, identification and prognostication of acute renal transplant rejection. Early preliminary research indicates extracellular vesicles (EVs) in urine may constitute qualitative biomarkers⁴, but the potential of EVs released by rejection-mediating immune cells to act as quantitative biomarkers has not yet been explored. An increasing body of recent evidence suggests immune-cell EVs to have a role in augmenting inflammatory responses⁵. Based on this we hypothesised that M1 macrophages and CD4⁺ T cells, cellular mediators of acute rejection⁶, upregulate expression of exosomes and microvesicles (key EV subsets) upon activation, and sought to test this hypothesis in vitro. If so, it would indicate future potential for immune cell EVs to act as quantitative biomarkers of renal transplant rejection.

Methods CD4⁺ T cells were magnetically isolated from peripheral blood of 4 healthy human donors and purified using flow cytometry. CD4⁺ T cells were cultured and split into 2 groups: unstimulated (received media alone) and stimulated (received aCD3 and aCD28). Monocytes were harvested from bone marrow of 3 C57BL/6 WT mice and cultured to stimulate macrophage differentiation. Macrophages were split into 2 groups: unstimulated (received media alone) and stimulated (received LPS and IFN- γ). Transmission electron microscopy was performed on supernatant of all cell groups to confirm release of EVs into cellular supernatant. The concentration of exosomes and microvesicles released into supernatant by activated and un-activated human CD4⁺ T cells and murine M1 macrophages was quantified using Nanoparticle Tracking Analysis and compared.

Results Supernatant from activated CD4⁺ T cells contained a significantly greater concentration of exosomes than that of unstimulated T cells (mean unstimulated = 286x10⁶/ml; mean stimulated = 998x10⁶/ml, P < 0.05). Supernatant from M1 macrophages contained a greater concentration of microvesicles than that of unstimulated macrophages, although statistical significance could not be demonstrated (mean unstimulated = 440x10⁶/ml; mean stimulated = 750x10⁶/ml).

Conclusions This project provides exciting preliminary evidence suggesting that macrophages and CD4⁺ T cells, key mediators of acute renal rejection, upregulate expression of at least one subset of EV upon activation. As these cell types have direct interface with the urinary space during acute rejection, we propose that with further optimisation and increasing technological advance, quantification of immune cell EVs in urine could constitute a novel biomarker of acute renal transplant rejection.

References

- 1 Matas AJ, Smith JM, Skeans MA et al. OPTN/SRTR 2012 Annual Data Report: Kidney. *Am J Transplant.* 2014; 14(1):11-14.
- 2 Racusen LC. Protocol Biopsies in kidney allografts: why and when are they indicated? *Clin J Am Soc Nephrol.* 2006; 1(1):144-7.
- 3 Ahhmad I. Biopsy of the transplanted kidney. *Semin Invent Radiol.* 2004; 21(4): 275-81.
- 4 Gámez-Valero A, Lozano-Ramos SI, Bancu I et al. Urinary extracellular vesicles as source of biomarkers in kidney diseases. *Front Immunol.* 2015; 6(1):1-10.
- 5 Robbins PD, Morelli AE. Regulation of immune responses by extracellular vesicles. *Nat Rev Immunol.* 2014; 14(3):195-208.
- 6 Nankivell BJ, Alexander SI. Rejection of the kidney allograft. *N Eng J Med.* 2010; 363(15):1451-62.

Best postgraduate oral presentation winner

Is metabolic syndrome in mid-life associated with increased risk of frailty at age 69? Findings from a British birth cohort study

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Introduction Recent evidence suggests that metabolic syndrome (MS) and frailty may have a shared pathogenesis. Early detection and treatment of MS in midlife may therefore present new opportunities to minimise risk of developing frailty in later life⁴. However there is limited evidence on the association between MS in mid-life and risk of frailty in later life. This study aimed to assess the association between MS at age 53 and risk of frailty at age 69. A secondary aim was to investigate whether prolonged exposure to MS was associated with greater frailty risk.

Patients and methods A total of 1676 participants from the MRC National Survey of Health and Development, a British birth cohort study, were included in analyses. MS was assessed at ages 53 and 60-64 and operationalised using a modified version of the ATP III definition. Frailty status was assigned at age 69 as non-frail, pre-frail or frail using an adapted 4-item phenotype. Cumulative exposure to MS was assessed from 53 to 60-64 years. Multinomial logistic regression was used to test the associations between both MS at 53 and cumulative exposure to MS and frailty with adjustment for potential confounders including gender, socioeconomic position and lifestyle factors.

Results Prevalence of MS at age 53 was 14%, rising to 27% by age 60-64. The prevalence of frailty and pre-frailty at age 69 was 3% and 33%, respectively. Participants with MS at age 53 had increased relative risks of pre-frailty and frailty at age 69 when compared with those without MS; these associations were only partially attenuated after adjustments. In a fully adjusted model the relative risk ratios (RRR) of pre-frailty and frailty when comparing those with and without MS at age 53 were 1.57 (95% CI: 1.16-2.10) and 4.90 (2.51-9.55), respectively. Greater length of exposure to MS was also associated with higher relative risk of frailty; RRR of frailty=4.20 (1.85-9.52) and 1.11 (0.36-3.48) when comparing those with 15 years and 5-8 years of exposure with those with no exposure to MS, respectively.

Conclusions MS at age 53 was associated with increased risk of frailty at 69 and there was evidence that this association was cumulative. This suggests that preventing or controlling MS in mid-life may be an important strategy to reduce subsequent risk of frailty.

References

- 1 Viscogliosi G, et al (2016). The metabolic syndrome and the phenotype of frailty: A causal link? *J Am Med Dir Assoc.* **17**(10):956-7.
- 2 Pérez-Tasigchana R, et al (2017). Metabolic syndrome and insulin resistance are associated with frailty in older adults: a prospective cohort study. *Age Ageing* (1):1-6.
- 3 Barzilay et al. (2007). Insulin Resistance and Inflammation as Precursors of Frailty. *JAMA Internal Medicine.* **167** (7) 635-641.
- 4 Jeffery et al, Emerging drug therapies for frailty. *Maturitas.* 2013 Jan;**74**(1):21-5.

Undergraduate abstracts

A cross-sectional analysis of undergraduate medical student attitudes towards interprofessional education

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Introduction This paper aims to assess medical student's attitudes towards interprofessional education (IPE), and how these attitudes may alter as students' progress through a curriculum integrated with structured interprofessional scenarios and clinical placements.

In a higher education setting, IPE refers to scenarios where students from different professional disciplines learn together, with the overall aim of cultivating a more collaborative and communicative healthcare workforce in the future¹. IPE has been outlined as a fundamental strategy in addressing health needs globally and locally, with initiatives across the world providing an evidence base that demonstrates the advantages IPE has on an educational, social, and professional basis.

Patients and methods This cross-sectional study used a total of 660 questionnaire responses and two focus groups to evaluate attitudes towards IPE in medical students from first to fifth (final) year at the University of Glasgow.

Results The study identified very strong support for IPE in students yet to undergo clinical placements, with a distinct trend towards a more neutral response as students progressed to the clinical years of their teaching.

Conclusions This study outlined that the implementation of IPE in the early stages of higher education is vital, with the greatest perceived advantages seen prior to students entering their clinical years. As studies have shown, optimising the benefits of IPE is resource-heavy, and requires careful collaboration between departments to produce an interprofessional programme that benefits all disciplines involved.

References

Framework for Action on Interprofessional Education & Collaborative Practice. (2010). World Health Organisation, p.7. http://www.who.int/hrh/nursing_midwifery/en/ [Accessed 3 Apr. 2017].

Adverse Left Ventricular Remodelling in Patients with Aortic Stenosis

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Introduction Aortic stenosis (AS) is the most common type of primary valvular heart disease in the elderly with an increasing prevalence in Scotland. Its impact on public health and health care resources is expected to increase due to our aging population. There is increasing appreciation that AS is also a disease of the left ventricle (LV) involving a maladaptive process with potentially irreversible consequences that impact on LV function and on the development of symptoms. We have conducted 2 studies to better understand the pathophysiology of this maladaptive process. In

the first study (**Study 1**), we investigated the prevalence and demographics of adverse LV remodeling in patients with AS in Tayside, Scotland. Recognising that not all patients with AS develop adverse LV remodelling, in our second study (**Study 2**), we explored the genetics of AS and adverse LV remodelling in a cohort of diabetic patients with AS with available DNA for analysis.

Patients and methods Study 1. Following Caldicott Guardian approval, we performed a retrospective analysis of 200 consecutive patients diagnosed with AS in NHS Tayside. ECGs from these patients were analysed for ECG evidence of LVH and ECG strain, defined as ≥ 1 -mm concave down-sloping ST-segment depression with asymmetrical T-wave inversion in the lateral leads. ECG strain has previously been shown to be a specific marker of midwall myocardial fibrosis, a feature of LV remodeling that predicts adverse clinical outcomes in AS (1). **Study 2.** This was an approved record linkage study of the Genetics of Diabetes Audit and Research in Tayside Scotland (GoDARTS) cohort. Patients with AS were identified from the GoDARTS echocardiographic database that was further phenotypically interrogated to identify patients with bicuspid and chronic degenerative aortic stenosis and those with LVH and left ventricular systolic dysfunction (LVSD) as reported by British Society of Echocardiography accredited echocardiographers. The echocardiographic parameters was analysed with genome-wide genotypes for LVH and LVSD.

Results Study 1. 200 consecutive patients with AS (mean age 69 ± 22 yrs, 48% females, 23% Diabetes, 65% hypertension, 29% CAD, 7% NYHA class III and IV) were identified for study. 46 (23%) were found to have ECG strain pattern. ECG strain was associated with more severe AS ($P=0.001$) and more atrial fibrillation (30% vs 16%, $P=0.05$). **Study 2.** From the GoDARTS echocardiographic database, 1686 patients with AS were identified with 21 patients with bicuspid AS and 1665 patients chronic degenerative AS. Further investigation for maladaptive LV remodeling in patients with chronic degenerative AS identified 1005 (60%) patients had LVH and 419 (25%) patients had LVSD. The association between the adverse LV remodeling phenotypes and single nucleotide polymorphisms (SNPs) that had previously been reported associated with LVH (rs17132261, rs2292462, rs4343, rs4291, rs9838915 and rs6796325) and heart failure (rs6696224, rs2466052, and rs3823879) was examined with calculation for a genetic risk score (GRS) for adverse LV remodeling in AS.

Conclusions We have shown that ECG strain, an ECG feature of adverse LV remodelling, is relatively prevalent in AS patients and is associated with more severe AS and more prevalent atrial fibrillation. Ongoing work exploring the genetics of AS will help us to better understand the pathophysiology of the disease. This understanding may help us to better define treatment strategies for patients with AS.

References

1. Shah ASV, Chin CWL, Vassiliou V et al. Left ventricular hypertrophy with strain and aortic stenosis. *Circulation*. 2014 Oct 28;130(18):1607–16.

Is the response to cartilage injury altered in mice that have reduced adipose tissue in the knee?

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Introduction Osteoarthritis is the most common degenerative joint disease in the UK and comprises loss of articular cartilage, subchondral bone changes and inflammation of the joint tissues. Articular adipose tissue, including the infrapatellar fat pad in the knee, is known to contribute to joint tissue

inflammation by releasing adipokines and cytokines, but it is unknown to what extent these influence the response to cartilage injury. The thin membrane that covers the surface of the infrapatellar fat pad facing the cartilage, called synovium, undergoes hyperplasia after joint surface injury.

Patients and methods To investigate the role of the adipose tissue in the knee on the synovial hyperplasia in response to cartilage injury, a transgenic mouse model with less articular adipose tissue was used. The mice underwent surgery on one knee to injure the cartilage (Eltawil et al., 2009), and the other knee was left as an uninjured control. The same procedure was repeated on littermate control mice. Synovial hyperplasia was assessed in histological sections of the knees using two parameters: cell proliferation in the synovium was measured using immunohistochemical detection of the proliferation marker BrdU, and synovial cell number changes were quantified from haematoxylin and eosin-stained sections using histological image analysis.

Results Validation of the transgenic mouse model was carried out by histology showing an approximately 50% reduction in the size of the infrapatellar fat pad of the knee compared to littermate controls. Following cartilage injury in control mice, immunohistochemical analysis of BrdU incorporation into proliferating cells showed a significant increase in synovial cell proliferation after cartilage injury, as previously reported (Kurth et al., 2011). Quantification of synovial cell number demonstrated increased cellularity of the synovium. There was no significant difference in either parameter of synovial hyperplasia between control mice and their littermates with reduced joint fat.

Conclusions These findings demonstrate that joint fat reduction has no measureable effect on the degree of synovial hyperplasia in response to cartilage injury in the knee in this model, suggesting that articular adipose tissue may not play a key role in the synovial response to joint injury.

References

- 1 Eltawil, N. M., De Bari, C et al. (2009). A novel in vivo murine model of cartilage regeneration. Age and strain-dependent outcome after joint surface injury. *Osteoarthritis and Cartilage* **17**, 695-704.
- 2 Kurth, T. B., Dell'Accio, F., Crouch, V et al. (2011). Functional mesenchymal stem cell niches in adult mouse knee joint synovium in vivo. *Arthritis and Rheumatism* **63**, 1289-1300.

Evaluation of Learning Styles in a Surgical Unit

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Introduction In this article, the dominant learning styles present in a surgical department and the importance of knowing one's own learning style, especially in a field like surgery, in order to enhance surgical education will be discussed.

Patients and methods A Kolb's learning style questionnaire was administered to 5 grades, in total 43 people. The scores of the questionnaire was totalled and their dominant learning style was identified.

Results Most dominant styles were pragmatist and activist. Theorist and reflector styles only found in Medical students and FY doctors, and one senior middle grader. This fits well with a medical student who has just begun their process of learning and therefore is at the start of the learning cycle

Conclusions The various learning styles of different grades in a surgical unit were identified. It was understood from this research that there is no uniform learning style for surgeons in this particular surgical setting. No particular learning style correlated to surgeons and consultants but there was a progression shown from medical students to consultants.

References

- 1 What is a Learning Style? International Learning Styles. [Cited 30th May 2017]
<http://www.ilsa-learningstyles.com/Learning+Styles/What+is+Learning+Style.html>
- 2 What are learning styles? [Cited 30th May 2017]
<http://web.cortland.edu/andersmd/learning/Introduction.htm>
- 3 Kolb's learning cycle. Mirjam S. Glessmer. [Internet]. 2014, 8th Oct. Cited 30th May 2017].
<http://mirjamglessmer.com/2014/10/08/kolbs-learning-cycle/>
- 4 Kolb – Learning Styles. Simply Psychology. 2013. [Cited 30th May, 2017].

The Significance of Injury Combinations in Children Referred for a Forensic Medical Examination

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Introduction Although multiple researchers have investigated injuries in physical child abuse, the significance and predictive value of injuries in combination is generally not well documented. This study investigated whether the presence of multiple types of injury is suggestive of abuse, and considered whether external injuries can predict or exclude internal ones.

Patients and methods Clinical case files of forensic medical examinations of children in Tayside between 2011 and 2016 were retrospectively reviewed. Details of injuries were recorded.

Results There was a statistically significant difference ($P < 0.05$) between the proportion of abused (66.04%) and accidentally injured (37.50%) children who had multiple types of 'standard' injury. Abused children were also significantly more likely to have multiple types of injury in the same body region than accidentally injured children (52.83% vs 20.83%). There was no significant difference in the proportion of abused and accidentally injured children with bruises and abrasions in combination; however, abused children were significantly more likely to have spatially related bruises and abrasions (44.30% vs 20.83%). Overlying bruising was rare in abusive fractures (1/58 fractures), but 7/9 abused children had bruising elsewhere on the body. 2/2 children with accidental fractures had overlying swelling, compared to only 2/9 abused children.

Conclusions The presence of multiple injury types in children referred for forensic medicine examinations is suggestive of abuse, especially if located in the same body region. However, injuries in combination are not completely sensitive for, and specific to, abuse. Cutaneous injuries appear to poorly predict internal ones.

References

- 1 FFLM (2013). Proforma – Body Diagrams. <https://fflm.ac.uk/publications/pro-forma-body-diagrams/> [Accessed 14 May 2017].
- 2 National Institute for Health and Clinical Excellence (2009). Child maltreatment: when to suspect maltreatment in under-18s. NICE Guidelines [CG89].

- 3 RCPCH (2013). Child Protection Companion. <http://www.rcpch.ac.uk/child-protection-companion> [Accessed 14 May 2017].

NAFLD Fibrosis Score to Diagnose Patients without Significant Fibrosis

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Introduction NAFLD Fibrosis Score has been suggested to be an accurate diagnostic tool to determine patients with or without advanced fibrosis, rendering unnecessary liver biopsy for identification of advanced fibrosis. This study was aimed to investigate the utility of NAFLD Fibrosis Score by comparing the possible relationships between FibroScan and NAFLD Fibrosis Score.

Patients and methods We collected a total of 132 sets of mandatory measured parameters (age, diabetes mellitus status, BMI, platelet count, albumin, AST/ALT ratio) to calculate the NAFLD Fibrosis Score and FibroScan result from 58 liver-biopsy diagnosed NAFLD patients with regular follow ups at Ninewells Hospital.

Results Our results suggest that, by applying the NAFLD Fibrosis Score, the NAFLD Fibrosis Score that lies in the range of F0-F1 was most reliable. From our study, 80% of the total collected data with FibroScan Score of F1 matched with NAFLD Fibrosis Score of F0-F1. On the contrary, results were almost equally distributed between NAFLD Fibrosis Score of F0-F2 & Indeterminate for both FibroScan score, F2 & F3. In this study, there was no NAFLD Fibrosis Score of F1-F2 in conjunction with FibroScan Score of F4 and no NAFLD Fibrosis Score of F3-F4 in conjunction with FibroScan Score of F1. This deduces the possible accuracy of the NAFLD Fibrosis Score in diagnosing patients without severe fibrosis. Based on this study, the sensitivity and specificity of NAFLD Fibrosis Score to diagnose significant fibrosis were 40% and 98.7%, respectively. Positive and negative predictive values were 0.80 and 0.93, respectively.

Conclusions NAFLD Fibrosis Score constructed from routine clinical and laboratory variables can accurately predict the absence of advanced fibrosis in NAFLD, rendering liver biopsy and FibroScan unnecessary in the vast majority of the patients.

Patient-specific simulation of pneumoperitoneum for laparoscopic surgical planning

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Introduction Laparoscopy is a minimally invasive method of abdominal surgery. A workspace for instrumentation is created by insufflating the abdominal cavity with gas, which distends the abdominal wall and separates it from the viscera (creating a temporary pneumoperitoneum). Well-placed trocars are an essential determinant of the operative ease and quality of laparoscopy. Surgical planning is often based on preoperative images, which do not account for the deformations caused by pneumoperitoneum, making pre-planned trocar positions inconsistent with their true positions in the final operation setup. This research aims to develop a platform that simulates the anatomical changes resulting from gas insufflation during laparoscopy in a patient-specific manner, using preoperative CT scans as the input data. This intends to improve surgical planning by providing a more realistic representation of the intraoperative scenario and guide trocar positioning in a way that optimises the ergonomics of laparoscopic instrumentation.

Patients and methods The simulation was developed by generating 3D reconstructions of insufflated and deflated porcine CT scans and simulating an artificial pneumoperitoneum on the deflated model. Simulation parameters were optimised by minimising the discrepancy between the simulated pneumoperitoneum and the ground truth model extracted from insufflated porcine scans. Insufflation modelling in humans was investigated by correlating the simulation's output to real post-insufflation measurements obtained from patients in theatre.

Results The simulation successfully modelled pneumoperitoneum in the porcine dataset, producing an average error of 7.26mm in the most accurate and 10.5mm in the least accurate simulations. The framework was demonstrated to be capable of simulating pneumoperitoneum in humans by inputting a patient's preoperative image data.

Conclusions This project initiated the development of a technology that could guide trocar placement in a way that achieves the optimal operative ergonomics for the laparoscopic surgeon. The benefits of a patient-specific simulation of pneumoperitoneum for image guidance systems in laparoscopy are discussed.

References

- 1 Alkatout I, Mettler L, Maass N, Noé GK, Elessawy M. *Abdominal anatomy in the context of port placement and trocars*. [Online] Journal of the Turkish German Gynecology Association. 2015. p. 241–251. Available from: doi:10.5152/jtgga.2015.0148
- 2 Chang C, Steinberg Z, Shah A, Gundeti MS. Patient Positioning and Port Placement for Robot-Assisted Surgery. *Journal of Endourology*. [Online] 2014;28(6): 631–638. Available from: doi:10.1089/end.2013.0733
- 3 Supe AN, Kulkarni G V, Supe PA. Ergonomics in laparoscopic surgery. *Journal of minimal access surgery*. [Online] 2010;6(2): 31–36. Available from: doi:10.4103/0972-9941.65161
- 4 Jafari MD, Stamos MJ, Mills S. Patient Positioning, Instrumentation, and Trocar Placement. In: Ross MD FACS FASCRS HM, Lee MD FACS FSW, Mutch MD FACS FMG, Rivadeneira MD MBA FFDE, Steele M.D. FACS FSR (eds.) *Minimally Invasive Approaches to Colon and Rectal Disease: Technique and Best Practices*. [Online] New York, NY: Springer New York; 2015. p. 15–24. Available from: doi:10.1007/978-1-4939-1581-1_2
- 5 Thepsuwan J, Huang K-G, Wilamarta M, Adlan A-S, Manvelyan V, Lee C-L. Principles of safe abdominal entry in laparoscopic gynecologic surgery. *Gynecology and Minimally Invasive Therapy*. [Online] 2013;2(4): 105–109. Available from: doi:10.1016/j.gmit.2013.07.003 [Accessed: 25th March 2017]
- 6 Krishnakumar S, Tambe P. Entry Complications in Laparoscopic Surgery. *Journal of Gynecological Endoscopy and Surgery*. [Online] India: Medknow Publications & Media Pvt Ltd; 2009;1(1): 4–11. Available from: doi:10.4103/0974-1216.51902
- 7 Sánchez-Margallo FM, Moyano-Cuevas JL, Latorre R, Maestre J, Correa L, Pagador JB, et al. Anatomical changes due to pneumoperitoneum analyzed by MRI: An experimental study in pigs. *Surgical and Radiologic Anatomy*. [Online] 2011;33(5): 389–396. Available from: doi:10.1007/s00276-010-0763-9

- 8 Elliott RC, Kirberger RM. Computed Tomography Determined Changes in Position of the Urogenital System After CO₂ Insufflation to Determine Optimal Positioning for Abdominal Laparoscopy. *Veterinary Surgery*. [Online] 2015;44(S1): 91–99. Available from: doi:10.1111/vsu.12351
- 9 Song C, Alijani A, Frank T, Hanna GB, Cuschieri A. Mechanical properties of the human abdominal wall measured in vivo during insufflation for laparoscopic surgery. *Surg Endosc*. [Online] 2006;20(6): 987–990. Available from: doi:10.1007/s00464-005-0676-6
- 10 Soler L, Marescaux J. Patient-specific surgical simulation. *World Journal of Surgery*. [Online] 2008;32(2): 208–212. Available from: doi:10.1007/s00268-007-9329-3
- 11 Zevin B, Aggarwal R, Grantcharov TP. Surgical Simulation in 2013: Why Is It Still Not the Standard in Surgical Training? *Journal of the American College of Surgeons*. [Online] 2014;218(2): 294–301. Available from: doi:http://dx.doi.org/10.1016/j.jamcollsurg.2013.09.016
- 12 Abboudi H, Khan MS, Aboumarzouk O, Guru KA, Challacombe B, Dasgupta P, et al. *Current status of validation for robotic surgery simulators a systematic review*. [Online] BJU International. 2013. p. 194–205. Available from: doi:10.1111/j.1464-410X.2012.11270.x
- 13 Makiyama K, Nagasaka M, Inuiya T, Takanami K, Ogata M, Kubota Y. Development of a patient-specific simulator for laparoscopic renal surgery. *International Journal of Urology*. [Online] Blackwell Publishing Asia; 2012;19(9): 829–835. Available from: doi:10.1111/j.1442-2042.2012.03053.x
- 14 Kitasaka T, Mori K, Hayashi Y, Suenaga Y, Hashizume M, Toriwaki J. Virtual Pneumoperitoneum for Generating Virtual Laparoscopic Views Based on Volumetric Deformation. In: Barillot C, Haynor DR, Hellier P (eds.) *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2004: 7th International Conference, Saint-Malo, France, September 26-29, 2004. Proceedings, Part II*. [Online] Berlin, Heidelberg: Springer Berlin Heidelberg; 2004. p. 559–567. Available from: doi:10.1007/978-3-540-30136-3_69
- 15 Bano J, Hostettler A, Nicolau SA, Cotin S, Doignon C, Wu HS, et al. Simulation of Pneumoperitoneum for Laparoscopic Surgery Planning. *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2012*. [Online] 2012. p. 91–98. Available from: http://link.springer.com/chapter/10.1007/978-3-642-33415-3_12
- 16 Bano J, Hostettler A, Nicolau SA, Doignon C, Wu HS, Huang MH, et al. Simulation of the Abdominal Wall and Its Arteries after Pneumoperitoneum for Guidance of Port Positioning in Laparoscopic Surgery. In: Bebis G, Boyle R, Parvin B, Koracin D, Fowlkes C, Wang S, et al. (eds.) *Advances in Visual Computing: 8th International Symposium, ISVC 2012, Rethymnon, Crete, Greece, July 16-18, 2012, Revised Selected Papers, Part I*. [Online] Berlin, Heidelberg: Springer Berlin Heidelberg; 2012. p. 1–11. Available from: doi:10.1007/978-3-642-33179-4_1
- 17 Oktay O, Zhang L, Mansi T, Mountney P, Mewes P, Nicolau S, et al. Biomechanically driven registration of pre- to intra-operative 3D images for laparoscopic surgery. *Lecture*

Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics). [Online] 2013. p. 1–9. Available from: doi:10.1007/978-3-642-40763-5_1

- 18 Nimura Y, Di Qu J, Hayashi Y, Oda M, Kitasaka T, Hashizume M, et al. Pneumoperitoneum simulation based on mass-spring-damper models for laparoscopic surgical planning. *Journal of Medical Imaging*. [Online] Society of Photo-Optical Instrumentation Engineers; 2015;2(4): 44004. Available from: doi:10.1117/1.JMI.2.4.044004
- 19 Müller M, Heidelberger B, Hennix M, Ratcliff J. Position based dynamics. *Journal of Visual Communication and Image Representation*. [Online] 2007;18(2): 109–118. Available from: doi:10.1016/j.jvcir.2007.01.005
- 20 Peters TM. Image-guidance for surgical procedures. *Physics in medicine and biology*. [Online] 2006;51(14): R505–R540. Available from: doi:10.1088/0031-9155/51/14/R01
- 21 Mårvik R, Langø T, Tangen GA, Andersen JO, Kaspersen JH, Ystgaard B, et al. Laparoscopic navigation pointer for three-dimensional image-guided surgery. *Surgical Endoscopy and Other Interventional Techniques*. [Online] 2004;18(8): 1242–1248. Available from: doi:10.1007/s00464-003-9190-x
- 22 Goldman LW. Principles of CT: radiation dose and image quality. *Journal of nuclear medicine technology*. [Online] 2007;35(4): 213-225-228. Available from: doi:10.2967/jnmt.106.037846
- 23 Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, et al. User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. *NeuroImage*. [Online] 2006;31(3): 1116–1128. Available from: doi:10.1016/j.neuroimage.2006.01.015
- 24 Cignoni P, Cignoni P, Callieri M, Callieri M, Corsini M, Corsini M, et al. MeshLab: an Open-Source Mesh Processing Tool. *Sixth Eurographics Italian Chapter Conference*. [Online] 2008; 129–136. Available from: doi:10.2312/LocalChapterEvents/ItalChap/ItalianChapConf2008/129-136
- 25 Camara M, Mayer E, Darzi A, Pratt P. Soft tissue deformation for surgical simulation: a position-based dynamics approach. *International Journal of Computer Assisted Radiology and Surgery*. [Online] 2016;11(6): 919–928. Available from: doi:10.1007/s11548-016-1373-8
- 26 Lee JS, Hong TH. In vivo porcine training model for laparoscopic Roux-en-Y choledochojejunostomy. *Annals of Surgical Treatment and Research*. [Online] The Korean Surgical Society; 2015;88(6): 306–310. Available from: doi:10.4174/astr.2015.88.6.306
- 27 Sung GT, Sun Y. Animal Laboratory Training: Current Status and How Essential Is It? In: Hemal AK, Menon M (eds.) *Robotics in Genitourinary Surgery*. [Online] London: Springer London; 2011. p. 147–156. Available from: doi:10.1007/978-1-84882-114-9_12
- 28 Dondelinger RF, Ghysels MP, Brisbois D, Donkers E, Snaps FR, Saunders J, et al. Relevant

- radiological anatomy of the pig as a training model in interventional radiology. *European Radiology*. [Online] 1998;8(7): 1254–1273. Available from: doi:10.1007/s003300050545
- 29 Ansell J, Goddard S, Gupta V, Warren N, Williams G, Haray P, et al. A new ex vivo animal simulation model for skills training in laparoscopic colorectal surgery. *The Bulletin of the Royal College of Surgeons of England*. [Online] The Royal College of Surgeons of England; 2014;96(4): 122–124. Available from: doi:10.1308/rcsbull.2014.96.4.122
- 30 Miller K, Lu J. On the prospect of patient-specific biomechanics without patient-specific properties of tissues. *Journal of the Mechanical Behavior of Biomedical Materials*. [Online] 2013;27: 154–166. Available from: doi:10.1016/j.jmbbm.2013.01.013
- 31 Hughes-Hallett A, Pratt P, Mayer E, Clark M, Vale J, Darzi A. Using preoperative imaging for intraoperative guidance: a case of mistaken identity. *International Journal of Medical Robotics and Computer Assisted Surgery*. [Online] 2016;12(2): 262–267. Available from: doi:10.1002/rcs.1654
- 32 Ahmad G, Gent D, Henderson D, O’Flynn H, Phillips K, Watson A. Laparoscopic entry techniques. *The Cochrane database of systematic reviews*. [Online] 2015;8: CD006583. Available from: doi:10.1002/14651858.CD006583.pub4
- 33 Saber A a, Mesleman AM, Davis R, Pimentel R. Safety zones for anterior abdominal wall entry during laparoscopy: a CT scan mapping of epigastric vessels. *Annals of surgery*. [Online] 2004;239(2): 182–185. Available from: doi:10.1097/01.sla.0000109151.53296.07
- 34 Balzer KM, Witte H, Recknagel S, Kozianka J, Waleczek H. Anatomic guidelines for the prevention of abdominal wall hematoma induced by trocar placement. *Surgical and Radiologic Anatomy*. [Online] 1999;21(2): 87–89. Available from: doi:10.1007/s00276-999-0087-9
- 35 Sugimoto M, Yasuda H, Koda K, Suzuki M, Yamazaki M, Tezuka T, et al. Image overlay navigation by markerless surface registration in gastrointestinal, hepatobiliary and pancreatic surgery. *Journal of Hepato-Biliary-Pancreatic Sciences*. [Online] 2010;17(5): 629–636. Available from: doi:10.1007/s00534-009-0199-y
- 36 Bernhardt S, Nicolau SA, Soler L, Doignon C. The status of augmented reality in laparoscopic surgery as of 2016. *Medical Image Analysis*. [Online] Elsevier; 2017;37: 66–90. Available from: doi:10.1016/j.media.2017.01.007
- 37 Kim HL, Schulam P. *The PAKY, HERMES, AESOP, ZEUS, and da Vinci robotic systems*. [Online] Urologic Clinics of North America. 2004. p. 659–669. Available from: doi:10.1016/j.ucl.2004.06.008

The role of O-GlcNAcylation of CRMP2 on cognitive function and behaviour

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Introduction Collapsin response mediator protein-2 (CRMP2)¹ is a key protein in the central nervous system involved in neuronal development, axon growth and cell migration. Recent evidence has linked CRMP2 to a range of neurodegenerative and psychiatric diseases¹ though the exact relationship and mechanism of this remains elusive. O-GlcNAcylation involves the post-translational modification (PTM) of proteins with a single sugar modification at serine or threonine residues². Interest in this PTM lies in its therapeutic potential for the treatment of neurodegenerative and psychiatric diseases³. CRMP2 contains a serine residue and has been shown to be one of the main neuronal proteins to undergo O-GlcNAcylation⁴. However, the relationship between CRMP2 and O-GlcNAcylation is poorly understood and the effect (or lack of) O-GlcNAcylation on CRMP2 has not been well characterised. Therefore the aim of this study was to characterise the cognitive and behavioural phenotype of O-GlcNAcylation of CRMP2.

Patients and methods Genetically altered CRMP2 mice were bred in which the serine residue was replaced with alanine (S517A knock-in; CRMP2^{S517A/S517A}). This created a functional CRMP2 protein but one which could not undergo O-GlcNAcylation therefore allowing for the cognitive and behavioural effects of O-GlcNAcylation on CRMP2 to be determined. Male CRMP2^{S517A/S517A} and WT littermate matched control animals (n=10-12 per group) underwent a series of behavioural and cognitive tests to assess cognition and behaviour. The Novel object recognition (NOR), open field and spontaneous alternation test were used to assess recognition memory, anxiety and spatial memory respectively. Data are expressed as mean +/- SEM and statistical analysis performed using Graphpad prism with significance of p<0.05.

Results The NOR test was performed twice and in both trials, the CRMP2^{S517A/S517A} knock-in mice were unable to perform the task having a significantly lower discrimination index (D3) compared with the WT (p<0.05). CRMP2^{S517A/S517A} knock-in mice were also less mobile during the test phase (p<0.01). Of note there was a significant positive correlation between D3 index and distance travelled (r= p<0.05). Despite the CRMP2^{S517A/S517A} knock-in mice travelling less distance than the WT in the NOR test there was no difference in the open field in terms of duration of movement or time spent in the central zone. Likewise there was no significant difference in the spontaneous alternation task between genotypes.

Conclusions The results of this study show that CRMP2^{S517A/S517A} knock-in mice have a specific deficit in recognition memory. No other behavioural or cognitive deficits were found. This suggests that O-GlcNAcylation of CRMP2 within the entorhinal cortex is important for the creation and storage of certain aspects of memory⁵. As CRMP2 and O-GlcNAcylation are implicated in neurodegenerative diseases, this may help shed light upon the role of CRMP2 and O-GlcNAcylation in these conditions.

References

- 1 Hensley, K. & Kursula, P. (2016). *J Alzheimers Dis.* 53(1): 1 – 14.
- 2 Zeidan, Q. & Hart, G. W. (2010). *J Cell Sci.* 123(1): 13 – 22.
- 3 Zhu, Y., et al. (2014). *J. Biol. Chem.* 289: 34472 – 34481.
- 4 Yamashita, N., et al. (2012). *J. Neurosci.* 32(4): 1360 – 1365.
- 5 Tallent, M. K., et al. (2009). *J. Biol. Chem.* 284: 174 – 181.

Is Intelligence Associated with the Presence of Internalising Traits in Adolescents with Autism Spectrum Disorder? A Meta-analysis.

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Introduction Intelligence, defined by intelligence quotient (IQ), has been found to relate to the presence of internalising symptoms in autism spectrum disorder (ASD). However, existing evidence disagrees on the direction of this relationship. This study sought to clarify the association between IQ and two prevailing internalising traits, anxiety and depression, in adolescents with ASD. It also aimed to highlight methodological factors contributing to inconsistent findings in existing research.

Patients and methods A meta-analysis, with anxiety and depression as separate outcomes, was performed to investigate the relationship between these internalising traits and IQ. A systematic literature search in 3 electronic databases identified 13 studies for the anxiety outcome and 4 studies for the depression outcome. Additionally, sub-group analyses were undertaken for the anxiety outcome to test the potential moderating effects of: self versus caregiver-reported anxiety; psychiatric medication use; IQ range analysed; age; gender; effect size type, and criteria used by the anxiety measure.

Results Overall, no significant correlation was found between anxiety and IQ in youth with ASD. However, self versus caregiver-reported anxiety significantly affected this result. When self-reported, anxiety was higher in those with a lower IQ. Tentative findings also suggested that adolescents with an IQ closer to 70 experience greater anxiety, warranting more research. Depression was positively associated with IQ in adolescents with ASD.

Conclusions Further research investigating anxiety subtypes separately, using both caregiver and self-reports, will advance the understanding of the relationship between IQ and anxiety. Parents and clinicians should be cautious of underestimating anxiety and depression levels in youth with a lower IQ. Equally, care should be taken to ensure that autistic adolescents without significant intellectual disabilities are not overlooked in terms of social and emotional support.

Discharge Letters: Improving Accuracy & Content

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Introduction Immediate discharge letters (IDLs) are the initial documents provided to patients and GPs detailing a patient's stay. In Scotland, they may be the only documentation received by the GP and are essential for informed management of a patient's ongoing care following discharge. In addition, *'the preparation and sharing of accurate and timely records of care and treatment are central aspects of good clinical practice and the principles of good medical practice set out by the General Medical Council (GMC).'*¹

The audit was conducted to establish current practice in regards to IDL scribing amongst patients who were discharged from a general surgical ward at the Queen Elizabeth University Hospital.

Patients and methods Criteria from the SIGN Guideline 128 - The Discharge Document, which provides a template for both IDLs and FDLs (final discharge letters), and the general surgical departmental standardised co morbidity list, were used.

The audit involved a retrospective case note review of electronic patient records of eligible patients discharged during a four week period. Then a simple intervention was implemented and a repeat audit of IDLs of patients discharged during the same length of time was conducted to compare whether there was a change in practice.

Results Compliance with the guideline was variable, with some criteria such as presenting complaint being documented 99% of the time, whilst source of referral was poor at 3%. Patients who self-discharged often had less compliant IDLs. In addition, some IDLs were headed with 'unfinished' but had been authorised and printed.

The re-audit demonstrated variable improvement. However, this may have been affected by the change in FY1s as a result of the end of the rota block; the intervention may have had a shorter impact or reduced impact. In addition, often paper interventions on the wards were removed from the nursing stations and may not have been noticed by the new FY1s.

Conclusions IDL scribing on this surgical ward during this period were variable but a simple paper based intervention highlighting the SIGN guideline and departmental requirements showed an overall improvement in compliance. Recommendations for further improvement include providing teaching to FY1s on IDL scribing, focusing on what content is required with feedback to scribes on their IDL scribing.

References

- 1 Scottish Intercollegiate Guidelines Network. SIGN 128 The SIGN discharge document. <http://www.sign.ac.uk/pdf/sign128.pdf> (accessed 12 December 2016)
- 2 General Medical Council. Professionalism in action. http://www.gmc-uk.org/guidance/good_medical_practice/professionalism_in_action.asp (accessed 18 May 2017)

The human urothelial tight junction: ZO3 function

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Introduction Human urothelium is the highly specialised transitional epithelium lining the ureters, bladder and proximal urethra. Its function as a permeability barrier against urine is important in minimising cell dissociation; a phenomenon associated with metastatic progression of bladder cancer and pathophysiology of UTI and interstitial cystitis (Haynes 2005, Keay 2014). Tight junction (TJ) proteins afford this epithelium the tightest barrier function of all epithelia and following previous research showing localisation of TJ protein ZO3 to terminal TJ regions (Hinley, pers.comm2016), this research aims to investigate the role of ZO3 in establishing and maintaining this barrier.

Patients and methods Knockdown study (k/d) – Normal human urothelial (NHU) cells derived and cultured from patient ureter samples were retrovirally transduced to knockdown ZO3. To achieve this shRNAs were designed against three ZO3 mRNA regions alongside a scrambled control and

ligated into pSIREN-RetroQ vectors. Following cloning by bacterial transformation, these vectors were used to transfect the shRNAs into PT67 cells for viral packaging. Viral PT67 supernatant was applied to proliferating NHU cells to achieve the ZO3 knockdown. Successfully transduced cells were selected for using Puromycin and cultured with Ca^{2+} to induce stratification and barrier formation (Southgate 1994). [Diagram available at request]

Barrier function was assessed by measuring transepithelial resistance (TER) via electrodes placed on either side of the cell layer. Cell layers were also scratched and TER measured to assess barrier recovery. Finally, immunoblotting techniques were used to determine expression and quantity of other relevant TJ proteins.

Results ZO3 k/d at mRNA location #1 showed insufficient growth to run barrier studies. ZO3 k/d at mRNA location #2 revealed earlier and tighter formation of a barrier compared with the control. This result was important as lysates showed k/d #2 to have achieved the best ZO3 silencing. ZO3 k/d #3 revealed a barrier formation similar to the scrambled control. Lysate analysis suggests low k/d efficiency with possible retained ZO3 function. Expression of other TJ proteins (ZO1/2, Claudin 3/5) in each cell line was comparable to the control. Barrier recovery analysis for ZO3 k/d cells demonstrated a reduced response in reforming a competent barrier following scratch compared to the control (Over 24 hours).

Conclusions Preliminary results suggest k/d of ZO3 may be linked with more rapid development of a tight barrier in cultured NHU cells. This implies that ZO3 itself hinders TJ formation however further investigation as to whether this is a direct effect is required as results may also be attributable to: shRNA off-target effects or a possible feedback response to ZO3 k/d in place to protect barrier function. Expression of ZO1, ZO2, Claudin 3 and Claudin 5 remained unchanged following ZO3 k/d such that their influence on achieving the earlier tighter barrier or forming a feedback response is considered negligible. Finally, barrier recovery results suggest ZO3 may be critical in achieving functional barrier formation following damage. Results are, however, difficult to interpret without further investigation into any ZO3 influence on cell migration and sheet healing independent of barrier formation. This, alongside replication of current work and conducting ZO3 overexpression studies are the next steps.

References

- 1 Haynes, MD et al 2005 '*Tight junctions and bladder cancer (Review)*' Int J Mol Med 16(1):3-9.
- 2 Keay, SK. et al 2014 '*Evidence For Bladder Urothelial Pathophysiology In Functional Bladder Disorders*'. BioMed Research International 2014: 1-15./ Hinley pers.comm 20th January 2016.
- 3 Southgate, J et al 1994 '*NHU Cells In vitro: Proliferation & Induction of Stratification.*' Laboratory investigation 77(4):583-94.

Patient Carer Community (PCC) at University of Leeds: exploring the impact on patients and carers, students and staff.

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Introduction Patients as educators have been an integral part of medical education since the 1960s.

Since then, patients' roles have developed from not only being used in teaching as passive 'subjects' but as actual teachers such as giving formal feedback and improving students' learning. ⁽¹⁾ Research has shown that there is definite benefit which has been shown in integrating patients' input and care into medical education. However, we know very little about how to optimise its impact or the processes involved in preparing, developing and evaluating patients' roles as educators.

The Patient Carer Community (PCC) is an organisation based in the University of Leeds providing students first-hand experience to speak to individuals who are living or caring for someone with a disability or medical condition.

In this study we aim to explore how the PCC recruits and trains patients and carers alongside an analysis of how the system has evolved and continuously improve to provide a high level of medical education. We also aim to study the impact the PCC has on students, staff and patients and carers who work with the Leeds Medical School.

Patients and methods Ethical approval for the study was obtained from the School of Medicine Research Ethics Committee (No: MREC16-013).

Data collection: A qualitative study was employed for data collection. Prior to the meetings all participants were sent copies of information sheets and consent forms, and these were revisited and signed on the day of the meeting. Data was recorded using our University iPhones and audio files were immediately transferred to our secure University drives. We then transcribed the audio files and performed theme analysis of the transcripts under the guidance of our supervisors. The first few transcripts were theme analysed together to reach consensus. The remainder were divided among us and analysed separately, however, at the end we reviewed each other's analysis as a quality control measure.

Results An analysis of the organisation which includes recruitment, training and development.

Theme analysis of our research brought forward the following major themes: Preserving spontaneity, truth and originality; patients and carers taking on more roles and responsibilities; enhancing student confidence; improving students' communication skills; providing tailored training and support; building friendships and supporting one another; shaping future doctors.

Conclusions The PCC at Leeds is constantly changing and improving to provide the best possible experience for its stakeholders. Theme analysis has enabled us to see the positive impact the PCC has had on the communication skills and the confidence of medical students of years 2-5. It has also shown that patients and carers themselves attain transferable skills from this experience that has enabled them to pursue their own aspirations and get back into employment. Suggestions for improvement to the existing system were made such as the introduction of a database with profiles of the patients and carers of the PCC for student reference prior to sessions, providing more history/examination based communication skills sessions towards the end of the year in preparation for the OSCE examinations.

In addition to the themes identified we discovered areas which future research could focus on. The impact of the PCC on the first year medical students, in particularly the home visits would be interesting to explore. Both PCC members and students echoed that they valued the input because it was 'spontaneous, truthful and original. Hence, the changing attitudes and roles of members who are involved with the PCC for a number of years in comparison to new members would be quite interesting to explore. Another area which could be explored would be how the feedback, received by both students and PCC members, is utilized and how to maximize the usefulness of this resource. In conclusion the PCC has positively impacted students, staff and patients and carers alike and has helped revolutionize the medical education provided at Leeds Medical School.

References

Towle, A., Bainbridge, L., Godolphin, W., Katz, A., Kline, C., Lown, B., Madularu, I., Solomon, P. And Thistlethwaite, J. (2010) Active patient involvement in the education of health professionals. *Medical Education* Vol. 44 (1) pp. 64-74.

The Mechanism of Action of Urocortin I, a Novel Anti-resorptive Agent

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Introduction Osteoporosis is a systemic skeletal disease attributed to cellular uncoupling between osteoblasts which deposit bone and osteoclasts which resorb bone, resulting in fragility fractures and excessive mortality^(1,2). Current osteoporosis therapies have significant side-effects such as osteonecrosis of the jaw and therefore further treatments are necessary⁽³⁾. Urocortin (UCN1), a Corticotrophin Releasing Factor (CRF) related peptide, inhibits both osteoclast resorption and motility; however, the mechanisms by which these effects are achieved is currently unknown⁽⁴⁾.

Methods and results Firstly, we aimed to comprehensively determine the presence of the urocortin system in murine osteoclasts, stromal cells and brain as a positive control. Utilising reverse transcriptase polymerase chain reaction, we found that both stromal cells and osteoclasts expressed UCN1 and CRF receptor 2β , with stromal cells also expressing Urocortin II and III, and osteoclasts also expressing Oestrogen receptor alpha. No other CRF or Oestrogen receptors or CRF binding protein were expressed by stromal cells or osteoclasts.

To determine the mechanisms by which UCN1 inhibits osteoclast resorption and motility we used the following pharmacological agents: the Phospholipase C activator m-3M3FBS, the Adenylate Cyclase activator Forskolin (which activate the $G\alpha_q$ and the $G\alpha_s$ pathway respectively) and the non-selective cation channel blocker Gadolinium. Dentine resorption assays determined that UCN1, m-3M3FBS and Gadolinium significantly inhibited osteoclast resorption compared to the control and Forskolin groups. Similarly, time lapse photography identified that UCN1, m-3M3FBS and Gadolinium-treated osteoclasts exhibited a loss of membrane ruffling and cytoskeletal membrane retraction after treatment, whereas the control and Forskolin groups did not. Phalloidin and cytofluorescence staining revealed that all treatments induced podosome belt loss, however, only m-3M3FBS and UCN1-treated osteoclasts displayed centralised actin rings.

Conclusions These findings demonstrate the fully characterised expression of the urocortin system in osteoclasts and that the anti-resorptive effects of UCN1 are mediated through the $G\alpha_q$ pathway. Therefore, manipulation of this pathway could generate new, novel osteoporosis therapies.

References

- 1 Sandhu SK, Hampson G. The pathogenesis, diagnosis, investigation and management of osteoporosis. *Journal of Clinical Pathology*. 2011;64(12):1042-50.
- 2 The British Menopause Society. Osteoporosis in the UK at Breaking Point. Buckinghamshire: 2010.

- 3 Sampalis JS, Adachi JD, Rampakakis E, Vaillancourt J, Karellis A, Kindundu C. Long-term impact of adherence to oral bisphosphonates on osteoporotic fracture incidence. *Journal of Bone and Mineral Research*. 2012;27(1):202-10.
- 4 Combs CE, Fuller K, Kumar H, Albert AP, Pirianov G, McCormick J, et al. Urocortin is a novel regulator of osteoclast differentiation and function through inhibition of a canonical transient receptor potential 1-like cation channel. *Journal of Endocrinology*. 2012;212(2):187-97.

Producing Cadaveric Anatomy Models for Laparoscopic Right Hemicolectomy of Colorectal Cancer

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Introduction Colorectal cancer is the third most commonly diagnosed world-wide malignancy and the fourth leading cause of oncological death in the world. In Europe and Northern America the incidence is 40 in every 100,000 and expected to increase 60% by 2030. Despite the significant mortality, 70-80% of cases are detected with localised disease, where resection of the site is potentially curable with adjunctive therapies. Although used, the laparoscopic technique for right hemicolectomies had been less readily accepted than in other abdominal surgeries, due to the technical challenges presenting a steep learning curve.

Patients and methods The aim of this study was the development of cadaveric pro-sections which demonstrate the anatomical challenges faced when performing a laparoscopic right hemicolectomy. Cadaveric dissection followed the medial-to-lateral approach of the laparoscopic procedure with mobilisation of the caecum from the abdominal wall followed by dissection of the attachments of the ascending and proximal transverse colon and lastly ligation and dissection of the associated vasculature.

Results The result of the study was the production of pro-sections which demonstrate the surgical path of the operation, highlight the surrounding structures which must be appreciated in order to avoid complication and provide a detailed demonstration of the variable vascular supply to area.

Conclusions The study has produced cadaveric pro-sections which allow key anatomic features pertinent to laparoscopic right hemicolectomies to be demonstrated clearly. As such these pro-sections may be used by surgical trainees to improve their knowledge, familiarity and confidence with the procedure, leading to an overall increase in the frequency of its use.

References

- 1 Arnold M., Sierra M.S., Laversanne M. *et al* (2016) Global patterns and trends in colorectal cancer incidence and mortality. *Gut* **0**:1-9.
- 2 Gustavsson B., Carlsson G., Machover D., *et al.* (2015). A review of the evolution of systemic chemotherapy in the management of colorectal cancer. *Clinical Colorectal Cancer*. **14**(1):1-10.

- 3 Witkiewicz W., Zawadzki M., Rzaca M., *et al.* (2013). Robot-assisted right colectomy: surgical technique and review of the literature. *Video Surgery and Other Miniinvasive Techniques*. **8**(3):254-257.

A Comparison of the Open and Laparoscopic Techniques Used in Right Hemicolectomies for Colorectal Cancer

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Introduction Benefits of laparoscopy in abdominal surgery are widely documented, yet a lack of papers reporting the intra-operative, post-operative and long term oncological outcomes of its use in right hemicolectomies for colorectal cancer currently exists. The aim of this study was to compare these outcomes between laparoscopic right hemicolectomies and the open alternative. In addition, there was intention to document the complexities and potential intra-operative complications of the operation.

Patients and methods Cadaveric dissection and observation of surgeries revealed three key areas of potential complication; division of the attachments of the caecum, division of the attachments of the proximal transverse colon and division of the highly variable blood vessels supplying the area. Surgeries were compared via extensive literature review.

Results Laparoscopic surgery was found to be 14.4% more expensive than the open alternative, whilst having a longer operative time (192.3 vs. 150.5 minutes). Lymph node yield was comparable (19.5 vs. 19.2), however, post-operative hospital stay (7.6 vs. 9.7 days), return to bowel function (2.6 vs. 3.7 days), return to diet (3.7 vs. 5.0 days) and return to ambulation (3.8 vs. 5.4 days) were all quicker following laparoscopic surgery. The blood lost (110.1 vs. 128.9 mls), rate of post-surgical complications (13.5% vs. 22.1%) and recurrence (13.8% vs. 17.2%) were all superior with laparoscopic surgery.

Conclusions A 7.7% rate of conversion was found, with conversions associated with worse outcomes than either laparoscopic or open surgeries. Future research is required to identify methods of determining which patients should undergo laparoscopic surgery, and which should undergo open surgery in order to avoid conversion.

References

- 1 Arnold M., Sierra M.S., Laversanne M. *et al* (2016) Global patterns and trends in colorectal cancer incidence and mortality. *Gut* **0**:1-9.
- 2 Gustavsson B., Carlsson G., Machover D., *et al.* (2015). A review of the evolution of systemic chemotherapy in the management of colorectal cancer. *Clinical Colorectal Cancer*. **14**(1):1-10.
- 3 Witkiewicz W., Zawadzki M., Rzaca M., *et al.* (2013). Robot-assisted right colectomy: surgical technique and review of the literature. *Video Surgery and Other Miniinvasive Techniques*. **8**(3):254-257.

Audit and re-audit of clinical details on urine request forms submitted to Monklands Microbiology laboratory 2015-2017

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Introduction Urine samples constitute the largest category of specimens examined in the Microbiology laboratory at Monklands hospital. The SIGN 88 guideline states that samples should only be sent in patients with symptoms of a urinary tract infection.

We audited compliance with SIGN 88 on 3 separate occasions between 2015 and 2017. Initially less than half of urine samples had appropriate clinical details. There was no improvement following educational intervention. A regional policy was introduced in April 2017 of only accepting samples with appropriate clinical details. Subsequent re-audit demonstrated a marked improvement in inclusion of appropriate clinical details. This translates into improved antimicrobial stewardship and patient management and more efficient use of laboratory resources.

Patients and methods Our objective was to improve the appropriateness and quality of requests for laboratory analysis of urine samples, in line with SIGN 88. The broader aim was to optimise antimicrobial stewardship and improve laboratory efficiency.

We audited performance on 3 occasions with 2 separate interventions to improve performance. 100 stored request forms scanned with the laboratory worksheets on the lab information system for urine culture on adult patients between December 2016 and March 2017 were used. Data from the first week in December, February and March were selected and the first 6 samples (4 on the final day) alphabetically by patient names were selected for each day. The same categorization of appropriate, inappropriate and no clinical details was used.

This process was then repeated for the first two weeks in April after the intervention (1st April to 16th April). Six samples were taken each day and 4 on the final day resulting in 100 samples in total.

Results A 32% increase in numbers of samples with appropriate details which leads to improved patient care through avoidance of unnecessary antibiotics. Therefore, improving hospital stewardship of antibiotics. It also translates into a cost saving of £1100 and 16 hours of laboratory time saved per week.

Conclusions This quality improvement project has enhanced antibiotic stewardship, patient care and saved time and money in the microbiology lab. This simple intervention has been soon to improve the hospital standards compared to SIGN 88.

References

Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary tract infection in adults. Edinburgh: SIGN; 2012. (SIGN publication no. 88). [July 2012]. Available from URL: <http://www.sign.ac.uk>

Treatment outcomes of oral immunosuppressants in the treatment of atopic dermatitis

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Introduction Ciclosporin and azathioprine are used to treat atopic dermatitis (AD) that are not adequately managed with standard topical treatments such as emollients and topical immunosuppressants.

Patients and methods The aim of this study is to evaluate the treatment outcomes of using ciclosporin and azathioprine to manage children with severe AD. A retrospective survey was conducted involving a cohort of 58 children with recalcitrant AD. There were 47 participants on ciclosporin and 18 on azathioprine because seven participants who were initially treated with ciclosporin switched to azathioprine after no improvement was observed with ciclosporin. 5 parameters including degree of improvement in eczema, time required to observe a clinical improvement, treatment duration, difficulty in weaning off and adverse events were used to evaluate treatment outcomes.

Results Children treated with Ciclosporin required a significantly shorter time to observe a clinical improvement (3 weeks) as compared to children on Azathioprine (8 weeks). (P-value < 0.001) Treatment duration was also significantly shorter for children managed with Ciclosporin (18 weeks) as compared to those on Azathioprine (37 weeks). (P-value = 0.02) Participants on Ciclosporin who have allergy-related triggers were found to be 4.8 times more likely to have difficulty in weaning off Ciclosporin as compared to those who do not have allergy-related triggers (95 % confidence interval).

Conclusions 82-85% of all patients had major improvements with oral immunosuppressants. in this cohort, ciclosporin induced a more rapid clinical effect and could be weaned off more quickly than azathioprine.

References

- 1 Ballard, D. (2001). Molecular mechanisms in lymphocyte activation and growth. *Immunologic Research*, 23(2-3), 157-166.
- 2 Beaumont, D., & Arkwright, P. (2012). Factors determining the effectiveness of oral ciclosporin in the treatment of severe childhood atopic dermatitis. *Journal of Dermatological Treatment*, 23(5), 318-322.
- 3 Bergfelt, L., Larko, O., & Blohme, I. (1993). Skin disease in immunosuppressed patients in relation to epidermal Langerhans' cells. *Acta Dermato-Venerologica*, 73(5), 330-334.
- 4 Berth-Jones, J., Finlay, A., Zaki, I., Tan, B., Goodyear, H., Lewis-Jones, S., . . . Graham-Brown, R. (1996). Cyclosporine in severe childhood atopic dermatitis: a multicenter study. *Journal of the American Academy of Dermatology*, 34(6), 1016-1021.
- 5 Blaker, P. (2017, January). *The Mechanism and drug interaction - Allopurinol and Azathioprine and risk of bone marrow suppression*. Retrieved from Evidence-based Medicine Consult: <https://www.ebmconsult.com/articles/allopurinol-azathioprine-interaction-mechanism-wbc>
- 6 Bunikowski, R., Mielke, M., Bräutigam, M., Renz, H., & Wahn, U. (2003). Effect of oral cyclosporin A in children with Staphylococcus aureus-colonized vs S aureus-infected severe atopic dermatitis. *Pediatric Allergy and Immunology*, 14(1), 55-59.
- 7 Bunikowski, R., Staab, D., Kussebi, F., Bräutigam, M., Weidinger, G., Renz, H., & Wahn, U. (2001). Low-dose cyclosporin A microemulsion in children with severe atopic dermatitis: clinical and immunological effects. *Pediatric Allergy and Immunology*, 12(4), 216-223.

- 8 Caufield , M., & Tom, W. (2013). Oral Azathioprine for recalcitrant pediatric atopic dermatitis: clinical response and thiopurine monitoring. *Journal of the American Academy of Dermatology*, 68(1), 29-35.
- 9 Chernyshov, P. (2009). B7-2/CD28 costimulatory pathway in children with atopic dermatitis and its connection with immunoglobulin E, intracellular interleukin-4 and interferon-gamma production by T cells during a 1-month follow-up. *Journal of the European Academy of Dermatology and Venerology*, 23(6), 656-659.
- 10 Chong, J., & Koh, M. (2017). Non-topical management of recalcitrant paediatric atopic dermatitis. *Archives of diseases in childhood*, 102(7), 0.
- 11 Deo, M., Yung, A., Hill, S., & Rademaker, M. (2014). Methotrexate for treatment of atopic dermatitis in children and adolescents. *International Journal of Dermatology*, 53(8), 1037-1041.
- 12 El-Khalawany, M., Hassan, H., Shaaban, D., Ghonaim, N., & Eassa, B. (2013). Methotrexate versus cyclosporine in the treatment of severe atopic dermatitis in children: a multicenter experience from Egypt. *European Journal of Pediatrics*, 172(3), 351-356.
- 13 Flohr, C., & Mann, J. (2014). New insights into the epidemiology of childhood atopic dermatitis. *Allergy*, 69(1), 3-16.
- 14 Fuggle, N., Bragoli, W., Mahto, A., Glover, M., Martinez, A., & Kinsler, V. (2015). The adverse effect profile of oral azathioprine in pediatric atopic dermatitis, and recommendations for monitoring. *Journal of the American Academy of Dermatology*, 72(1), 108-114.
- 15 Garrido Colmenero , C., Blasco Morente , G., & Tercedor Sánchez , J. (2015). Oral Cyclosporine Weekend therapy: a new maintenance therapeutic option in patients with severe atopic dermatitis. *Pediatric dermatology*, 32(4), 551-552.
- 16 GJ, N. (1999). A transformed view of cyclosporine. *Nature*, 397(6719), 471-472.
- 17 Harper, J., Ahmed, I., Barclay, G., Lacour, M., Hoeger, P., Cork, M., . . . Berth-Jones, J. (2000). Cyclosporin for severe childhood atopic dermatitis: short course versus continuous therapy. *British Journal of Dermatology*, 142, 52-58.
- 18 Hernández-Martín , A., Noguera-Morel , L., Bernardino-Cuesta , B., Torrelo , A., Pérez-Martin , M., Aparicio-López , C., & de Lucas-Collantes , C. (2017). Cyclosporine A for severe atopic dermatitis in children. efficacy and safety in a retrospective study of 63 patients. *Journal of the European Academy of Dermatology and Venereology*, 31(5), 837-842.
- 19 Hon, K., Ching, G., Leung, T., Chow , C., Lee, K., & Ng, P. (2009). Efficacy and tolerability at 3 and 6 months following use of azathioprine for recalcitrant atopic dermatitis in children and young adults. *Journal of Dermatological Treatment*, 20(3), 141-145.
- 20 Jin, S., Lim, W., Sung, N., Cheong, K., & Lee, A. (2015). Combination of glucosamine and low-dose cyclosporine for atopic dermatitis treatment: a randomized, placebo-controlled, double-blind, parallel clinical trial. *Dermatologic therapy*, 28(1), 44-51.
- 21 Kocarnik, J. (2015, April 20). *Common supplements found to lower circulating inflammation levels*. Retrieved from Fred Hutchinson Cancer Research Center: <https://www.fredhutch.org/en/news/spotlight/imports/common-supplements-found-to-lower-circulating-inflammation-level.html>
- 22 Kuo, C., & Leiden, J. (1999). Transcriptional regulation of T lymphocyte development and function. *Annual Review of Immunology*, 17, 149-187.

- 23 Kwon , H., Ahn, B., Choi, Y., Jin , S., Cheong, K., Lee, J., & Lee, A. (2013). Combination of glucosamine improved therapeutic effect of low-dose cyclosporin A in patients with atopic dermatitis: a pilot study. *The Journal of Dermatology*, 40(3), 207-210.
- 24 Leitner, J., Drobits, K., Pickl, W., Majdic, O., Zlabinger , G., & Steinberger, P. (2011). The effects of Cyclosporine A and azathioprine on human T cells activated by different costimulatory signals. *Immunology Letters*, 74-80.
- 25 Ma, D., & Jones, G. (2003). The association between bone mineral density, metacarpal morphometry, and upper limb fractures in children: a population-based case-control study. *Journal of Clinical Endocrinology and Metabolism* , 88(4), 1486-1491.
- 26 Maltzman, J., & Koretzky, G. (2003). Azathioprine: old drug, new actions. *Journal of Clinical Investigation*, 111(8), 1122-1124.
- 27 Matsuda , S., & Koyasu, S. (2000). Mechanisms of action of cyclosporine. *Immunopharmacology*, 47(2-3), 119-125.
- 28 Murphy, L., & Atherton , D. (2003). Azathioprine as a treatment for severe atopic eczema in children with a partial thiopurine methyl transferase (TPMT) deficiency. *Pediatric Dermatology*, 20(6), 531-534.
- 29 Notaro , E., & Sidbury , R. (2015). Systemic agents for severe atopic dermatitis in children. *Paediatric Drugs*, 17(6), 449-457.
- 30 Pedreira, C., King , E., Jones, G., Moore, E., Zacharin, M., Varigos, G., & Cameron , F. (2007). Oral cyclosporin plus topical corticosteroid therapy diminishes bone mass in children with eczema. *Pediatric Dermatology*, 24(6), 613-620.
- 31 Schmitt , J., Schmitt, N., & Meurer, M. (2007). Cyclosporin in the treatment of patients with atopic eczema - a systematic review and meta-analysis. *Journal of the European Academy of Dermatology and Venereology*, 21(5), 606-619.
- 32 Senra, M., & Wollenberg, A. (2014). Psychodermatological aspects of atopic dermatitis. *British Journal of Dermatology*, 170(Suppl 1), 38-43.
- 33 Shen, S., O'Brien, T., Yap, L., Prince, H., & McCormack, C. (2012). The use of methotrexate in dermatology: a review. *The Australasian Journal of Dermatology*, 53(1), 1-18.
- 34 Sibbald, C., Pope, E., Ho, N., & Weinstein , M. (2015). Retrospective review of relapse after systemic cyclosporine in children with atopic dermatitis. *Pediatric Dermatology*, 32(1), 36-40.
- 35 Slater, N., & Morrell , D. (2015). Systemic therapy of childhood atopic dermatitis. *Clinics in Dermatology*, 33(3), 289-299.
- 36 Waxweiler, W., Agans, R., & Morrell, D. (2011). Systemic treatment of pediatric atopic dermatitis with azathioprine and mycophenolate mofetil. *Pediatric Dermatology*, 28(6), 689-694.
- 37 Zaki , I., Emerson , R., & Allen, B. (1996). Treatment of severe atopic dermatitis in childhood with cyclosporin. *British Journal of Dermatology*, 135(Suppl 48), 21-24.

Teaching scientific principles using High-Fidelity Simulation

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Introduction High Fidelity Simulation, in the form of part or full-scale mannequin which is computer controlled to reproduce realistic physiological signs [1], is frequently employed in healthcare education to teach skills [2]. Its application in Biomedical Sciences education has been limited [3,4]. This study investigated whether High-Fidelity Simulation could be applied to teach scientific concepts.

Patients and methods A simulation scenario based on sepsis has been developed. The SimMan 3G mannequin was selected as a suitable form of High-Fidelity Simulation. 36 student volunteers from Biomedical Sciences and Medical backgrounds were recruited. Assessment of knowledge was accomplished using pre- and post-testing. The simulation involved following sepsis treatment pathways with a short interactive explanation of underlying pathophysiology at the end. The participants filled out feedback questionnaires at the end of the simulation.

Results 78% of participants were medical students and 17% of participants had received formal teaching on sepsis prior to the simulation. The simulation increased test results from 5.03 ± 0.29 to 9.39 ± 0.27 ($p < 0.0001$, total score of 12). Using a 10 point Likert scale, the average score for the overall impression of the simulation is 9.11. Participants reported higher perceived levels of engagement using simulation compared to lectures (8.75 versus 5.58 respectively, $p < 0.0001$).

Conclusions High-Fidelity Simulation can increase knowledge and engagement of students, and can be utilised to teach scientific concepts.

References

- 1 Al-Elq AH. Simulation-based medical teaching and learning. *J Family Community Med* 2010;17(1):35-40.
- 2 Nicksa GA, Anderson C, Fidler R, Stewart L. Innovative Approach Using Interprofessional Simulation to Educate Surgical Residents in Technical and Nontechnical Skills in High-Risk Clinical Scenarios. *JAMA Surg.* 2015;150(3):201–207.
- 3 Harris JR, Helyer RJ, Lloyd E. Using high-fidelity human patient simulators to teach physiology. *Med Educ* 2011;45(11):1159-1160.
- 4 Zvara DA, Olympio MA, MacGregor DA. Teaching cardiovascular physiology using patient simulation. *Acad Med* 2001;76(5):534.

Mortality and Functional Recovery in TSCI patients over 80 years old

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Introduction There is an upwards trend in age of patients presenting with Traumatic Spinal Cord Injury (TSCI)¹, which could cause strain on NHS services in years to come. With a recent focus on 'realistic medicine'², the main objective of this study is to provide prognostic information to inform management decisions for the elderly TSCI population by describing:

1. The demographics of TSCI in the extreme elderly population.

2. The mortality of TSCI patients over the age of 80 who are discharged from the Queen Elizabeth National Spinal Injury Unit (QENSIU).

The functional improvements the extreme elderly population make during their rehabilitation at QENSIU.

Patients and methods A retrospective review of the QENSIU database was performed. Patients over 80 years old with TSCI between 1994 and 2013 were selected for analysis. Data collection included dates of discharge and death; admission and discharge neurological classification of spinal cord injury (ASIA score) and admission and discharge motor function (FIM score). Survival time after discharge was calculated for each patient and a Cox regression for survival time was performed using ASIA grade and sex as covariates. Life expectancy in years for each patient after discharge was estimated from the National Life Tables³ and then compared with actual life years lived. Change in patients FIM score during their stay was calculated. A two-tailed unpaired t-test was used to compare group means, significance at $p < 0.05$. Confidence Intervals calculated at 95%.

Results In-hospital mortality is around 50% in patients with ASIA A-C (group ABC). Those patients that survive until discharge have a mean survival time in the community of 493 days (95% CI 39-946, $n=12$), compared to 1542 days (95% CI 1185-1899, $p < 0.05$, $n=51$) in group DE. Mean reduction in life years is 3.7 years (95% CI 2.5-4.9, $n=12$) relative to an age and sex matched Scottish population for group ABC, compared to 1.2 years (95% CI 0.3-2.2, $p < 0.05$, $n=51$) for group DE. Cox regression showed survival probability of group ABC patients after discharge from the unit is 50% at around one year. Group DE perform better with a 50% survival probability at around 5 years. Functional improvements during inpatient rehabilitation were poor, with mean FIM improvement of only 4 points in group ABC ($n=5$).

Conclusions TSCI in the elderly is a life-threatening and life-limiting condition. These data aid prognostication and treatment discussions. With a view to provide realistic medicine, tailored rehabilitation should be undertaken to focus on those tasks that are of the most benefit e.g. hand function and self-care, rather than an aim for raw motor score improvement. Meeting care needs and maximising independence in a homely environment is likely to be more beneficial than a prolonged hospital stay.

References

- 1 McCaughey EJ, Purcell M, McLean AN, Fraser MH, Bewick A, Borotkanics RJ, Allan DB. Changing demographics of spinal cord injury over a 20-year period: A longitudinal population-based study in Scotland. *Spinal Cord*; 2016; 54:270–276.
- 2 Calderwood C. Chief medical officer's annual report 2014-15. Scotland: Scottish Executive; 2016.
- 3 Office for National Statistics. National life tables, Scotland. United Kingdom: Office for National Statistics; 2016.

Single cell analysis of the interaction between transcription factors Nrf2 and Hsf1, master regulators of the cellular stress response

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Introduction Transcription factors nuclear factor-erythroid 2 p45-related factor 2 (Nrf2) and heat shock factor 1 (Hsf1) are the main regulators of the cellular stress response. Nrf2 regulates genes encoding a large array of antioxidant, drug metabolising and detoxifying enzymes¹. Hsf1 activates the heat shock response to thermal stress, but its over-activation has been shown to support highly malignant human cancers². Shared transcriptional targets and inducer molecules have been found between Nrf2 and Hsf1, however interactions between Nrf2 and Hsf1 are still not fully understood³. This project aimed to investigate the effect of heat shock on Nrf2.

Patients and methods Human cervical cancer HeLa Hsf1-wild-type (HWT) cells and HeLa Hsf1 knock-out (HKO) cells, originally grown at 37°C, were transferred into a 42°C incubator for either 1, 2 or 3h. The cells were then either lysed immediately or allowed to recover at 37°C for 3h before lysis. Western blot analysis was performed on the lysates obtained.

Next, another heat shock experiment was conducted using human osteosarcoma U2OS cells, which were similarly incubated at 42°C for either 1, 2 or 3h. Cells were then either lysed immediately or allowed to recover at 37°C for either 3 or 6h before lysis. Western blot analysis was performed on all lysates. Quantitative real-time PCR was also performed on the 6h-recovery samples.

Results In the HeLa cells which were lysed immediately, Nrf2 levels displayed a positive correlation with heat shock duration, and this was observed to a far greater extent in HWT cells compared to HKO cells. For the HeLa cells allowed to recover for 3h, Nrf2 levels were uniform in HWT cells, indicating a return to basal levels, while induction was still evident in HKO cells. As for the U2OS cells, a clear relationship was not observed between Nrf2 levels and heat shock duration. However, PCR revealed a 5.5-fold increase in mRNA levels of the shared Nrf2 and Hsf1 transcriptional target, heme oxygenase-1 (HO-1).

Conclusions The observed stabilization of Nrf2 upon heat shock in HeLa cells supports the idea that Nrf2 may contribute to some of the actions of Hsf1 during the heat shock response. While similar results were not observed with Western blot analysis of lysates from U2OS cells subjected to heat shock, the significant increase observed in HO-1 mRNA levels after heat shock is consistent with the idea that Nrf2 has the potential to compensate for Hsf1.

References

- 1 Talalay, P. Chemoprotection against cancer by induction of Phase 2 enzymes. *BioFactors* **12**, 5–11 (2000).
- 2 Mendillo, M. L. *et al.* HSF1 drives a transcriptional program distinct from heat shock to support highly malignant human cancers. **150**, 549–562 (2012).
- 3 Naidu, S. D., Kostov, R. V & Dinkova-Kostova, A. T. Transcription factors Hsf1 and Nrf2 engage in crosstalk for cytoprotection. *Trends Pharmacol. Sci.* **36**, 6–14 (2015).

Retinal Vascular Parameters and Blood Pressure Genetic Risk Scores as Predictors of Diabetic Retinopathy and Maculopathy in Type 2 Diabetes: a GoDARTS-VAMPIRE Prospective Study

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Introduction Diabetic retinopathy and maculopathy (DR/ DM) affect up to 50% of people with Type 2 diabetes (T2DM).¹ It is one of the major causes of blindness worldwide². Being able to identify those at greatest risk early is important. Only a few prospective studies have considered the potential of using retinal vascular parameters (RVPs) such as Central Retinal Artery or Vein Equivalent (CRAE and CRVE), their ratio (AVR) and retinal venular or arteriolar tortuosity (TortV and TortA) to predict the development of DR & DM.³ Blood pressure is strongly associated with several commonly measured RVPs as well as with DR and DM. Whether these associations are causal is not known. The use of a genetic risk score for blood pressure (BPGRS) as an instrumental variable to explore causality provide a means of understanding the relationship of blood pressure with both RVPs, DR and DM. This study sought to determine the potential of using RVPs extracted from diabetes retinal screening photographs to predict of DR and DM and the use of BPGRS as an instrument to explore the pathophysiological role of blood pressure.

Patients and methods 7,962 T2DM patients in the 'GoDARTS' cohort were included. The first available retinal screening photographs of 4,465 patients were obtained from the Scottish National Screening programme. RVPs were measured semi-automatically using the VAMPIRE⁴ platform including CRAE, CRVE, AVR, TortA, TortV and Optic Disc Radius (ODR). A 262 SNPs weighted BPGRS was constructed. Cox proportional hazard were used to model the incidence and progression of DR &DM, using recorded blood pressure, BPGRS and RVPs.

Results CRVE and TortV were found to be significant predictors of incidence of DR, whereas ODR was a significant predictor of incidence of DM. AVR and TortV significantly predicted progression of DR, whereas ODR significantly predicted progression of DM. Mean HbA1c level and age at T2DM diagnosis were both strong predictors of incidence of DR and DM, and DR progression, which concurred with other studies. While the BPGRS was significantly associated with TortA, it was not a significant predictor of incidence or progression of DR and DM, while blood pressure measurements were.

Conclusions Our study has demonstrated the potential use of CRVE, AVR, TortV and ODR as promising predictors of DR & DM. These associations do not seem to be linked to blood pressure as the common underlying pathophysiological driver. Furthermore, BPGRS did not predict development of DR/DM, indicating blood pressure lowering in T2DM may not be a major factor in reducing risk of DR/DM.

References

- 1 Ahmed K, Karim M, Bhowmik B, Habib S, Bukht M, et. al. Incidence of diabetic retinopathy in Bangladesh: A 15-year follow-up study. *Journal of Diabetes* (2012) 4(4): 386-391. doi: 10.1111/j.1753-0407.2012.00208.x
- 2 Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. *Bulletin of the World Health Organization* (2004) 82: 844-851. doi: 10.1590/s0042-96862004001100009
- 3 Crosby-Nwaobi R, Heng L, Sivaprasad S. Retinal vascular calibre, geometry and progression of diabetic retinopathy in type 2 diabetes mellitus. *Ophthalmologica* (2012) 228: 84-92. doi: 10.1159/000337252
- 4 Trucco, E. et al. Morphometric measurements of the retinal vasculature in fundus images with VAMPIRE. *Biomed. Image Underst. Methods Appl.* 91–111 (2015).

Radial Access: Training Model Development

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Introduction Increasing evidence has shown that the use of radial over femoral access for percutaneous interventions confers better patient outcomes in terms of safety & effectiveness including reduced access-site complications and early notice and control of subcutaneous bleed¹. However, there is little opportunity for life-like interventional radiology training in radial access. The aim of the study was to evaluate the potential of Thiel-embalmed cadavers as models for training in radial access.

Patients and methods The right common carotid artery (CCA) and both femoral arteries were cannulated and connected to a heart-lung bypass machine. Continuous, extracorporeal perfusion of the cardiac system was achieved, with inflow through the right CCA and a Y-port connection provided a single outflow system through the femoral arteries. The model was tested by an interventional radiologist who performed percutaneous coronary angioplasty (PCA) via radial access under fluoroscopic guidance.

Results Fluoroscopy showed perfusion of left coronary artery. PCA was successfully carried out by an interventional radiologist under fluoroscopic guidance. The right coronary artery however, was not visualised. Increasing oedema of the cadaver, restricting antegrade flow through the arterial system also proved to be a limiting factor during longer interventions.

Conclusions The Thiel-embalmed human cadaveric model serves as an anatomically accurate and life-like model for simulation training in radial access. Future plans would see this model also being used for training of other endovascular interventions as well as testing of new endovascular devices. Further development of this model would include model optimisation in terms of reducing oedema, the use of CT imaging and improvement of RCA visualisation.

References

¹ Hamon M, Pristipino C, Di Mario C, Nolan J, Ludwig J, Tubaro M, et al. Consensus document on the radial approach in percutaneous cardiovascular interventions: position paper by the European Association of Percutaneous Cardiovascular Interventions and Working Groups on Acute Cardiac Care and Thrombosis of the European Society of Cardiology. *Euro Intervention*. 8(11):1242–51

A new method for the performance of external chest compressions during hypogravity Simulation.

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Introduction 2015 UK resuscitation guidelines aim for 50-60mm depth when giving external chest compressions (ECCs). This is achievable in hypogravity if the rescuer flexes and extends their arms during CPR, or using a new method trialed; the 'Mackaill- Russomano' (MR) method.

Patients and methods 10 subjects performed 3 sets of 30 ECCs in accordance with 2015 guidelines. A control was used at 1Gz, with eight further conditions using Mars and Moon simulations, with and without braces in the terrestrial position and using the MR method. The MR method involved

straddling the mannequin, using its legs for stabilization. A body suspension device, with counterweights, simulated hypogravity environments. ECC depth, rate, angle of arm flexion and heart rate (HR) were measured.

Results Volunteers completed all conditions, and ECC rate was achieved throughout. Mean (\pm SD) ECC depth using the MR method at 0.38Gz was 54.1 \pm 0.55mm with braces; 50.5 \pm 1.7mm without. ECCs were below 50mm at 0.17Gz using the MR method (47.5 \pm 1.47mm with braces; 47.4 \pm 0.87mm without). In the terrestrial position, ECCs were more effective without braces (49.4 \pm 0.26mm at 0.38Gz; 43.9 \pm 0.87mm at 0.17Gz) than with braces (48.5 \pm 0.28mm at 0.38Gz; 42.4 \pm 0.3mm at 0.17Gz). Flexion increased from approximately 2°-8° with and without braces respectively. HR did not change significantly from control.

Conclusions 2015 guidelines were achieved using the MR method at 0.38Gz, with no significant difference with and without braces. Volunteers were closer to achieving the required ECC depth in the terrestrial position without braces. ECC depth was not achieved at 0.17Gz, due to a greater reduction in effective body weight.

References

- 1 Baers J, Velho R, Ashcroft A, Rehnberg L, Baptista R, Russomano T. Is Weight a Pivotal Factor for the Performance of External Chest Compressions on Earth and in Space. *Journal of Exercise Physiology*. 2016; 19(2): 1-16.
- 2 Baker ES, Barratt MR, Wear ML. Human response to space flight. *Principles of clinical medicine for space flight*. New York: Springer. 2008; 27–58.
- 3 Baskett PJF. Peter Safar, the early years 1924 – 1961, the birth of CPR. *Resuscitation*. 2001; 50:17-22.
- 4 Cheskes S, Schmicker RH, Verbeek PR, Salcido DD, Brown SP, Brooks S, Menegazzi JJ, Vaillancourt C, Powell J, May S, Berg RA, Sell R, Idris A, Kampp M, Schmidt T, Christenson J. The impact of peri-shock pause on survival from out-of-hospital shockable cardiac arrest during the Resuscitation Outcomes Consortium PRIMED trial. *Resuscitation*. 2014; 85: 336-42.
- 5 Dalmarco G, Calder A, Falcao F, Azevedo DFG, Sarker S, Evetts S, Moniz S, Russomano T. Evaluation of external cardiac massage performance during hypogravity simulation. *Conf Proc IEEE Eng Med Biol Soc*. 2006; 1: 2904-7.
- 6 Davey P. The effect of paramedic position on external chest compression quality: A simulation study. School of Clinical Sciences, Department of Paramedicine, Auckland University of Technology. 2014.
- 7 Idris AH, Guffey D, Pepe PE, Brown SP, Brooks SC, Callaway CW, Christenson J, Davis DP, Daya MR, Gray R, Kudenchuk PJ, Larsen, J, Lin S, Menegazzi JJ, Sheehan K, Sopko G, Stiell I, Nichol G, Aufderheide TP. Chest compression rates and survival following out-of-hospital cardiac arrest. *Crit Care Med*. 2015; 43: 840-8.
- 8 Johnson RS, Dietlein LF & Barry CA. Biomedical results of Apollo. Washington, DC: NASA. 1975; SP-386.

- 9 Johnston SL, Marshburn TH, Lindgren K. Predicted incidence of evacuation level illness/injury during space station operation. *Aviat. Space Environ. Med.* 2000; 71: 333.
- 10 Kouwenhoven W, Jude J, Knickerbocker G. Closed-chest cardiac massage. *JAMA.* 1960; 173: 1064-7.
- 11 Krygiel RG, Waye AB, Baptista R, Heidner GS, Rehnberg L, Russomano T. The Evaluation of Upper Body Muscle Activity during the Performance of External Chest Compressions in Simulated Hypogravity. *Life Sciences in Space Research.* 2014; 1: 60-66.
- 12 Lei Z, Qing H, Yaxiong Z. The efficacy of straddling external chest compression on a moving stretcher. *Resuscitation.* 2010; 81(11): 1562-1565.
- 13 Nasiri E, Nasiri R. A comparison between over-the-head and lateral cardiopulmonary resuscitation with a single rescuer by bag-valve mask. *Saudi Journal of Anaesthesia.* 2014; 8(1): 30-37.
- 14 Niles DE, Sutton RM, Nadkarni VM, Glatz A, Zuercher M, Maltese MR, Eilevstjønn J, Abella BS, Becker LB, Berg RA. Prevalence and hemodynamic effects of leaning during CPR. *Resuscitation.* 2011. 82(2): 23- 26.
- 15 Perkins GD, Travers AH, Berg RA, Castren M, Considine J, Escalante R, Gazmuri RJ, Koster RW, Lim SH, Nation KJ, Olasveengen TM, Sakamoto T, Sayre MR, Sierra A, Smyth MA, Stanton D, Vaillancourt C. Basic Life Support Chapter Collaborators. Part 3: Adult basic life support and automated external defibrillation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Resuscitation.* 2015; 95: 43-69.
- 16 Rajab TK, Pozner CN, Conrad C, Cohn LH, Schmitto JD. Technique for chest compressions in adult CPR. *World Journal of Emergency Surgery.* 2011; 6(41).
- 17 Rehnberg L, Russomano T, Baers J, VelhoR, CardosoR, Ashcroft A, GehrkeR, Dias M, Baptista R. Free Paper Session - [AS005]. What can CPR in simulated hypogravity teach us about CPR on Earth? Abstracts / *Resuscitation.* 2014; 85: 4-14.
- 18 Resuscitation Council (UK). *Resuscitation Guidelines.* 2017; Available at: <https://www.resus.org.uk/resuscitation-guidelines/> (Accessed: 15/04/2017).
- 19 Rowe WJ. The Apollo 15 space syndrome. *Circulation.* 1998; 97: 119 -20.
- 20 Russomano T, Baers J, Velho R, Cardoso RB, Ashcroft A, Rehnberg L, Gehrke RD, Dias MKP, Baptista RR. A comparison between the 2010 and 2005 basic life support guidelines during simulated hypogravity and microgravity. *Extreme Physiology & Medicine.* 2013; 2(11).
- 21 Stiell IG, Brown SP, Nichol G, Cheskes S, Vaillancourt C, Callaway CW, Morrison LJ, Christenson J, Aufderheide TP, Davis DP, Free C, Hostler D, Stouffer JA, Idris AH. What is the optimal chest compression depth during out-of-hospital cardiac arrest resuscitation of adult patients? *Circulation.* 2014; 130:1962-70.

- 22 Trappe S, Costill D, Gallagher P, Creer A, Peters JR, Evans H, Riley DA, Fitts RH. Exercise in space: human skeletal muscle after 6 months aboard the International Space Station. *J Appl Physiol.* 2009; 106(4):1159–68.
- 23 Vadeboncoeur T, Stolz U, Panchal A, Silver A, Venuti M, Tobin J, Smith G, Nunez M, Karamooz M, Spaite D, Bobrow B. Chest compression depth and survival in out-of-hospital cardiac arrest. *Resuscitation.* 2014; 85:182-8.
- 24 Vaillancourt C, Everson-Stewart S, Christenson J, Andrusiek D, Powell J, Nichol G, Cheskes S, Aufderheide TP, Berg R, Stiell IG. The impact of increased chest compression fraction on return of spontaneous circulation for out-of-hospital cardiac arrest patients not in ventricular fibrillation. *Resuscitation.* 2011; 82:1501-7.
- 25 Waye AB, Krygiel RG, Susin TB, Baptista R, Rehnberg L, Heidner GS, Campos F, Falcão FP, Russomano T. Evaluation of upper body muscle activity during cardiopulmonary resuscitation performance in simulated microgravity. *Advances in Space Research.* 2013; 53: 971-978.

Investigating the effect of dietary nitrate supplementation on placental angiogenesis in fetal growth restriction.

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Introduction Fetal growth restriction (FGR), compromised growth in utero, is a risk factor for stillbirth and preterm birth, in addition to long term adverse effects including an increased risk of cardiovascular disease in adulthood (1-3).

Placental insufficiency associated with aberrant placental vasculature frequently underlies FGR (4). Nitric oxide (NO) stimulates the production of pro-angiogenic factors including vascular endothelial growth factor (VEGF) and placental growth factor (PlGF) (5, 6). FGR is associated with low NO levels compared to healthy pregnancies (7). Therefore, elevation of placental NO bioavailability is a target in the development of therapies for FGR. Dietary nitrate is a source of NO generating potential via the nitrate-nitrite-NO pathway in which nitrate is reduced to nitrite by commensal bacteria in the oral cavity; nitrite is subsequently further reduced to NO in the tissues and circulation (8).

It was hypothesised that dietary nitrate supplementation, in the form of beetroot juice, would increase NO bioavailability in the placenta and therefore upregulate VEGF and PlGF expression, which in turn would augment placental angiogenesis.

Patients and methods To address this, the endothelial nitric oxide synthase knockout (eNOS^{-/-}) model, a mouse model of FGR associated with aberrant placental vasculature, was used(9). Pregnant eNOS^{-/-} mice and C57 wildtype controls were treated with nitrate replete (~1mmol/kg/day) or depleted beetroot juice or water (n=6/genotype/treatment). Placental VEGF and PlGF mRNA expression were measured using RT-qPCR.

A human umbilical vein endothelial cell (HUVEC) tube formation assay was performed to investigate the effect of sodium nitrite on angiogenesis *in vitro*. Nitrite, rather than nitrate, was tested to bypass the initial reduction of nitrate as this is performed by bacteria *in vivo*.

Results No differences were found in the expression of VEGF or PlGF mRNA across the different treatment groups, however PlGF expression was higher in the eNOS^{-/-} mice compared to the C57 mice ($p < 0.001$).

Sodium nitrite increased the length of tubes formed in a concentration dependent manner, and tube length was significantly higher than the untreated control cells at 100 μ M (16.62mm vs 29.47mm, respectively $p = 0.0062$).

Conclusions These data show that nitrite exposure can augment angiogenesis in human endothelial cells *in vitro*, however further work is required to demonstrate this effect in an *in vivo* model of FGR. This project has also shown that PlGF expression is higher in the eNOS^{-/-} mouse compared to the background wild-type strain. This is a previously unreported observation which may further the understanding of the development of FGR in the eNOS^{-/-} model.

References

- 1 Sharma D, Shastri S, Farahbakhsh N, Sharma P. Intrauterine growth restriction - part 1. J Matern Fetal Neonatal Med. 2016;29(24):3977-87.
- 2 Bukowski R, Hansen NI, Willinger M, Reddy UM, Parker CB, Pinar H, et al. Fetal Growth and Risk of Stillbirth: A Population-Based Case–Control Study. PLoS Medicine. 2014;11(4):e1001633.
- 3 Barker DJ. Adult consequences of fetal growth restriction. Clin Obstet Gynecol. 2006;49(2):270-83.
- 4 Salafia CM. Placental pathology of fetal growth restriction. Clin Obstet Gynecol. 1997;40(4):740-9.
- 5 Kimura H, Esumi H. Reciprocal regulation between nitric oxide and vascular endothelial growth factor in angiogenesis. Acta Biochim Pol. 2003;50(1):49-59.
- 6 Groesch KA, Torry RJ, Wilber AC, Abrams R, Bieniarz A, Guilbert LJ, et al. Nitric oxide generation affects pro- and anti-angiogenic growth factor expression in primary human trophoblast. Placenta. 2011;32(12):926-31.
- 7 Schiessl B, Strasburger C, Bidlingmaier M, Mylonas I, Jeschke U, Kainer F, et al. Plasma- and urine concentrations of nitrite/nitrate and cyclic Guanosinemonophosphate in intrauterine growth restricted and preeclamptic pregnancies. Arch Gynecol Obstet. 2006;274(3):150-4.
- 8 Lundberg JO, Weitzberg E, Gladwin MT. The nitrate-nitrite-nitric oxide pathway in physiology and therapeutics. Nat Rev Drug Discov. 2008;7(2):156-67.
- 9 Kulandavelu S, Whiteley KJ, Bainbridge SA, Qu D, Adamson SL. Endothelial NO synthase augments fetoplacental blood flow, placental vascularization, and fetal growth in mice. Hypertension. 2013;61(1):259-66.

Inter-pregnancy BMI change and the risk of preeclampsia (PE) and small for gestational age (SGA) babies: Analysis of the first two pregnancies in women from three European countries

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Introduction Although maternal weight gain is strongly associated with the risk of adverse pregnancy outcomes, research on the effect of inter-pregnancy weight change on the risk of pregnancy complications is limited.

Objective To assess whether the risk of PE and SGA is influenced by inter-pregnancy body mass index (BMI) changes between first and second pregnancy.

Patients and methods A cohort study of 551,592 women from three European datasets (Finland, Malta, and Aberdeen) was undertaken. Inter-pregnancy weight change was calculated from the difference between BMI recorded in the first two pregnancies. Weight change was characterised as an increase or decrease of ≥ 2 BMI units between pregnancies and compared with weight-stable women who remained within 2 units. Univariate and multivariate logistic regression analyses were employed to examine the associations.

Results The adjusted odds ratio (AOR) for PE was 1.22 (95% confidence interval 1.09-1.37) for inter-pregnancy weight gain when compared to weight-stable women. A decrease in BMI showed no significant reduction in risk of PE (AOR 1.07 (0.87-1.32)). In contrast, increase of >2 BMI units suggested a protective role against SGA (AOR 0.83(0.73-0.95). Reduced BMI resulted in an increased risk of SGA (OR 1.18(1.04-1.34). However, this relationship was not evident once adjusted for confounding factors (AOR 1.03(0.85-1.23). SGA and PE in first pregnancy were found to greatly increase the risk of recurrence in the second pregnancy (AOR 15.24 (13.80-16.84) & AOR 2.69 (2.11-3.44), respectively). Having either SGA or PE during second pregnancy resulted in an increased risk of the other occurring; PE risk AOR 3.99 (3.27-4.87) and SGA AOR 4.10 (3.40-4.95).

Conclusions We show that a weight gain >2 BMI units was associated with an increased risk of PE but reduced the risk of SGA. While weight loss of 2 units did not affect PE risk, it did increase the risk of SGA on unadjusted analyses. Additionally, women who have had previous PE or SGA have an increased risk of recurrence.

Is GluK2 the Atypical PLD-GluR in Muscle Spindles?

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Abstract The primary mechanosensory nerve terminals of muscle spindles express an unusual glutamate receptor (GluR) (Maren and Baudry, 1995). Termed the PLD-GluR, this receptor atypically results in the activation of phospholipase D (PLD), and has been found to play a role in the maintenance of stretch sensitivity in sensory nerve endings (Bewick, 2015). Despite pharmacological characterisation, this receptor has not been isolated. As such, this thesis aims to examine the literature available to determine likely candidates for the PLD-GluR. PLD-GluR ligand binding properties do not match those of canonical iGluRs, which suggests it is metabotropic GluR (mGluR). However, its pharmacological profile is highly unusual and does not match that of any canonical mGluRs (Ruiz *et al.*, 2005), either. Recent research has revealed that GluK2, an ionotropic kainate receptor subunit, is the only GluR subunit present in the mechanosensory nerve terminals (Thompson *et al.*, (2016). Although as a homotetrameric complex the kainate receptor composed of GluK2 subunits is ionotropic, the individual subunit itself has been proven to also display metabotropic properties (Bewick and Banks, 2015) which is consistent with the actions of the PLD-GluR. The mechanism by which the PLD-GluR activates PLD in muscle spindles and maintains stretch

sensitivity, is largely unknown. Moreover, GluK2 does not have an appropriate intracellular G-protein binding motif. However, the Neto accessory proteins – Neto1 and Neto2 - may act as an intermediary for G-protein interactions when co-expressed with GluK2 (Thompson *et al.*, (2016). However, whether this happens in spindles remains unproven.

Conclusions In conclusion, recent evidence has shown that GluK2 is expressed in the sensory nerve endings of muscle spindles and it seems a likely component of the PLD-GluR. However, further research is required to determine how GluK2 activates metabotropic signalling.

References

- 1 Bewick, G. (2015). Synaptic-like vesicles and candidate transduction channels in mechanosensory terminals. *Journal of Anatomy*, **227**(2): 194-213.
- 2 Bewick, G. and Banks, R. (2015). Mechanotransduction in the muscle spindle. *Pflügers Archiv - European Journal of Physiology*, **467**(1): 175-190.
- 3 K. J. Thompson, C. Zanato, M. Llaveró, T. M. Wishart, M. Zanda & G. S. Bewick (2016). Glutamatergic regulation of mechanosensitivity: isolating the atypical receptor from muscle spindles. *Proc Physiol Soc* 37: SA010.
- 4 Maren, S. and Baudry, M. (1995). Properties and mechanisms of long-term synaptic plasticity in the mammalian brain: relationships to learning and memory. *Neurobiology of Learning and Memory*, **63**(1): 1-18.
- 5 Ruiz, A., Sachidhanandam, S., Utvik, J., Coussen, F. and Mulle, C. (2005). Distinct Subunits in Heteromeric Kainate Receptors Mediate Ionotropic and Metabotropic Function at Hippocampal Mossy Fiber Synapses. *Journal of Neuroscience*, **25**(50): 11710-11718.

Assessing how cAMP-binding proteins influence invasion of non-small cell lung cancer cells

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Introduction Popeye domain containing (POPDC) proteins are cAMP-binding proteins that have been discovered to affect cancer cell signalling. POPDCs are novel proteins that show downregulation in breast malignancy that correlates with the aggressiveness and metastasis of cancer in vitro and in vivo. The role of these proteins in non-small cell lung cancer (NSCLC) has not yet been identified. The project examined these traits in NSCLC adenocarcinoma sub-type and focused on developing an invasion assay to establish the invasive potential. This involved preparing a layer of basement extract and then assessing the cancer's ability to breach this as a means of determining how likely these cell types are to escape normal tissue boundaries and begin to spread.

Patients and methods Immunohistochemistry, western blot, Boyden chamber migration assay, Transwell migration and invasion assay, measuring migration and invasion index via crystal violet, Transfection with siRNA.

Results POPDC 1, 2 and 3 were shown to be expressed within the NSCLC cell line A549. Boyden chamber and transwell assays showed migration potential of NSCLC cell line A549 in complete

medium. Transwell invasion assay was developed to show invasion potential of NSCLC cell line A549. POPDC1 knockdown A549 cell line showed an increase in invasive potential

Conclusions POPDC proteins have been identified within NSCLC cell line A549. Migration and invasion index of A549 was shown in complete medium. A transwell invasion assay was developed POPDC1 suppression in NSCLC suggests increases invasive potential.

The effectiveness of the Airsonett device in treating severe asthma patients

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Introduction Airsonett is a temperature-controlled, laminar airflow device that provides filtered, allergen-free air to the breathing zone of severe asthmatic patients as they sleep, resulting in fewer asthma attacks during the night. This audit was used to determine its effectiveness on 9 patients at a severe asthma clinic in Glasgow, in terms of their health and quality of life.

Patients and methods Baseline measurements were recorded, and the same measurements were recorded at the patients' annual review. The measurements recorded included: IgE levels for different allergens and spirometry results. Scores from a mini-AQLQ (asthma quality of life questionnaire), ACT (asthma control test), ACQ (asthma control questionnaire) were also used to assess patients' quality of life. Extra information regarding quality of life was also gleaned from clinical letters.

Results The audit revealed that 5 out of 7 patients who filled out the Mini-AQLQ saw an improvement in their score ($p=0.0156$). The IgE results, lung function tests, and number of hospital/GP visits showed no significant improvements. The clinical letters described that 6/9 patients felt they benefitted from the device and they all described:

- ❖ Fewer nocturnal symptoms
- ❖ Improved nasal symptoms
- ❖ Better quality of life
- ❖ Brought up less mucus

The other 3 patients had poor adherence and did not feel an improvement

Conclusions The quality of life of the patients appears to have improved and is shown by improved M-AQLQ results. This is backed up by the improved symptoms described in the clinical letters. This, coupled with the fact that 6 out of 9 patients saw benefit, implies that Airsonett is an effective treatment for severe asthma. 2 previous studies, from Boyle et al and Pedroletti et al, also concluded significant improvements in quality of life after Airsonett use ^{1,2}

References

- 1 Boyle RJ, Pedroletti C, Wickman M, Bjermer L, Valovirta E, Dahl R, von Berg A, Zetterström O, Warner JO. Nocturnal temperature controlled laminar airflow for treating atopic asthma: a randomised controlled trial. *Thorax* (2011). doi:10.1136/thoraxjnl-2011-200665 <http://thorax.bmj.com/content/early/2011/11/07/thoraxjnl-2011-200665.long>
- 2 Pedroletti C, Millinger E, Dahlén B, Söderman P, Zetterström O. Clinical effects of purified air administered to the breathing zone in allergic asthma: A double-blind randomized cross-over

The mechanisms of Th2 cell intrinsic tolerance during chronic helminth infection

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Introduction Filarial nematodes carry a high human disease burden. Their ability to immunosuppress their hosts promotes parasite survival and helps them establish chronic infections. Host Th2 cells become hyporesponsive during infection, undergoing an intrinsic change with downregulation of GATA3¹, IL-4 and IL-5². This is thought to be induced via PD-L2 acting on the Th2 inhibitory receptor PD-1, possibly expressed by macrophages, which upregulate PD-L2 over the course of infection. Elucidating the molecular mechanism of helminth-mediated Th2 hyporesponsiveness could assist the development of anti-helminth vaccinations, and treatments for other conditions in which the PD-1 ligands and/or Th2 cells are implicated, such as atopy³ and cancer⁴.

Patients and methods *Litomosoides sigmodontis*-infected BALB/c mice were employed as a murine model of filariasis. GATA3 and Th2 cytokine expression levels over the course of infection were assessed via flow cytometry. Macrophages were co-cultured with CD4⁺ T cells to assess their role in Th2 hyporesponsiveness. PD-L2^{-/-} mice, α PD-1 and α PD-L2 antibodies were utilised to determine whether PD-L2 mediates Th2 hyporesponsiveness.

Results In WT mice a two-fold decrease in GATA3 was seen from 35-41 days post-infection (dpi). In PDL2^{-/-} mice, GATA3 expression at 50 dpi was preserved, however worm burden was not significantly lower. There was no change in Th2 cytokine expression by 50 dpi. Co-cultured Th2 cells retained their Gata3 expression when treated with α PD-1 antibody.

Conclusions Th2 hyporesponsiveness developed sequentially, with GATA3 and IL-4 suppressed in turn. Although IL-4/IL-5 expression was not decreased by 50 dpi, previous studies² have shown that Th2 cytokine expression is impaired by 60 dpi. Blocking PD-1, but not PD-L2, reversed Th2 hyporesponsiveness in co-cultured cells at 60 dpi, implying that both PD-L1 and PD-L2 may be expressed by macrophages to induce Th2 hyporesponsiveness.

Whereas IL-4 expression is dependent on macrophage PDL2, GATA3 expression appears dependent on PD-1 but not PD-L2 alone, suggesting a role for macrophage PD-L1 in Th2 hyporesponsiveness.

References

- 1 Knipper JA, Campbell SM, Taylor MD. PD-L2 and B cells independently regulate Th2 cell expansion and functional quality during filarial nematode infection. *WIRM*. 2016.
- 2 van der Werf N, Redpath SA, Azuma M, Yagita H, Taylor MD. Th2 cell-intrinsic hyporesponsiveness determines susceptibility to helminth infection. *PLoS Pathog*. 2013; 9(3): e1003215.
- 3 Dittrich AM, Erbacher A, Specht S, Diesner F, Krokowski M, Avagyan A, et al. Helminth infection with *Litomosoides sigmodontis* induces regulatory T cells and inhibits allergic

sensitization, airway inflammation, and hyperreactivity in a murine asthma model. *J Immunol.* 2008; 180(3): 1792–9.

- 4 Francisco LM, Sage PT, Sharpe AH. The PD-1 pathway in tolerance and autoimmunity. *Immunol Rev.* 2010 Jul; 236: 219–42.

Sacral Nerve Stimulation - Current Concepts and Future Trends

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Introduction Sacral nerve stimulation is a relatively new therapy that is being increasingly used to treat both bowel and bladder dysfunction. Currently more than 200,000 people have been treated worldwide, largely comprising of patients in whom conservative treatments have proven ineffective. Successful SNS can avoid the need for more invasive surgery. We have undertaken a literature review on the current evidence base for SNS and also outline future trends regarding this exciting new technique.

Patients and methods We conducted a literature and internet review and focussed on a set of core papers including a meta-analysis carried out by Tan et al, and a systematic review performed by Carrington. Our poster presents a summary of the results contained in seminal publications on the subject.

Results Tan et al looked at all studies from 1995-2008, evaluating functional, physiological and QOL outcomes and comparing them to conservative management. Significant improvements were noted overall, especially in those less than 56 years of age, while complication rates were calculated at 15%.

Carrington on the other hand looked at 161 articles - of which 53 were deemed suitable for analysis. Results supported the hypothesis of peripheral motor nerve stimulation.

A further Cochrane review in 2015 by Thaha et al confirmed benefits for patients with faecal incontinence but not for those with constipation.

Conclusions My analysis under Professor Ronan O’Connell’s supervision at St. Vincent’s University Hospital in Dublin elaborates on the now widespread use of a treatment, initially aimed only at those with urinary incontinence, as a first-line for both urinary as well as bowel symptoms. This literature review article aims to address the fact that the mechanism of action still remains largely unpublished. Professor O’Connell’s important article in 2010 cautions that PNE evaluation is highly subjective and subject to a considerable placebo effect. Technological advances and a deeper understanding of the underlying dysfunction in such patients will undoubtedly improve outcomes in the future.

References

- 1 Suboptimal outcome following sacral nerve stimulation for faecal incontinence, O’Connell, P. Ronan (*Br J Surg*2011; 98: 140–147)

- 2 A review of sacral nerve stimulation parameters used in the treatment of faecal incontinence. Devane LA1, Evers J2, Jones JF3, Ronan O'Connell. Surgeon. 2015 Jun;13(3):156-62
- 3 <https://www.nice.org.uk/guidance/cg49/evidence/full-guideline-195116653>

HMGB1 expression in oesophageal neoplastic progression and gastric cancer

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Introduction Barrett's oesophagus (BO), defined by metaplastic columnar epithelium in the distal oesophagus, is a pre-malignant lesion for oesophageal adenocarcinoma, an aggressive late-presenting cancer. There is no associated biomarker to predict progression. High Mobility Group Box-1 (HMGB1) is a ubiquitous nuclear protein that regulates gene expression. When phosphorylated, it translocates to the cytoplasm and extracellular space to stimulate pro-inflammatory responses and influence epithelial cell behaviour. Expression of HMGB1 has been associated with malignancy at many sites. Lymphocytes, and downstream effector proteins p53 and RUNX3, are linked to HMGB1 function. There are no data on the expression or clinical significance of HMGB1 in oesophageal neoplastic progression. The role of HMGB1 in gastric cancer is also unknown.

Patients and methods Epithelial subcellular HMGB1, p53 and RUNX3 expression was assessed immunohistochemically in a tissue microarray containing 313, 30 and 48 cores of upper gastrointestinal cancer, normal oesophageal and normal gastric mucosa. 79 and 15 biopsies of non-dysplastic and dysplastic BO were also assessed. Normal and BO specimens were assessed for CD20⁺, CD4⁺, CD8⁺, and Foxp3⁺ lymphocyte infiltrate. Data was analysed by relative frequencies of staining correlated to clinico-pathological data, Fisher's exact test, Mann-Whitney U test and Log Rank test with Kaplan Meier survival analysis.

Results Normal oesophageal mucosa expressed strong nuclear and absent cytoplasmic HMGB1. There was loss of nuclear ($p=0.019$) and emergence of cytoplasmic ($p<0.001$) HMGB1 in BO. Compared to non-dysplastic BO, dysplasia was associated with stronger nuclear ($p=0.002$) and cytoplasmic ($p<0.001$) HMGB1. Cytoplasmic expression was reduced upon malignant transformation ($p=0.002$). Background non-dysplastic BO in those who progressed to cancer expressed weaker cytoplasmic HMGB1 compared to those who had not progressed ($p=0.015$). Downstream effector protein p53 emerged in dysplasia ($p<0.001$) and was reduced upon malignant transformation ($p=0.006$). Weak epithelial nuclear RUNX3 also emerged in dysplasia ($p=0.001$) and was lost upon malignant transformation ($p<0.001$). BO was associated with reduced CD20⁺ B-cells ($p<0.001$) and CD4⁺ ($p<0.001$) and CD8⁺ ($p<0.001$) T-cells. Dysplasia was associated with emergence of Foxp3⁺ regulatory T-cells ($p<0.001$). In gastric adenocarcinoma, expression of cytoplasmic HMGB1 ($p=0.010$) and nuclear p53 ($p<0.001$) provided significant survival benefit.

Conclusions This study demonstrates dynamic subcellular localisation of HMGB1 in upper gastrointestinal cancers, alongside a dynamic stromal lymphocyte infiltrate. This warrants further investigation to determine a protective or pathogenic biological consequence. HMGB1 may be a future biomarker for oesophageal neoplastic progression.

References

Wu T, Zhang W, Yang G, Li H, Chen Q, Song R, Zhao L, Wu T, Zhang W, Yang G, Li H, Chen Q, Song R, Zhao L, Tengyun Wu (2016) HMGB1 overexpression as a prognostic factor for survival in cancer: a meta-analysis and systematic review. *Oncotarget* 7: 50435–50445, doi:10.18632/oncotarget.10413.

Assessment and outcome of patients with colorectal cancer that do not undergo surgery.

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Introduction Surgery is the staple curative method of treatment of colorectal cancer however not all patients will undergo major operations. More patients are regarded as too frail/too much cancer for operations at Lancashire Teaching Hospital Trusts (LTHT) than the national average. This study aims to determine the outcomes of these non-operative patients.

Patients and methods All patients in colorectal multidisciplinary team discussions over a 2-year period (April 2013 – March 2015) were categorised into the National Bowel Cancer Audit (NBOCA) groups of major resection, too little cancer, too much cancer, too frail for surgery or others. Patient demographics were then documented and survival time post diagnosis recorded.

Results Four hundred and fifty three patients (mean age 69.9 years (range 23-98 years)) were found to have colorectal cancer and classified into major resection (n=285), too little cancer (n=38), too much cancer (n=81), too frail (n=41) and others (n=8). Frail and too much cancer patients had a higher proportion of patients with more co-morbidities and a higher performance status than patients that had too little cancer. Median survival times for patients who had too much cancer or were too frail were 8.3 months and 10.4 months respectively.

Conclusions Patients with too much cancer or that are too frail for resection surgeries have a poorer prognosis than those who are fit enough for operations. Pre-operative frailty assessment still has room to be improved with the introduction of the quantification of frailty using frailty scores and geriatric assessment. Further studies comparing non-operative outcomes and frailty assessment will aid future decision-making.

References

- 1 Bethune R, Sbaih M, Brosnan C, Arulampalam T. What happens when we do not operate? Survival following conservative bowel cancer management. *Ann R Coll Surg Engl.* 2016 Jul; **98**(6): 409-12.
- 2 Caldararo MD, Stein DE, Poggio JL. Nursing home status is an independent risk factor for adverse 30-day postoperative outcomes after common, non-emergent inpatient procedures. *J Surg.* 2016 Aug; **212**(2): 202-8.
- 3 Healthcare Quality Improvement Partnership. *National Bowel Cancer Audit* 2016. London, UK: 2016.

Does sepsis fall victim to the weekend effect?

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Introduction The weekend effect is the occurrence that mortality is increased if admitted at the weekend (1). One theory, the 'quality theory' suggests this is due to a reduction in appropriate care (2); an alternative idea the 'volume theory' pins it on a selective bias leading to a smaller volume of sicker patients causing increased mortality rates. The study tests the 'volume theory' by assessing mortality rates from sepsis in different regions of the country whilst factoring in the spread of admissions over the week (3). Sepsis was the chosen condition as it has a high mortality rate, needs timely admission and is not expected to strike at particular rates throughout the week.

Patients and methods This retrospective study includes data from the Health Episode Statistics database and used 15433 patients admitted to hospital trusts in England with a diagnosis of Sepsis from the financial year 2015-2016. We looked at the difference in weekday and weekend mortality at 7 and 30 days post-admission using a multiple logistic regression that was risk adjusted for factors known to have an effect on mortality (age, gender, ethnicity, co-morbidity and deprivation)

Results Overall in England a statistically significant weekend effect was found at both 7 and 30 days post admission (odds ratio (OR) 1.146, confidence intervals (CI) [1.037, 1.265]; OR 1.130 CI[1.028, 1.242] respectively). No regions had an equal proportion of admissions at the weekend as in the week, those that came close were East Midlands and North East. A small weekend effect was noted in both of these regions (East Midlands OR 1.033 CI[0.759, 1.443] and North East OR 1.072 CI[0.728, 1.577]).

Conclusions Our results show that even in regions of the country where volumes of admissions are steady a small weekend effect is demonstrated, although it is not statistically significant. It is naive however to suggest that the weekend effect is simply due to a reduction in healthcare services alone as there are still regions of the country where the weekend effect is lessened, even when the volumes of admissions in these areas are lower at the weekend suggesting an increased severity of illness. It is prudent that more research is carried out on the weekend effect in order to truly understand this phenomenon before it is used as evidence to change NHS working practice.

References

- 1 Bell, C. M. & Redelmeier, D. A., 2001. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *New England Journal of Medicine*, 345(9), pp. 663-668.
- 2 Freemantle, N. et al., 2015. Increased mortality associated with weekend hospital admission: a case for expanded seven day services. *The BMJ*, 351(h4596), pp. 1-6.
- 3 Meacock, R. et al., 2017. Higher mortality rates amongst emergency patients admitted to hospital at weekends reflect a lower probability of admission. *Journal of Health Services, Research and Policy*, 22(1), pp. 12-19.

General practitioners attitudes towards routinely offering long acting reversible contraceptives immediately in the postpartum period

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Introduction There is a demand for insertion of an intrauterine contraceptive device immediately in the postpartum period. Routinely offering long acting reversible contraceptives (LARC) in this period

is safe and effective in women who have undergone an elective caesarean section. This could improve accessibility to contraception in this demanding period of time. However, there is a need to assess whether primary care has the understanding, skills and resources to manage the post-insertion 6-week LARC check.

Patients and methods Practitioners in NHS Lothian attending the annual Sexual Health Update for GP's in NHS Lothian in 2016 completed a self-completed questionnaire. There were 92 delegates at the meeting and 85 individuals responded to the questionnaire (response rate= 92.4%).

Results The GP's served a range of demographics seen in the NHS Lothian population, with the majority having been practising for >10 years (70.2%, 59/84) and 64.7% (55/85) of the respondents being trained IUD fitters. Overall, 73.8% (59/80) of respondents were in favour of LARC insertion post-caesarean and those whom reported concerns (23.8%, 19/80) did so primarily due to the lack of long-term data and the availability of resources. Most of those concerned had been practising between 10-20 years. Affluence of the practice did not affect the GP's outlook. Most respondents felt it would be manageable to cut threads during the post-partum 6-week check (77.1%, 64/83) and felt confident in understanding their role in the process (70.6%, 60/85).

Conclusions Primary care teams largely view LARC insertion post caesarean section favourably, which is promising for the expansion of this practice, allowing a greater choice to women. Further sampling of GPs' views would enable a greater understanding of this issue.

Investigating the Ultrastructure of the Purkinje – Ventricular Muscle Junction Using Serial Block Face Scanning Electron Microscopy

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Introduction The cardiac conduction system is responsible for generating and propagating action potentials in the heart which leads to synchronised contraction of the myocardium (1). The large ventricular masses are activated by the His-Purkinje system (2). Free running Purkinje fibres emerge from the bundle branches and form an intricate network inside the ventricular cavities (3). These terminal fibres are coupled to the myocardium at sites termed the Purkinje – ventricular muscle junction (4). Currently, uncertainty remains as to the structural characteristics of the junction. Therefore, the aim of this project is to establish the morphological relationship between the Purkinje fibre, junctional region and ventricular myocardium.

Patients and methods Serial block face scanning electron microscopy was performed on rabbit Purkinje fibre tissue. This novel technique allows the generation of high resolution 3D reconstructions of large tissue samples. 2 tissue blocks were scanned and subsequently followed by data analysis. Block 1 contained free running Purkinje fibre cells, and block 2 a Purkinje – ventricular muscle junction.

Results Free running Purkinje fibre cells are long and narrow cells designed for fast action potential propagation. Strong electrical coupling between cells was demonstrated via the expression of large Intercalated discs. Terminal free running Purkinje fibre cells transition into Type 1 Junctional cells. These cells are weakly electrically coupled and hence begin to slow propagation of the action potential. Then, type 2 junctional cells emerge. Following 3D reconstruction, type 2 junctional cells manifest as flat structures with a small cellular length. Small intercalated discs are expressed in these

cells which further delays action potential propagation. Lastly, ventricular cardiomyocytes are classically arranged in uniform layers along the same axis.

Conclusions The findings of this novel study demonstrate for the first time the structural relationship between the free running Purkinje fibre cells and ventricular myocardium. The junctional region serves as a high resistance barrier protecting the Purkinje fibres from the large electrical load imposed by the ventricles. Moreover, by inducing a delay to action potential propagation, junctional cells build up the intracellular electrical charge which allows them to sufficiently activate the large ventricles.

References

- 1 Van Weerd JH, Christoffels VM. The formation and function of the cardiac conduction system. *Development*. 2016;143:197–210.
- 2 Boyett MR. ‘And the beat goes on’ The cardiac conduction system: the wiring system of the heart. *Exp Physiol*. 2009;94:1035–49.
- 3 Atkinson A, Inada S, Li J, Tellez JO, Yanni J, Sleiman R, et al. Anatomical and molecular mapping of the left and right ventricular His–Purkinje conduction networks. *J Mol Cell Cardiol*. 2011;51:689–701.
- 4 Vigmond EJ, Stuyvers BD. Modeling our understanding of the His-Purkinje system. *Prog Biophys Mol Biol*. 2016;120:179–88.

Meaningful activities in a dementia unit can reduce the frequency of hallucinations and sleep disturbance

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Introduction The behavioural and psychological symptoms in dementia are an important factor in determining quality of life. Mounting evidence has emerged supporting the reduction of antipsychotic-based pharmacotherapy. It is suggested that increased mortality rate is related to pharmacological-based therapeutic strategies.

Patients and methods Patients with a clinical diagnosis of dementia in an acute assessment and treatment facility for older people at Hayworth House, St Peter’s Hospital, Chertsey were included in this pilot study. The assessment of the behavioural and psychological symptoms of dementia was mediated by the administration of the Neuropsychiatry Inventory (NPI), which evaluates 12 behavioural and neurovegetative symptoms.

Results The primary finding of this pilot study demonstrated that there is a strong negative correlation between the NPI score and the meaningful activities that each patient undertook weekly for the 6-week duration of the study. More specifically, this study demonstrates that meaningful engagement reduces the manifestation of a range of behavioural disturbances, including psychotic symptoms, irritability and sleep disturbances.

Conclusions These findings indicate that participating in activities that are meaningful to the patient could elicit positive emotions and, as a result, ameliorate behavioural disturbances in dementia. Therefore, involvement in meaningful activities could be an effective non-pharmacological intervention strategy in managing behavioural disturbances in dementia. A major implication of this novel pilot study could be the evaluation of the effectiveness of non-pharmacological strategies focused on person-centred interventions in hospital settings.

References

- 1 Banerjee, S. (2010). *Living well with dementia; development of the national dementia strategy for England*. International journal of geriatric psychiatry, 25(9), pp.917–22.
- 2 Chancellor, B., Duncan, A. & Chatterjee, A. (2014). *Art therapy for Alzheimer's disease and other dementias*. Journal of Alzheimer's disease : JAD, 39(1), pp.1–11.
- 3 Chen, R.-C. et al. (2014). *Non-pharmacological treatment reducing not only behavioral symptoms but also psychotic symptoms of older adults with dementia: a prospective cohort study in Taiwan*. Geriatrics & gerontology international, 14(2), pp.440–6.
- 4 Cowles, A. et al. (2003). *Musical skill in dementia: a violinist presumed to have Alzheimer's disease learns to play a new song*. Neurocase: case studies in neuropsychology, neuropsychiatry, and behavioural neurology, 9(6), pp.493–503.
- 5 Dementia UK (2007). A report into the prevalence and cost of dementia prepared by the Personal Social Services Unit (PSSRU) at the London School of Economics and the Institute of Psychiatry at King's College London, for the Alzheimer's society. Alzheimer's Society, 2007.
- 6 Evans-Roberts, C.E.Y. & Turnbull, O.H. (2011). *Remembering relationships: preserved Emotion-based learning in Alzheimer's disease*. Experimental aging research, 37(1), pp.1–16.
- 7 Gori, G., Pientini, S. & Vespa. (2001). *The selection of meaningful activities as a treatment for day-care in dementia*. Archives of Gerontology and Geriatrics, 33(SUPPL.), pp.207–212.
- 8 Harmer, B.J. & Orrell, M. (2008). *What is meaningful activity for people with dementia living in care homes? A comparison of the views of older people with dementia, staff and family carers*. Aging & mental health, 12(5), pp.548–558.
- 9 Kazui, H., Mori, E. & Hashimoto, M. (2000). *Impact of emotion on memory. Controlled study of the influence of emotionally charged material on declarative memory in Alzheimer's disease*. British Journal of Psychiatry 2000 Oct; 177: pp.343–347.
- 10 Lai, C.K.Y. (2014). *The merits and problems of Neuropsychiatric Inventory as an assessment tool in people with dementia and other neurological disorders*. Clinical Interventions in Aging, 9, pp.1051–1061.
- 11 Leibenluft, E. & Stoddard, J. (2013). *The developmental psychopathology of irritability*. Development and psychopathology, 25(4 Pt 2), pp.1473–87.
- 12 Mather, M. & Carstensen, L.L. (2005). *Aging and motivated cognition: the positivity effect in attention and memory*. Trends in cognitive sciences, 9(10), pp.496–502.

- 13 Prince, M. et al. (2014). Dementia UK: Update. Retrieved from alzheimers.org.uk/dementiauk
- 14 Ragneskog, H. & Kihlgren, M. (1997). *Music and other strategies to improve the care of agitated patients with dementia. Interviews with experienced staff.* Scandinavian journal of caring sciences, 11(3), pp.176–182.
- 15 Safar, L.T. & Press, D.Z. (2011). *Art and the Brain: Effects of Dementia on Art Production in Art Therapy.* Art Therapy, 28(3), pp.96–103.
- 16 Schiamborg, L.B. et al. (2012). *Physical abuse of older adults in nursing homes: a random sample survey of adults with an elderly family member in a nursing home.* Journal of elder abuse & neglect, 24(1), pp.65–83.
- 17 Sung, H.C. et al. (2012). *A group music intervention using percussion instruments with familiar music to reduce anxiety and agitation of institutionalized older adults with dementia.* International Journal of Geriatric Psychiatry, 27(6), pp.621–627.
- 18 Taher, A.V., Ahmadi, M.K. & Zamir, F.P. (2015). *Effects of multi-sensory stimulation on cognition function, depression, anxiety and quality of life in elderly persons with dementia.* International Journal of Sport Studies, 5(3), pp.355–360.
- 19 Thies, W. & Bleiler, L. (2013). *Alzheimer's disease facts and figures. Alzheimer's & dementia: the journal of the Alzheimer's Association,* 9(2), pp.208–45.
- 20 Vink, a C. et al. (2004). Music therapy for people with dementia. Cochrane database of systematic reviews (Online), (3), p.CD003477.
- 21 World Alzheimer report (2015). *The global impact of dementia, an analysis of prevalence, incidence, cost and trends. 2015.* Alzheimer's Disease International.
- 22 Yamamoto-Mitani, N., Aneshensel, C.S. & Levy-Storms, L. (2002). *Patterns of family visiting with institutionalized elders: the case of dementia.* The journals of gerontology.

An audit into the optimum time for Neisseria gonorrhoeae test of cure following treatment in sexual health centres

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Introduction *Neisseria gonorrhoeae* is the second most common bacterial sexually transmitted infection worldwide and has evolved resistance to several antibiotic classes². BASHH Guidelines 2011¹ currently recommend ceftriaxone 500mg IM plus azithromycin 1g stat as first line treatment and also recommend a test of cure (TOC) at 14 days. In our centre the time period between treatment and TOC was reduced to 14 days in July 2016. Anecdotal evidence suggests that this may be producing a higher false positive rate.

Patients and methods Clinical notes for all 197 positive gonorrhoea tests (pharyngeal, rectal, urethral, cervical) in a 3-month period were reviewed, from 161 individual patients. Data was

collected about gender, gender of partners, antibiotic used for treatment, antibiotic resistance of cultured organisms and site of infection. Positive TOC were identified and reasons for these assessed (reinfection, treatment failure, false positive). Cycle threshold (CT) values were used to help identify false positives.

Results 7.5% of TOC results performed at 14 days were likely false positive (no risk of reinfection or treatment failure, high CT values), compared to 2.7% of TOC performed after 14 days. 8.3% of pharyngeal samples and 12.5% of urinary samples were false positive. There were no false positives found for rectal and vulvovaginal samples.

Conclusions There is a significantly higher rate of false positives when a TOC is performed at 14 days and they are more prevalent in pharyngeal and urinary samples. This has a negative impact on both patient and health care provider time and can lead to unnecessary retreatment. Potential interventions could be to extend the TOC time period, include CT values for all TOC results or move to a less sensitive NAAT for TOC.

References

- 1 Bignell C, Fitzgerald M. UK national guideline for the management of gonorrhoea in adults. BASHH Guidelines: BASHH Guidelines, 2011
- 2 Chisholm SA, Wilson J, Alexander S, et al. An outbreak of high-level azithromycin resistant *Neisseria gonorrhoeae* in England. *Sexually Transmitted Infections* 2016;92(5):365-67. doi: 10.1136/sextrans-2015-052312

Chronic inflammatory disease: The effects and mechanisms of cyclin-dependent kinase

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Introduction Neutrophils are key effectors of the inflammatory response that strives to resolve injury or infection-induced tissue damage [1]. However, the excessive accumulation of activated neutrophils is implicated in many chronic inflammatory diseases (e.g. COPD, asthma, atherosclerosis)[2]. This becomes problematic when neutrophil apoptosis and/or phagocytic clearance are disrupted and the increasing concentration of neutrophils release histotoxic contents, perpetuating inflammation. Inflammatory sites are typically hypoxic (<5% O₂) compared to normal tissue homeostatic oxygen levels (~8-12% O₂). Hypoxia enhances neutrophil survival by a mechanism not yet fully understood. This research investigates the ability of cyclin-dependent kinase inhibitors (CDKi) to induce neutrophil apoptosis with a view to circumvent persistent inflammation and drive resolution in a hypoxic microenvironment [3].

Patients and methods Isolated human neutrophils from healthy donors were cultured *in vitro* with two novel CDKi drugs, AT7519 and R-roscovitine. Hypoxic conditions were induced pharmacologically with dimethyloxaloylglycine (DMOG), a competitive antagonist of prolyl hydroxylase enzymes, and environmentally with a hypoxia chamber. The extent of neutrophil viability, apoptosis and necrosis was measured by morphological analysis and flow cytometry that measured the degree of Annexin-V (conjugated with fluorescein isothiocyanate) and propidium iodide binding. The mechanism of hypoxia-mediated neutrophil survival was probed by measuring hypoxia-inducible factor 1 alpha (HIF-1a) expression in pharmacologically induced hypoxic conditions.

Results CDKi drugs AT7519 and R-roscovitine induce human neutrophil apoptosis and R-roscovitine overrides the enhanced neutrophil survival induced by DMOG, the pharmacological mimic of hypoxia after 20h culture. The hypoxia chamber did not show significantly enhanced neutrophil survival. HIF-1a expression as assessed by western blotting was up-regulated in DMOG-treated neutrophils.

Conclusions The ability of CDK novel CDKi drug AT7519 and the prototype CDKi R-roscovitine efficiently induce apoptosis in isolated human neutrophils. Their ability to override the prolonged viability of neutrophils in hypoxic environments warrants future research and application to the treatment of chronic inflammatory disease. Further experimentation with the hypoxia chamber working at optimal conditions should be carried out, in addition to exploration of the role of the transcription factor NF- κ B pro-survival influences on neutrophil survival

References

- 1 Duffin R, Leitch AE, Fox S, Haslett C, Rossi AG (2010). Targeting granulocyte apoptosis: mechanisms, models, and therapies. *Immunological Reviews* 236:28-40.
- 2 Leitch AE, Duffin R, Haslett C, Rossi AG (2008). Relevance of granulocyte apoptosis to resolution of inflammation at the respiratory mucosa. *Nature* 1:350-368.
- 3 Rossi AG, Sawatzky DA et.al. (2006). Cyclin-dependent kinase inhibitors enhance the resolution of inflammation by promoting inflammatory cell apoptosis. *Nature Medicine* 12:1056-1064.

The effect of SGLT2 inhibitors on HbA1c, weight reduction, and systolic BP, and the impact of SGLT2 inhibitors on 10-year cardiovascular and stroke risk

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Introduction Despite the array of medications currently available for Type 2 Diabetes Mellitus, achieving treatment goals remains a great challenge. Sodium glucose cotransporter 2 (SGLT2) inhibitors has not only proved itself effective in glycaemic control but also shown to improve blood pressure, weight, and cardiovascular and stroke risks.

Patients and methods Through the SCI-Diabetes database, we gathered data from 155 patients who were commenced on dapagliflozin and 117 patients who were commenced on empagliflozin between its initial release in the UK until May 2017. Paired and unpaired t-tests were used to analyse the effects of SGLT2 inhibitors.

Results HbA1c showed significant improvement in one year with dapagliflozin (83.45mmol/mol to 71.83mmol/mol, $p < 0.0001$). The same was seen in empagliflozin treatment in one year (85.50mmol/mol to 75.31mmol/mol, $p < 0.0001$). A significant reduction in weight was also seen in both dapagliflozin and empagliflozin (3.95kg and 4.96kg respectively, $p < 0.0001$) in one year. Patients on dapagliflozin experienced an average drop of SBP in one year (8.22mmHg, $p = 0.0001$), and patients on empagliflozin 5.41mmHg ($p = 0.0094$) in six months.

83 patients on dapagliflozin and 60 patients on empagliflozin were identified to calculate the 10-year risk of coronary heart disease (CHD), fatal CHD, stroke and fatal stroke using UKPDS software. Patients on dapagliflozin had significant reduced risk of CHD by 2.53% ($p=0.012$) after one year. Risk of fatal CHD was also reduced by 2.52% after one year. Patients on empagliflozin have significant reduction in the 10-year CHD risk by 4.19% after one year ($p<0.0001$). There was also a slight reduction in the 10-year stroke risk by 0.30% after one year ($p=0.0008$).

Conclusions This study demonstrates that dapagliflozin and empagliflozin are effective oral antidiabetic drugs that are able to achieve significant improvement in HbA1c, SBP, and weight, and have also significantly reduced cardiovascular and stroke risks.

Five-year longitudinal BP in treated hypertensive patients shows evidence for diastolic J-curve and cardiovascular outcomes

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Introduction Current guidelines recommend a BP target $<140/90$ mmHg irrespective of cardiovascular(CV) risk level. The SPRINT trial showed significant benefit of treating SBP to <120 mmHg. Concerns exist regarding the potential increased CV risk from intensive DBP lowering - the diastolic J-curve. We analysed the relationship between longitudinal on-treatment SBP and DBP on CV events.

Patients and methods Longitudinal BP was obtained from clinic records for hypertensive patients attending the Glasgow BP Clinic. AUC BP for the first year(Y1) and 2-5years(Y2-5) were calculated for patients who had at least 3 BP measurements during these periods. Survival analyses were performed using Cox proportional hazard model adjusted for age, sex, cholesterol, smoking status, BP(time-dependent) and Charlson comorbidity index(time-dependent).

Results There were 4813 eligible patients(mean age 54 ± 14 years; female 52%). The average baseline, Y1 and Y2-5 BPs were $167/97\pm 26/12$, $153/91\pm 19/9$ and $146/87\pm 16/8$ mmHg respectively. There were 398, 452 and 455 first admissions with IHD in 15, 25, 35 years ($31,563$, $39,255$ and $40,714$ person-years respectively). Survival analyses for 15-year follow-up period showed a linear relationship between SBP over the first 5 years with IHD, MI, HF and CVA while DBP demonstrated a non-linear J-shaped relationship with IHD and MI events but not for CVA (Figure). Similar results were observed for 25- and 35-year follow-up periods.

Conclusions Low DBP (<90 mmHg) is associated with increased risk of IHD but not CVA. Increasing SBP was linearly associated with increased risk of IHD and CVA. Intensive SBP reduction measures should recognise potential risks of concomitant DBP reduction.

Assessing the utility of simple measures of frailty in older hospital-based cardiology patients

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Introduction The cardiac population is ageing. Frailty describes a lack of physiological reserve in older adults that increases the risk of dependency or death.¹ While a strong association between cardiovascular diseases, frailty and risk of poor clinical outcomes has been established, a gold standard frailty assessment for cardiology patients is lacking. We tested four simple and rapid frailty tools in older cardiology patients at the point of hospital discharge.

Patients and methods Patients over 70 years old and under the care of a cardiology consultant at the Royal Infirmary of Edinburgh were eligible for inclusion. Twenty-four hours prior to planned hospital discharge, consented patients were screened for frailty using physical measures (Fried criteria² and Short Physical Performance Battery, SPPB³), holistic nursing assessment (Clinical Frailty Scale, CFS⁴) and self-report (PRISMA-7 questionnaire⁵). All patients were followed through electronic health records for a composite primary outcome of hospital readmission or all-cause mortality after discharge.

Results A total of 100 patients (66% males; mean age 79.9 ± 6.3 years) were recruited between January and April 2017. The Fried criteria classified 28% of the cohort as frail, while the SPPB, CFS and PRISMA-7 categorized 79%, 17% and 65% as frail respectively. Agreement between measures was poor (21/100 complete agreement, maximum Cohen's kappa between any two measures of 0.39). During a median follow-up period of 25 days (range 13–47 days), 21 patients were readmitted and 2 died. Used at the point of discharge, the Fried scale provided the greatest discrimination for the primary outcome (8/28 (29%) frail patients vs. 13/72 (18%) non-frail, $p=0.02$). Using the Fried criteria, frail patients less frequently attended cardiac rehabilitation after discharge although this did not reach statistical significance (18% vs. 35%, $p=0.10$). During the 30 days following hospital discharge, frail patients on average spent 4.0 ± 7.3 days readmitted to hospital for unscheduled care compared to 0.9 ± 2.9 days in those classified as non-frail ($p=0.04$).

Conclusions Measuring frailty in this population proved feasible and appeared acceptable to patients and staff. The early outcomes from this ongoing cohort study show that the Fried frailty status may identify patients at high-risk of poorer short-term outcomes after hospital discharge. Strategies to reduce hospital readmission or target anticipatory care planning should focus on this frail older group. Alternative frailty scales that do not measure physical attributes appear to lack the sensitivity to detect short-term risk, but longer follow-up is awaited.

References

- 1 Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: A call to action. *J Am Med Dir Assoc*. 2013; 14(6): 392–397.
- 2 Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol Med Sci* 2001; 56: M146–156.
- 3 Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home readmission. *J Gerontol*. 1994; 49: M85–94.
- 4 Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ*. 2005; 173(5): 489–495.
- 5 Hébert R, Bravo G, Korner-Bitensky N, et al. Refusal and information bias associated with postal questionnaires and face-to-face interviews in very elderly subjects. *J Clin Epidemiol*. 1996; 49(3): 373–381.

Short on change? The therapeutic potential of repurposing licenced voltage-gated sodium channel inhibitors in the treatment of cancer.

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Introduction Voltage gated sodium channels (VGSCs) are transmembrane proteins which regulate membrane current and cellular migration during nervous system organogenesis. VGSCs are also expressed in fibroblasts, immune cells, glia, and metastatic cancer cells. VGSCs regulate migration and invasion of breast, bowel, and prostate cancer cells, suggesting that they may be novel anti-metastatic targets. Thus, licenced VGSC-targeting drugs could be repurposed to prevent or inhibit tumour metastasis.

Patients and methods A systematic literature search was performed to identify studies using VGSC-inhibiting drugs as part of treatment for patients with colorectal, breast and prostate cancer. Medline and Embase (Ovid interface) databases were used from inception until 20th May 2015.

Results 204 publications were identified. 2 human, 2 mouse and 20 *in vitro* publications were included. The clinical studies did not directly report on the effect of the drugs on survival or relapse in metastasis. The 22 preclinical studies identified suggested that some licenced VGSC inhibiting drugs inhibit cancer proliferation, migration and invasion. There were no human studies that specifically investigated the effects of these drugs on VGSC activity. However, 6 preclinical studies did investigate drug effects on VGSC current.

Conclusions Due to the heterogeneity of studies and lack of standardisation it proved difficult to compare methods and outcome measures. The benefits of VGSC inhibitors require further investigation. Standardization of future studies and outcome measures should enable meaningful study comparisons.

References

- 1 Martin, F. et al. *Front. Pharmacol* **6**:273 (2015).
- 2 Raderer, M. et al. *Onkologie* **16**, 450-453 (1993).
- 3 Wheler, J. J. et al. *Cancer Chemother. Pharmacol.* **73**, 495-501 (2014).

Predictors of Operative Complications and Mortality in patients with Low Ejection Fraction undergoing Coronary Artery Bypass Grafting

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Introduction Left ventricular (LV) dysfunction by itself is insufficient as an independent predictor of post-operative complications and mortality following coronary artery bypass surgery (CABG). Our

objective was to assess the effect of other pre, peri- and post-operative factors that might identify patients with low ejection fraction (EF) at highest risk.

Patients and methods We retrospectively analysed 346 consecutive patients with low EF ($\leq 30\%$) who underwent isolated CABG between 2009 to 2015. Potential preoperative and perioperative predictors of outcomes were recorded and patients were stratified into 2 groups based on their status at 30 days (alive vs death).

Results Serum creatinine $>166 \mu\text{mol/l}$, <24 -hour interval between surgery and last MI, left main stem disease, pre-operative ventilation, pre-operative use of intra-aortic balloon pump (IABP) and non-elective CABG were univariate predictors of mortality post-CABG (all $p \leq 0.001$). Generalised structural equation model (gSEM) analysis showed pre-operative use of IABP [adjusted odds ratio (AOR), 3.64; 95% confidence interval (CI), 1.09-12.1; $p = 0.035$] revascularisation complications (AOR, 12.8; CI, 3.51-46.4; $p < 0.001$) and renal complications (AOR, 9.87; CI, 3.01-32.4; $p < 0.001$) were independent predictors of 30-day death. Operative urgency was not a direct predictor of death but its impact was manifested through revascularisation and renal complications. Pre-existing diabetes mellitus increased likelihood of both renal (AOR, 2.77; CI, 1.18-6.49; $p = 0.025$) and vascular complications (AOR, 3.71; CI, 0.190-72.5; $p = 0.388$), although the latter was non-significant.

Conclusions Patients with significant LV dysfunction undergoing isolated CABG have good short-term survival and CABG remains a viable option. After adjusting for other baseline predictors, pre-operative use of IABP, revascularisation complications and renal complications were strong independent predictors of mortality.

Determining the Role of Fitness vs Body Composition in Insulin Sensitivity

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Introduction Athletes are more insulin sensitive than their sedentary counterparts. However, it is not known if this is because they are more active or because they have lower body mass. Exercise allows insulin-independent glucose uptake into muscle cells. However, exercise also contributes to weight loss. This study aimed to investigate whether diabetics should be encouraged to improve cardiovascular fitness or lose weight by reducing their body mass, to improve their insulin sensitivity (S_i). To our knowledge, there have been no previous studies comparing insulin sensitivity in those with impaired S_i compared with sedentary controls and endurance trained athletes (ETA's). We investigated the relationship between S_i and fitness; and S_i and body composition. We then established whether S_i is determined predominantly by fitness or body composition.

Patients and methods We recruited 34 participants divided into three phenotypically distinct cohorts. The 120-minute value of glucose (mmol/L) during the oral glucose tolerance test was used to represent S_i . Fitness was determined from VO_2max , which was assessed using an incremental bicycle ergometer test. Body Fat Percentage (BFP) was calculated with BodPod (BODPOD 200A, LMI software), which uses bio-impedance and air displacement plethysmography to calculate body composition. Statistics were calculated using Minitab 17.

Results We recruited 16 Controls, 16 ETA's and 2 Diabetics. The ETA's had the lowest body fat percentage (mean 12.8%; SEM 1.54); followed by the controls (20.2%; SEM 1.15) and the diabetics

(32.6%; SEM 4.2). ETA's had the highest VO₂max (54.4ml/kg/min); followed by the controls (35.4ml/kg/min) and then the diabetics (31ml/kg/min).

ETA's were the most insulin sensitive, with a mean 120-minute glucose value of 4.41mmol/L. Controls had a mean 120-minute glucose value of 5.17mmol/L, and diabetics had the lowest insulin sensitivity with a value of 12.18mmol/L.

Linear Regression was performed. Body composition had an R² value of 35.3%, and VO₂max had an R² value of 11%. Correlations were calculated. With regards to insulin sensitivity, body composition had a Pearson Correlation Coefficient of 0.594 (p0.002) and VO₂max had a Coefficient of -0.332 (p 0.059). Interestingly, body composition and VO₂max had a Coefficient of -0.717 (p<0.0001).

Conclusions ETA's and controls have similar insulin sensitivity (p=0.328). Linear Regression showed that body composition is a greater predictor of insulin sensitivity than fitness, in keeping with previous studies[4]. Correlations showed that body composition and VO₂max are both statistically significant predictors of insulin sensitivity, however, body composition is a greater determinant. Further work is needed to confirm if clinicians should focus on body weight reduction primarily, as opposed to increasing cardiovascular fitness in diabetic patients.

References

- 1 [1] Human Kinetics: Normal Ranges of Weight and Body Fat.
- 2 [3] World Health Organisation; 2006. Accessed 10 April 2017.
- 3 [4] K. R. Segal, A. Edano, A. Abalos, J. Albu, L. Blando, M. B. Tomas, F. X. Pi-Sunyer (1991) (6), 2402-2411.

Patient survey in MSM attending the SRP clinic looking at their basic knowledge of HPV and the HPV vaccine

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Introduction From July 2017 the Scottish government are making the HPV vaccine available to MSM (men who have sex with men) under the age of 45 on the NHS at GUM and HIV clinics. The vaccine is currently available through secondary schools to girls aged 12-13 years old.

HPV is a common sexually transmitted infection, many of which are asymptomatic when infected. High risk HPV 16 and 18 are associated with cancers including cervical, anus, penile and oropharyngeal. Low risk HPV 6 and 11 is associated with genital warts. Whilst in Scotland girls aged 12-13 years are vaccinated against these strains HPV, men are not, resulting in MSM being out with the cohort of vaccination (unlike heterosexual men) and therefore at a much greater risk of infection and subsequent complications. In particular the associated cancers in MSM are on the rise.

Patients and methods Anonymous patient survey handed out to MSM at the Steve Retson Project (SRP) clinic at Sandyford central.

Results 27 out of 35 participants are aware of HPV, with media and schools being the main source of information. Out of the 27, 18 are aware of the vaccine, however in regards to information about

the vaccine this was minimal, with most participants wanting information in relation to potential side effects and reasons for vaccination. 28 out of 35 said they would have the vaccine due to health benefits and prevention of infection, with the remainder a no or unsure until more information can be provided.

Conclusions Many are aware of HPV, mainly through the media and schools, however more needs to be done, particularly by health professionals to get further information out to the public. Specifically, potential sides effects and why we want to vaccinate MSM. In general, MSM feel they would have the vaccine due to prevention of infection and overall benefits to their health.

Limitations: patient survey was handed out over a short space of time and limited to only the SRP clinic at Sandyford central, excluding other daily clinics which many MSM attend.

References

- 1 Cancer Research (2017) *HPV and cancer*, Available at: <http://www.cancerresearchuk.org/about-cancer/causes-of-cancer/infections-hpv-and-cancer/hpv-and-cancer> (Accessed: 23rd May 2017)
- 2 HPVaction.org (2015) *HPV*, Available at: <http://www.hpvaction.org/hpv.html> (Accessed: 23rd May 2017).
- 3 Immunisation Scotland (2017) *HPV Vaccine*, Available at: <http://www.immunisationscotland.org.uk/vaccines-and-diseases/hpv.aspx> (Accessed: 30th May 2017).
- 4 Pubmed (2017) *Human papillomavirus vaccine efficacy in the prevention of anogenital warts: systematic review and meta-analysis*, Available at: [https://www.ncbi.nlm.nih.gov/pubmed/28423114?log\\$=activity](https://www.ncbi.nlm.nih.gov/pubmed/28423114?log$=activity) (Accessed: 30th May 2017).
- 5 Immunisation Scotland (2017) *HPV vaccine for men who have sex with men (MSM)*, Available at: <http://www.immunisationscotland.org.uk/vaccines-and-diseases/hpvmism.aspx> (Accessed: 30th May 2017).

The Role of Palmitoylation in Glutamate-Mediated Excitotoxicity in Neurodegenerative Diseases.

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Introduction Chronic neurodegenerative disorders such as Alzheimer's and Huntington's disease are associated with neuronal degeneration due to glutamate-mediated excitotoxicity as a result of dysfunctional proteins in the glutamatergic tripartite synapse. Palmitoylation controls several synaptic proteins in physiological glutamate neurotransmission but the role of palmitoylation in neurodegenerative diseases is unknown.

Patients and methods An integrated approach was taken to review the published literature and to make novel predictions to determine whether synaptic protein palmitoylation was disrupted and contributed to excitotoxicity in neurodegenerative diseases, with a focus on proteins already implicated in these disorders.

Results The major findings is that disrupted palmitoylation to proteins throughout the tripartite synapse contributes to the mechanisms controlling excitotoxicity in Huntington's disease. The

majority of synaptic proteins implicated in disease are predicted to be palmitoylated. Therefore, aberrant palmitoylation in each component of the tripartite synapse is predicted to affect homeostatic glutamate neurotransmission.

Conclusions This research develops our understanding of the role of palmitoylation in neurodegenerative disease. Palmitoylation is disrupted in Huntington's disease which highlights a novel therapeutic target in the treatment of this disorder. But further research is necessary to establish whether aberrant palmitoylation is a common pathological mechanism in other life-limiting, neurodegenerative diseases.

References

- 1 Rudy C, et al (2015). The Role of the Tripartite Glutamatergic Synapse in the Pathophysiology of Alzheimer's disease. *J Aging Dis* 6(2), 131-48.
- 2 Wettschureck N & Offermanns S (2005). Mammalian G proteins and their cell type specific functions. *Physiol Rev* 85(4), 1159-204.
- 3 Miller LC, et al (2003). Cysteine String Protein (CSP) Inhibition of N-type Calcium Channels Is Blocked by Mutant Huntingtin. *J Biol Chem* 278(52), 53072-81.
- 4 El-Husseini AED & Brecht DS (2002). Protein palmitoylation: a regulator of neuronal development and function. *Nat Rev Neurosci* 3(10), 791-802.
- 5 Young FB, et al (2012). Putting proteins in their place: palmitoylation in Huntington disease and other neuropsychiatric diseases. *Prog Neurobiol* 97(2), 220-328.
- 6 Antinone SE, et al (2013). Palmitoylation of Superoxide Dismutase 1 (SOD1) is increased for Familial Amyotrophic Lateral Sclerosis-linked SOD1 mutants. *J Biol Chem* 288(30), 21606-17.
- 7 Kim KS, et al (2013). DJ-1 associates with lipid rafts by palmitoylation and regulates lipid rafts-dependent endocytosis in astrocytes. *Hum Mol Genet* 22(23), 4805-17.

Deprivation in relation to urgent suspicion of head and neck cancer referrals in Glasgow

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Introduction The aim of this audit was to examine deprivation measured by the Scottish Index of Multiple Deprivation (SIMD) and its relation to urgent suspicion of head and neck cancer referrals. A secondary aim was to examine the symptomatology generating urgent suspicion of cancer (USOC) referrals by SIMD category.

Patients and methods All 'Urgent Suspicion of Cancer' referrals to the GGC ENT department over a one-year period, between 2015-16, were reviewed. Information was recorded anonymously and included demographics and red flag referral symptoms.

Results 1998 patients were assessed, 43.4% (n=867) were male. 171 (8.6%) patients had primary head and neck cancer (HNC). 61 patients had other types of cancer, giving an all cause cancer rate of 11.6%. 71.3% of primary HNC patients were male. The most common SIMD category observed was

SIMD1, the most common SIMD category yielding a primary head and neck cancer diagnosis was SIMD1. *Neck lump* was the commonest symptom amongst all SIMD categories.

Conclusions A link between deprivation and USOC referrals has been established. A difference in gender distribution between referrals and primary HNC was observed, more females are referred but a significant higher number of primary HNC patients are males. HNC patients were older, more likely to smoke and drinking alcohol to excess/history of alcohol excess.

Neck lump is a very strong referral indicator for HNC and *intermittent hoarseness* is not. The findings from this analysis could be used to refine local referral patterns and priority of referral.

Postgraduate abstracts

Neural Regions Critical for Naming Recovery after Stroke

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Introduction Impaired naming is the most common post-stroke language disorder. Previous research has shown that damage to left inferior frontal gyrus, posterior superior temporal gyrus (pSTG) and posterior middle/ inferior temporal gyrus are critical for naming. In this longitudinal study, we investigated naming recovery by identifying i) areas of the brain damage responsible for low naming ability immediately after stroke and whether ii) different/additional areas of damage are associated with persistent low naming scores at 4-7 months post-stroke.

Patients and methods We included 19 patients with acute left hemispheric ischemic stroke, who were enrolled within 48 hours of symptom onset and returned for follow-up 4-7 months later. All participants had MRI with DWI acutely and naming evaluations at both acute and chronic (4-7 months) time points. None had recurrent stroke in the interim. Boston Naming Test was used to quantify naming ability. We performed atlas-based lesion-symptom mapping using the MRICron software and MATLAB to associate damaged brain regions with naming scores. Of the 189 regions of interest on the JHU atlas, 9 were considered in our analysis. Analysis was run using the general linear model (least squares' linear regression), corrected for lesion volumes and multiple comparisons (Bonferroni correction) at a level of significance of 0.05.

Results No region was associated with lower naming scores at acute time point after controlling for lesion volume and corrected for multiple comparisons. Two regions, when damaged acutely, were associated with impaired naming at 4-7 months: left pSTG ($Z = -2.540$) and superior longitudinal fasciculus (SLF; $Z = -2.660$).

Conclusions Findings are consistent with those from previous studies regarding the importance of pSTG in naming. Further, a lesioned SLF acutely is associated with long-term naming deficits (i.e., failure to recover naming). This suggests that both regions, when damaged acutely, contribute to naming recovery. As they are only associated with low naming scores at 4-7 months, but not acutely, this could mean that they independently/synergistically contribute to naming deterioration, or failure to improve, from acute to chronic stage (4 patients had worse naming at 4-7 months). Naming involves many cognitive processes and SLF and pSTG have been proposed to be part of language pathways. Results show that grey matter regions, as well as the status of white matter

tracts (e.g. SLF) that connect components of language cortex can influence language recovery in stroke survivors.

References

- 1 Indefrey P, Levelt WJ. The spatial and temporal signatures of word production components. *Cognition* 2004; 92(1-2): 101-144.
- 2 Kertesz A, McCabe P. Recovery patterns and prognosis in aphasia. *Brain*. 1977; 1;100(1):1-8.
- 3 Naeser MA, Helm-Estabrooks N, Haas G, Auerbach S, Srinivasan M. Relationship between lesion extent in 'Wernicke's area' on computed tomographic scan and predicting recovery of comprehension in Wernicke's aphasia. *Arch Neurol*. 1987; 44(1): 73-82.

Follow up studies and notes The findings from this study had recently been replicated in another cross-sectional study (under the same Principal Investigator) involving 159 patients, which concluded: SLF and pSTG need to be intact for patients to experience good recovery of naming ability.

*This abstract will also be presented at American Neurological Association (ANA) Annual Meeting in the USA this year, by my American co-authors. ANA is fine for this abstract to be presented elsewhere. Permission has been sought from Sara Collier, to submit this to MRS RCPE.

Improving the efficiency of cannulation at the Queen Elizabeth University Hospital, Glasgow

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Introduction Cannulation is a common task performed by foundation year one trainees (FY1s). At the Queen Elizabeth University Hospital (QEUH), different ward stockrooms have different layouts which can lead to difficulty locating equipment. Following frustration amongst junior doctors, who felt valuable time was wasted locating equipment for cannulation, we decided to quantify time spent collecting equipment and trial a 'cannulation drawer' in order to standardise and organise cannula equipment on wards in the QEUH.

Patients and methods In our first cycle, we distributed a questionnaire to 40 junior doctors and clinical support workers to gather information on estimated time taken to locate cannulation equipment, both on familiar and unfamiliar wards. To further validate these estimates, we timed a smaller group of respondents finding equipment. In cycle 2, we created a pilot 'Cannulation Drawer' on a medical ward and timed 10 participants locating equipment using the drawer. For our third cycle, we are currently running a feasibility trial, with the 'Cannulation Drawer' implemented on two different wards across the course of 4-6 weeks.

Results Over 85% of FY1s feel they waste time finding equipment. We calculated that an estimated 82 hours per week is spent simply locating cannulation equipment. FY1s spend almost double the time on unfamiliar wards compared to familiar wards (4.3 vs 2.3 minutes). Following the implementation of the 'Cannulation Drawer', time taken to assemble cannula trays reduced significantly to 11.4 seconds ($p=0.0055$). There was no significant difference between those who were familiar or unfamiliar with the 'Cannulation Drawer' ($p=0.39$). All participants found the drawer easy to use.

Conclusions A significant amount of time is wasted locating cannulation equipment. The implementation of a pilot 'Cannulation Drawer' has resulted in notable time saved and has been shown to be easy to use. Further feasibility trials in view of standardised implementation across all QEUH wards are in progress.

References

- 1 Bolton D. (2010). Improving peripheral cannulation practice at an NHS Trust. *Br J Nurs*. Volume 19, (21):1346-50.
- 2 Morris W, Heong Tay M. (2008). Strategies for preventing peripheral intravenous cannula infection. *Br J Nurs*. Volume 17(19):S14-21.
- 3 T Test (2017). Graphpad QuickCalcs version 7; copyright Graphpad Software, Inc. Available: URL: <https://www.graphpad.com> (accessed 30/05/17).

Intravenous Fluid Management in the Acute General Surgical Setting.

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Introduction Many patients requiring hospital admission for an acute surgical problem will require fluids for resuscitation, maintenance or to correct electrolyte imbalances. The responsibility of prescribing intravenous fluids (IVF) most often falls to the foundation year doctor on the team. Guidelines on fluid management are clear and yet The National Confidential Enquiry into Perioperative Deaths report in 1999, found that a significant proportion of inpatient deaths were due to incorrect fluid prescriptions¹. This audit aimed to identify the accuracy of fluid prescriptions on a busy surgical ward with regard to adherence to local guidelines.

Patients and methods 35 surgical inpatient fluid charts were reviewed in cycle one and 32 in cycle two. All surgical inpatients receiving IVF on ward 107, Edinburgh Royal Infirmary were included. Data were gathered on the IVF prescriptions in the preceding 24 hours and recorded on a data collection form.

In each cycle data were collected on: 1) potassium prescription as per the local guidelines, 2) documentation of patient weight, 3) appropriate rate of maintenance fluids according to patient weight and 4) case note documentation of further fluid management plan.

A poster displaying the results of cycle one and recommendations to improve IVF prescriptions was placed around the workplace. This was reinforced by informal ward based teaching to the foundation year doctors and nursing staff. The audit was repeated after two weeks. The results and a proposal of a new fluid balance chart were presented at a departmental meeting.

Results In the first cycle (1) 43% of patients were prescribed potassium when indicated. (2) 6% of the fluid balance charts had the patient's weight recorded and (3) 66% of maintenance fluids were prescribed at the correct rate. (4) 56% of patients had clear documentation regarding ongoing fluid management.

Following the intervention there was improvement in potassium prescription (66%) and rate (82%) but no substantial change in weight documentation (3%) and ongoing fluid management plan (44%).

Conclusions As demonstrated by the 23% improvement in cycle 2, education plays a role in encouraging doctors to prescribe potassium in fluids. Regular teaching sessions should therefore be implemented and aid memoirs introduced in the workplace.

The documentation of weight was identified as being a major issue. Making the recording of the weight mandatory, as is the case with many pharmaceutical agents, will ensure all charts have an accurate weight documented and will likely result in more IVF being prescribed at the correct rate. Following the completion of this audit electronic ward rounds were introduced. A repeat audit reviewing the efficacy of this as an intervention to improve the documentation of fluid management plans should be undertaken.

A new fluid chart with space to document up to date biochemistry and an ongoing management plan was designed. This received positive feedback and could be considered as a future way to improve IVF prescriptions.

This audit demonstrates that while fluid prescribing is regarded as a basic task it is not always being carried out as effectively as the guidelines recommend. The results of this audit and suggested interventions are relevant to all surgical units.

References

NICE. (2013). Intravenous fluid therapy in adults in hospital. Available: <https://www.nice.org.uk/guidance/cg174/chapter/Introduction>. Last accessed 9.9.17.

The Differentiation of Ependymal Cells In The Postnatal Neurogenic Niche Of The Spinal Cord

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Introduction Spinal cord injury and myelination disorders result in motor impairment, dysaesthesia, chronic pain and autonomic dysregulation. Such disease sequelae have a severe effect upon life quality and are a consequence of neuronal death, axonal damage and demyelination. Restoration of neurological function may be achieved by harnessing postnatal neurogenesis within the spinal cord. Previous studies have demonstrated that the ependymal cell population surrounding the spinal cord central canal can proliferate under cholinergic modulation. Endogenous retinoic acid (RA) has been identified within the neurogenic zones of the adult murine brain. Furthermore, exogenous RA increases the differentiation and proliferation of neuroblasts extracted from the subventricular zone of postnatal mice. Indeed, recent studies have demonstrated that RA can enhance the proliferation of ependymal progeny within the spinal cord.

Patients and methods The aim of this study is to determine whether RA, in combination with cholinergic modulation, can enhance the differentiation of proliferating ependymal cells within the spinal cord. C57/Bl6 mice received in vivo intraperitoneal injections of RA and the alpha7 nicotinic acetylcholine receptor modulator PNU120596 (PNU). The number of proliferating cells within the spinal cord was determined using intraperitoneal delivery of the cell proliferation marker 5-ethynyl-2'-deoxyuridine (EdU), and the phenotype of these cells was confirmed by immunohistochemistry.

Results The results showed a significant reduction in EdU labelled cells for the RA group in comparison to PNU treatment alone. Fewer proliferating cells were found to co-localise with markers of differentiation, particularly within the central canal, which was the main area of focus.

Conclusions In conclusion, RA has a negative effect upon neurogenesis in the murine spinal cord. This is shown by the significant reduction in stem cell proliferation for the RA group in comparison to the PNU & EdU group in all areas of the lumbar and thoracic spinal cord. The results may be affected by an RA degrading enzyme present within the spinal cord. Neurogenesis may have also failed due to unknown suboptimal factors within the microenvironment of the spinal cord, injection timing, or the interaction of RA and PNU.

References

Moreno-Manzano, V. et al. Activated Spinal Cord Ependymal Stem Cells Rescue Neurological Function. *Stem Cells* 27, 733-743 (2009).

The appropriate prescribing of pharmacological thromboprophylaxis for patients admitted to the Medical High Dependency Unit at Wishaw General Hospital

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Introduction In the United Kingdom 25,000 hospitalised patient deaths occur annually due to venous thromboembolism (VTE). Safe dosing of Enoxaparin is dependent upon weight and renal function. Severe renal insufficiency occurs in 30% of critical care patients therefore such consideration is imperative. The audit objective was to determine whether thromboprophylaxis dosing is carried out appropriately for extremes of weight and renal function on the medical high dependency unit (MHDU).

Patients and methods Retrospective data was collected for one month. Dose of Enoxaparin on admission to MHDU was recorded alongside weight and creatinine clearance.

Results 21% of patients receiving VTE prophylaxis were prescribed the incorrect dose; 50% of incorrect prescriptions were due to under-dosing of patients of 100-150kg; 25% of incorrect prescriptions were due to no adjustment in renal impairment.

Conclusions The audit demonstrated the need to improve thromboprophylaxis prescribing. The findings were disseminated locally at the medical journal club, to the pharmacy team and at FY1 teaching. The project was also presented at a hospital wide quality improvement event and a cross-site Haematology meeting. A weight based dosing guidance poster was designed and displayed in MHDU and receiving units. The second audit cycle is due to take place in July 2017.

References

- 1 BARBA, R., MARCO, J., MARTIN-ALVAREZ, H., RONDON, P., FERNANDEZ-CAPITAN, C., GARCIA-BRAGADO, F. & MONREAL, M. The influence of extreme body weight on clinical outcome of patients with venous thromboembolism: findings from a prospective registry (RIETE). *J Thromb Haemost* 2005; 3: 856-62.

- 2 COOK, D. J., CROWTHER, M. A., MEADE, M. O. & DOUKETIS, J. Prevalence, incidence, and risk factors for venous thromboembolism in medical-surgical intensive care unit patients. *J Crit Care* 2015; 20: 309-13.
- 3 LUDWIG, K. P., SIMONS, H. J., MONE, M., BARTON, R. G. & KIMBALL, E. J. Implementation of an enoxaparin protocol for venous thromboembolism prophylaxis in obese surgical intensive care unit patients. *Ann Pharmacother* 2011; 45: 1356-62.
- 4 NHS LANARKSHIRE JOINT FORMULARY. ANTICOAGULANTS AND PROTAMINE. NHS LANARKSHIRE. 2016.

The use of Ideal Body Weight guided lung protective ventilation for critical care patients at Wishaw General Hospital

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Introduction Large tidal volumes delivered by mechanical ventilators can cause high airway pressures, volutrauma, barotrauma and biotrauma. Numerous studies have highlighted the benefit of using tidal volumes calculated by IBW, whereby lung volume is deemed to depend upon height, weight and gender. Currently NHS Lanarkshire has no such specific guidelines for lung protective ventilation. This audit objective was to determine whether mechanically ventilated patients receive tidal volumes based upon the IBW target of 6-8ml/kg.

Patients and methods Prospective data collection occurred for one month. Tidal volumes were collected from hourly readings over a period of 24 hours and averages calculated. The IBW target tidal volume range was also calculated.

Results The audit showed that 43% of ventilated hours provided tidal volumes greater than the lung protective range. Overall 90% of patients experienced non-lung protective ventilation.

Conclusions Overall the audit demonstrated a lack of compliance with lung protective ventilation strategy. The results were disseminated at a departmental meeting and a hospital wide meeting to educate nurses, trainees and consultants. The bedside patient airway cards were modified to incorporate an ideal tidal volume range section which will improve ventilation management by staff. A second audit cycle is planned, alongside potential development of local lung protective tidal volume guidelines.

References

- 1 ARDSNet. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med*. 2000 May 4;342(18):1301-8.
- 2 Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, Marret E, Beaussier M, Gutton C, Lefrant JY, Allaouchiche B, Verzilli D, Leone M, De Jong A, Bazin JE, Pereira B, Jaber S; IMPROVE Study Group. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med*. 2013 Aug 1;369(5):428-37.

- 3 Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Espósito DC, Pasqualucci Mde O, Damasceno MC, Schultz MJ. Association between use of lung-protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: a meta-analysis. *JAMA*. 2012 Oct 24;308(16).

Pelvic sidewall node involvement in rectal adenocarcinoma; incidence and outcomes with current management.

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Introduction The management of pelvic side wall nodes (PSWN) in rectal cancer remains controversial. In the West, unlike Japan, PSWN are not routinely resected and are managed with neoadjuvant chemoradiotherapy. This study documents the incidence of PSWN in rectal cancer on staging MRI and the significance of these findings on patient outcomes.

Patients and methods A retrospective study was performed of 335 patients diagnosed with rectal adenocarcinoma who had staging MRI (January 2014 - December 2015). Patients were identified from the West of Scotland Managed Clinic Network Database and divided into 3 groups according to MRI lymph node status: PSWN, including iliac; mesorectal (MRN) or node negative. Patients with inguinal (9) or paraaortic (3) lymphadenopathy were excluded. Demographics, staging, surgical and oncological treatments and outcomes were collected.

Results Mean age was 70(26-93) years with 49.5% male. Node positive disease was reported on MRI in 212(65.6%): PSWN n=66(19.7%) and MRN n= 146(43.6%). PSWN were associated with a higher rate of radiological CRM involvement, higher incidence of locoregional or distant recurrent disease, and higher mortality (median 2 years follow up).

Conclusions Our results highlight the poorer outcomes associated with PSWN involvement in rectal adenocarcinoma and suggest a need to explore alternative management strategies.

References

- 1 Bell et al, Understanding the anatomy of lymphatic drainage of the use of blue-dye mapping to determine the extent of lymphadenectomy in rectal cancer surgery: unresolved issues, *The Authors Journal Compilation, The Association of Coloproctology of Great Britain and Ireland*, 2009; 11: 443-449.
- 2 Watanabe et al, Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for the treatment of colorectal cancer, *International Journal of Clinical Oncology*, March 2015; 20(2): 207-239.
- 3 MERCURY Study Group, Relevance of magnetic resonance imaging-detected pelvic sidewall lymph node involvement in rectal cancer, *British Journal of Surgery*, 2011; 98: 1798–1804.

Long-term outcomes for patients undergoing elective colorectal surgery as part of ERAS

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Introduction ERAS is a fast-track program widely used in surgical specialties that have shown to improve peri-operative outcomes. However, there is little information about recovery after discharge. This study aims to show how ERAS impacts on patient's long-term functional status.

Patients and methods A prospective dataset was collected for patients undergoing elective colorectal surgery from June 2013-July 2014. A telephone survey was conducted using standardised questionnaire including mobility, independence, employment and housing status at 1 year post-operation.

Results There were a total of 199 patients with mean age 61.7 years. 53.8 % were male. 78.4% (n=156) of patients responded to the telephone survey. At 1 year post-operatively: 24.4% (n=38) required increased assistance with daily living; 4.5% (n=7) required mobility aids that were not required pre-surgery and 0.6% (n=1) became bed-bound. 6.4% (n=10) of patients who were previously employed were unemployed 1 year post-op; of which only 2 were due to post-operative complications. All patients reported living in their same pre-operative residence with none admitted to nursing homes.

Conclusions This is the first study to look into long-term functional outcomes of ERAS patients. Majority of the patients maintained their pre-operative quality of life. However, almost a quarter required extended care package on discharge.

References

- 1 Mia DeBarros, MD and Scott R. Steele, MD (2013) 'Perioperative Protocols in Colorectal Surgery', US National Library of Medicine National Institutes of Health, [Online].
- 2 Teeuwen P, Bleichrodt R, Strik C, Groenewoud J, Brinkert W, van Laarhoven C Et al. Enhanced Recovery After Surgery (ERAS) Versus Conventional Postoperative Care in Colorectal Surgery. *Journal of Gastrointestinal Surgery* 2009;14(1)88-95.

Audit of ultrasound service: a cost-effective and streamlined referral pathway

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Introduction Demand for radiology diagnostic services has been growing steadily, surpassing the ability of current services to cope. This has a knock-on effect on various medical specialties given the importance of diagnostic imaging in modern medicine, inevitably leading to longer wait for scans and reports. Therefore as a sustainable way to rationalise and prioritise scans, an USS outpatient referral pathway has been designed on RefHelp. Hence the aim of this project is to find out if this USS referral pathway is effective in rationalising scans.

Patients and methods We retrospectively audited 50 patients who had their initial USS request rejected in 2016 based on the new Refhelp guidelines. The following variables were audited: reason

for request, if secondary referral was made in accordance to guidelines, any subsequent imaging, modality and results of subsequent imaging.

Results The results showed that majority (46%) of the indications for USS were for lumps/bumps, followed by 12% for groin/ hernia and 8% for knee and shoulder likewise. In a significant 18% of the requests, a wide variety of other indications included arm tingling, axillary pain and perceived foreign body. In 72% of the rejected requests, a secondary referral was made to various specialties as per guideline e.g. orthopaedics, combined tumour clinic.

In 64% of the cases, no subsequent imaging was deemed necessary. Majority of the subsequent imaging (14 pts) was USS while 4 pts had an MRI. In terms of results of subsequent imaging, it showed no serious pathology in relation to the initial clinical question hence reassuring that there was no delay in the diagnosis of any serious pathology.

Given that approximately 244 USS are rejected annually locally and extrapolating that the demand for scans was reduced by 64% with the RefHelp referral guidelines, an approximate savings of £9403 could be estimated with this new referral pathway.

Conclusions In conclusion, it is reassuring there is good uptake of this ongoing USS referral pathway from GPs as majority (72%) are referred to specialties according to the guideline.

Apart from cost savings and more efficient allocation of USS scanning slots, this also provides more holistic care as clinic referral to specialty allows the specialty to review the patient to decide relevance of scan and initiate diagnosis/treatment accordingly at the same time. While this has been a local initiative to streamline USS requests, it could be a useful reference and model for more widespread uptake of this model across NHS boards eventually.

References

- 1 The Royal College of Radiologists. Clinical Radiology UK Workforce census 2015 report [homepage on the Internet]. c2016 [cited 2017 Sept 12]. Available from: https://www.rcr.ac.uk/system/files/publication/field_publication_files/bfcr166_cr_census.pdf
- 2 ISD Scotland. File listings. c2016 [cited 2017 Sept 12]. Available from: http://www.isdscotland.org/Health-Topics/Finance/Publications/2016-11-22/Costs_R120X_2016.xlsx

The Negative Appendicectomy Rate: A new Gender Gap?

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Introduction The negative appendicectomy rate (NAR) in existing literature ranges from 5-30% and in recent years pre-op imaging has increasingly been used to aid diagnosis and lower the NAR. Historically NA's (Negative appendicectomies) have been more commonly associated with young females' due to mimicking gynaecological causes for lower abdominal pain. Our aims are to establish the NAR at a large Scottish DGH, to compare rates between men and women and to explore the factors which may account for a gender gap in the NAR.

Patients and methods All patients who underwent emergency appendicectomy during a 1 year period at our DGH were included. Data was collected from the OPERA theatre system and CHI numbers obtained were then used to perform a retrospective data collection from TRAKcare. Rates of pre-op imaging, surgical technique and grade of principal surgeon were then calculated for the NA cohort, PA (Positive appendicectomy) cohort and split by gender for comparison.

Results 146 patients underwent appendicectomy during a 1year period at our centre. 6 were excluded as non-emergent cases, 5 had grossly normal appendices on laparoscopy and did not proceed to appendicectomy, while 15 were found to be NA's on histopathological analysis (10.7%). On average inflammatory markers (WCC, CRP) were higher in the PA cohort compared with the NA cohort and a higher proportion of the NA cohort had no pre-op imaging (73.3%) compared with the positive cohort (42.4%). 60% of the NA cohort were found to be male. Pre-op imaging was more common in females (55.7% compared with 25.8% males). Males were more likely to undergo open appendicectomy (22.8% compared with 10% females) and a slightly greater proportion of the male cohort were found to undergo conversion from laparoscopic to open procedure (8.6% vs 5.7%).

Conclusions NAR at our centre (10.7%) is consistent with published rates. A greater proportion of this cohort being male is inconsistent with existing literature. Higher rates of pre-op imaging and laparoscopic appendicectomy in the female cohort could reflect increased awareness of mimicking gynaecological pathology where as males are much more likely to be taken to theatre based on a clinical diagnosis alone. We would therefore suggest males either have pre-operative imaging or a laparoscopic approach to reduce the male NAR.

References

- 1 Addiss DG, Schaffer N, Fowler BS, Tauxe RV (1990) 'The epidemiology of appendicitis and appendectomy in the United States', *Am J Epidemiol*, 132(5), pp. 910-925.
- 2 Sauvain, MO., Slankamenac, K., Muller, M.K. et al. *Langenbecks Arch Surg* (2016) 401: 643. doi:10.1007/s00423-016-1444-xvv.
- 3 Chen K, Arad A, Chen K, et al The clinical value of pathology tests and imaging study in the diagnosis of acute appendicitis *Postgraduate Medical Journal* 2016;92:611-619.
- 4 Misdiagnosing adult appendicitis: clinical, cost, and socioeconomic implications of negative appendectomy Mock, Kyle et al. *The American Journal of Surgery* , Volume 212 , Issue 6 , 1076 – 1082.
- 5 Lembcke B (2016) 'Ultrasonography for acute appendicitis - the way it looks today', *Z Gastroenterol*, 54(10), pp. 1151-1165.
- 6 Sauerland S, Jaschinski T, Neugebauer EAM. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database of Systematic Reviews* 2010, Issue 10. Art. No.: CD001546. DOI: 10.1002/14651858.CD001546.pub3

A multi-method systems approach to antimicrobial management in continuing care wards

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Introduction Nearly 50% of antibiotic use is unnecessary or inappropriate¹. Unnecessary use of antibiotics can lead to undesirable consequences such as Clostridium difficile infection (CDI) and antimicrobial resistance (AMR). Optimising antibiotic management, commonly referred to as antimicrobial stewardship², is one of the strategies adopted to reduce unnecessary and inappropriate use³. The Scottish Antimicrobial Prescribing Group (SAPG) developed four indicators which they expect all healthcare staff to comply with. A human factors approach using the Systems Engineering Initiative for Patient Safety (SEIPS) framework⁴ was applied to identify the systems barriers and facilitators to safe and effective antimicrobial management, using the SAPG indicators as a baseline definition of safe and effective use.

Patients and methods This study used a multi-method approach consisting of four methods to identify the systems barriers and facilitators to safe and effective antimicrobial management on two study wards within NHS Tayside; a medical ward and a surgical ward. The methods used included; a focus group with members of the Association of Scottish Antimicrobial Pharmacists (ASAP) group to identify the challenges and facilitators as identified by subject matter experts (SMEs), a point prevalence survey (PPS) as an objective measure of performance of the two study wards and semi-structured interviews with staff to identify how the team perceive antimicrobial management and coping strategies.

Results The focus group carried out with ASAP, to identify the challenges and facilitators to antimicrobial management from the perspective of SMEs, identified two sub-processes within the overall antimicrobial management process. These included (1) the collection of national indicator data, the four SAPG measures, and (2) compliance with these measures in clinical areas. Barriers to collecting data included; motivation, design of the data collection app, not checking whether choice is compliant with guidelines, the frequency of staff changeover, training and the time it takes to complete the task. Facilitators to collecting the data included nursing staff permanently on the ward collecting the data, training and organisational culture when a consultant is driving the audit. Many barriers were identified to compliance with the indicators including competing priorities on the ward, knowledge, decision making, patient characteristics, commitment, available space on prescribing tools to document required information, organisational culture, workload and not reviewing at appropriate times. Facilitators to compliance with the indicators include knowledge, motivation, having a ward champion, an antibiotic section on the kardex, organisational culture, feedback, incentive systems, training and weekly meeting to discuss performance.

The PPS was carried out to provide an objective measure of how each ward performs in relation to the four SAPG measures, the baseline definition of safe and effective management. Non-compliance with the indicators was identified on both study wards. Indication was documented more reliably than the duration or review date. Both wards had missed doses, however, reasons were documented for all.

The interviews with team members on the study wards identified many barriers and facilitators. Barriers included the consultants' priorities and perception of importance of management on the surgical ward and the confidence of the foundation year (FY) doctors on the medical ward. Facilitators included clear guidelines, the pharmacist reviewing antibiotics on the ward round and the consultants support on the medical ward.

Conclusions Complex systems such as healthcare are unpredictable, therefore the persons in the system must display performance variability in response to adapting situations. To optimise antimicrobial management, a whole system, user-centred approach should be used to design the work system and any improvements that can be made. System design and interventions to improve

system design may result in unintended consequences as work as imagined does not take the unpredictable nature of complex systems into consideration. By using a systems approach, some of these unintended consequences can be predicted and minimised.

References

1. Lee, TC., Frenette, C., Jayaraman, D., Green, L., Pilote, L. (2014). Antibiotic Self-Stewardship: Trainee-Led Structured Antibiotic Time-Outs To Improve Antimicrobial Use. *Annals of Internal Medicine*. 161.10_Supplement; pp.S53-S58.
2. Allerberger, F., Gareis, R., Jindrák, V., Struelens, MJ. (2009). Antibiotic stewardship implementation in the EU: the way forward. *Expert Review of Anti-infective Therapy*. 7(10), pp.1175-1183.
3. Aryee, A., Price, N. (2015). Antimicrobial stewardship - can we afford to do without it? *British Journal of Clinical Pharmacology*. 79(2), pp.173-181.
4. Holden, R., Carayon, P., Gurses, A., Hoonakker, P., Hundt, A., Ozok, A et al. (2013). SEIPS 2.0: a human factors framework for studying and improving the work of healthcare professionals and patients. *Ergonomics*. 56(11), pp.1669-1686.

The long-term risk of recurrent stroke in patients with lacunar versus non-lacunar ischaemic stroke

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Introduction Stroke is one of the leading causes of morbidity and mortality worldwide. [1] The lacunar subtype was once believed to have a relatively benign prognosis, but evidence of a strong association with subsequent vascular events and death is mounting. [2] However, there remains a dearth of data comparing morbidity in lacunar versus non-lacunar stroke patients in the very long-term. This study aims to investigate the long-term (>10 years) prognosis following an index ischaemic stroke in terms of the risk of recurrent stroke, and whether this risk varies between the lacunar and non-lacunar subtypes.

Patients and methods This is a secondary data analysis of the Edinburgh Stroke Study (ESS) (recruitment in 2002-2005), a prospective hospital-based cohort study designed to compare different ischaemic stroke subtypes. Data were recently linked to hospital admission and mortality records until 31 December 2015, providing a follow-up period of over 10 years. Cox regression analysis was conducted for three time periods (total follow-up period, onset of stroke to first year, and first year to end follow-up) after adjusting for age, sex, and other confounders. The Fine and Gray model was applied to account for the competing risk posed by mortality.

Results 812 participants were included in the analyses, 283 (34.9%) of whom had had lacunar strokes. Cumulative 30-day, 90-day, 1 year, 5 year, and 10-year rates of recurrent stroke were 2.1%, 4.2%, 8.5%, 17.4%, and 22.4%. The lacunar and non-lacunar groups had a similar risk of recurrent stroke in the first year following the index stroke (adjusted HR, 0.76; 95% CI 0.45–1.30), after the first year (adjusted HR, 0.81; 95% CI 0.55–1.21), and over the entire follow-up period (adjusted HR, 0.80; 95% CI, 0.58–1.10).

Further analyses will include competing risk analysis incorporating mortality data. The risk of other subsequent vascular events in this cohort will also be examined.

Conclusions Preliminary analyses demonstrate that lacunar and non-lacunar strokes have a similar risk of recurrence in the mid- and long-term. This lends credence to the theory that lacunar strokes are not 'mild' forms of the disease, and suggests that the management and follow-up of these patients should not be neglected.

References

- 1 Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, et al. Global and regional burden of stroke during 1990-2010: findings from the global burden of disease study 2010. *Lancet* 2014;383:245-54.
- 2 Norving B. Lacunar infarcts: no black holes in the brain are benign. *Pract Neurol* 2008, 8(4):222-8.

Diabetic Foods Survey

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Introduction The feeling of happiness and pleasure produced by the consumption of sweet food may lead health-conscious people with diabetes to search for alternatives which are better for their condition. The food industry has long ensured that these people have such alternatives available to them. Many foods found in major supermarkets and high street stores are targeted at people with diabetes, often claiming to be sugar free or low in sugar (Diabetes UK, 2013). Diabetes UK (Diabetes UK, 2013) has recommended that patients with diabetes avoid these foods and that manufacturers discontinue diabetic labelling due to the implied health benefit for which there is no definitive evidence.

This project assessed the contribution of an extended version of the theory of planned behaviour (TPB) in predicting intention to eat diabetic food among adults with diabetes. This theory was developed by Azjen (1991) in order to predict and understand human behaviour. The three components of this theory are attitude, subjective norms and perceived behavioural control. The general rule proposed by Azjen (1991) is that strength of intention should be strong if attitude and subjective norms are favourable toward performing the behaviour, in addition to holding a high degree of perceived behavioural control. A self-identity component was added as an extension. It was hypothesised that all four components would be significant in predicting intention to eat diabetic food.

There is currently no published data on the purchasing behaviour, beliefs and attitudes of people with diabetes towards diabetic food. This study developed a questionnaire based on the theory of planned behaviour constructs relevant to the consumption of diabetic foods to achieve an understanding of what factors influence their consumption.

Patients and methods Participants (n=103) were recruited from a diabetic retinal screening site and a diabetic outpatient clinic in NHS Greater Glasgow and Clyde. A questionnaire was developed based on the theory of planned behaviour following an elicitation study.

Results Regression tests were run to assess which predictors were significant in predicting intention to eat diabetic food. The results showed that attitude and subjective norms were significant in predicting intention to eat diabetic food. Perceived behavioural control and the self-identity

components were not significant. These results could be used by diabetes educators and doctors to tailor nutrition-related advice to patients. This theory can also be applied to many other health-related behaviours.

Conclusions The results of this study reveal that attitude and subjective norm are significant in predicting intention to eat diabetic food. Self-identity was not found to be significant in addition to the original TPB model in predicting intention to eat diabetic food. Although the findings from this study cannot be generalised to all patients with diabetes, they do offer insight into beliefs and the relative importance of the predictors of intention to eat diabetic food.

References

- 1 Azjen, (1991). The theory of planned behaviour. *Organizational Behavior and Human Decision Processes*, 50.
- 2 Diabetes UK, (2013). *Diabetes UK Position Statement on Diabetic Foods*. 1st ed. [ebook] Diabetes UK. Available at: <https://www.diabetes.org.uk/Documents/Position%20statements/Diabetes-UK-position-statement-Diabetic-foods-0213.pdf> [Accessed 31 Oct. 2015].

Attitudes to IV potassium amongst Foundation Doctors and Nursing Staff

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Introduction As many as 1 in 5 patients on suffer complications or morbidity due to the inappropriate administration of IV fluids¹. Poor prescribing can cause hypervolaemia, hyponatraemia and hyperchloraemia. Prescribers of IV fluids 'knew neither the needs of the individual patients, nor the specific composition of the many choices of IV fluid available to them' and IV fluid prescribing is 'often delegated to the most junior medical staff' on the team¹.

Current clinical guidelines¹ relating to the prescription of IV fluids for adults in hospital were developed in an attempt to correct these problems. They recommend that IV fluid plans should be reviewed by an expert daily and suggest the composition of routine maintenance fluid.

NHS Lothian changed its fluid prescription policy in August 2015 in order to be in line with current guidelines. The policy recommends the use of 4% Glucose and 0.18% sodium chloride for routine maintenance fluid and recommends a daily potassium intake of 1mmol/kg. After this changed policy, Pharmacy data showed no change in the use of Potassium containing fluids.

This survey was to find the reasons why Potassium prescribing did not follow the NHS Lothian policy.

Patients and methods A paper survey was delivered to FY1s and nursing staff on all medical and surgical wards in a District General Hospital in NHS Lothian during December/January 2017. We aimed to survey all FY1s and a minimum of 3 nursing staff per ward. Responses were anonymous. In addition, all maintenance fluid prescriptions in 3 medical wards were reviewed on one day in January 2017.

Results The study captured the opinions of 15 FY1s and 22 nursing staff. With regards to FY1s, 60% reported difficulty in calculating fluid balance on the ward. This was attributed to lack of accurate inputs, outputs and weights. Time pressures meant that 73% of FY1s admitted to not completing fluid reviews before prescribing maintenance fluids and most (73%) did not think that their fluid

prescriptions were adequately reviewed on ward rounds. Although 93% claimed to be happy to prescribe potassium in maintenance fluids, only 13% reported that they did so routinely.

Nursing staff reported that they did not get any formal training on the administration of IV potassium and the majority stated that they had learnt 'on the job'. However, most (91%) reported that they were completely comfortable administering IV fluids containing potassium. The most common reasons given for asking for prescriptions of IV potassium to be changed were lack of stock and concerns over the rate at which the fluid was prescribed.

On the day surveyed, 14 maintenance fluid prescriptions were found on the medical wards. Of these, only 5 included potassium. Of these, 3 were less than the suggested recommended dose and 2 were 2-3 times the recommended dose. Only 3 of the 14 fluid balance charts had inputs and outputs recorded.

Conclusions Despite new clinical guidelines, patients are not prescribed appropriate potassium in maintenance fluids. Barriers include lack of time for medical staff, inadequate charting of fluid balance and reported issues with ward stock.

References

National Institute for Health and Care Excellence (2013) Intravenous fluid therapy in adults in hospital, NICE Guideline [CG174]

A novel formula for personalised near-peer learning

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Introduction Near peer teaching is an established teaching method and can be as effective as faculty taught programmes, however it is often underutilised in comparison. There are numerous NPT programmes but its use is less established in undergraduate clinical skills teaching. We aim to identify the benefits of one-to-one clinical examination teaching using a mock OSCE and modified one minute preceptor model.

Patients and methods We recruited 75 second year students to sit six randomly assigned 5 minute OSCE stations followed by 2 and a half minutes of teaching by final year medical students or junior doctors. Data collected included pre and post intervention questionnaires which featured Likert psychometric and zero-ten satisfaction scales to look at overall satisfaction and confidence change. As a control, students were asked to rate their confidence before and after the OSCE for all stations, including those that they did not sit. In addition free text answers and demographic data were obtained as well as comparison to a recent faculty led mock OSCE which did not utilise micro skills teaching.

Results All stations showed a significant increase in confidence from baseline after teaching. Most stations had a small but significant increase from baseline even if the student hadn't been taught on that station. With the exception of one station (upper neurological), all stations had significant student confidence increases in those who received teaching in comparison to those who did not receive teaching. Student satisfaction for our event was significantly higher than the faculty mock OSCE. Written free text themes include favouring the course design, time to learn new skills and the realism of a mock OSCE helped their learning experience.

Conclusions Our study demonstrates a resource light and time efficient method of clinical skills teaching. 6 stations were taught to students in less than 60 minutes, offering personalised feedback and mentoring. The one station which did not show a significant increase in comparison to control could be explained by transferable skills as all students sat either upper or lower neurological examination. The upper neurological station also had the smallest control sample which could suggest it was underpowered. To identify if our program can achieve quantitative results, in addition to student impact, we aim to host an RCT with independent markers to ensure our teaching leads to better doctors.

References

- 1 E. Rees et al, How does peer teaching compare to faculty teaching? A systematic review and meta-analysis, *Medical Teacher* 2016; 38:829-837.
- 2 Neher JO, Gordon KC, Meyer B, Stevens N. A five-step 'microskills' model of clinical teaching. *Clin Teach.* 1992;5:419–24.

The ECG in Suspected Pulmonary Embolism: Case Control Study

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Introduction Pulmonary embolism is one of the most common cardiovascular disease with 47,594 cases reported in the UK in 2014. The clinical presentation varies depending on the number, size and distribution of emboli and on underlying cardiorespiratory reserve. The role of ECG is mainly to exclude alternative diagnoses such as acute coronary syndrome; a review of literature highlighted studies which correlated ECG changes with prognosis (Zhan et al, Icli et al) and clot location with incidence of ECG abnormalities (Zhang et al). We therefore formed the following questions for the case controlled study: A) What is the effect of clot load on the ECG? B) Do certain ECG changes have greater specificity and sensitivity in given clot loads? C) What is the use of the ECG in the diagnosis of PE?

Patients and methods This was a retrospective case controlled study, using a list of 1397 consecutive CTPAs done at DGRI (Nobes et al), of which 313 were positive. Positive CTPAs were then screened for whether ECG +/- 72 hours of CT could be located (217) and if this was the first PE (189). This group was age (+/- 3 years) and sex matched to patients with negative CTPAs. Medical histories for patients in both groups at time of admission were also screened for cardiorespiratory disease as we were concerned this could give alternate reasons for ECG findings. CT scans were reviewed by a consultant radiologist to determine clot load and ECGs were blinded and given to a consultant cardiologist for analysis of changes.

Results 20-25% patients with PE, including those with large clot load, had normal ECGs. The commonest ECG finding in patients with PE was sinus tachycardia though this was not invariable: around 70% patients with large clot load had heart rates <100/min. S1Q3T3, P pulmonale and right axis deviation were infrequent findings (<5%). Right ventricular (RV) strain pattern occurred more commonly in patients than controls (11.2% v 2.7%, p<0.005), particularly in those with large clot load (17.1% v 2.6%, p<0.005; specificity 97.4%, sensitivity 17.1%). Our findings were confounded, to a degree, by the presence of cardiorespiratory disease. Notwithstanding, we were able to show a significant association between RV strain and PE despite the inclusion of such patients.

Conclusions S1Q3T3 is an uncommon finding in PE. An ECG showing RV strain in a breathless patient is highly suggestive of PE with specificity 97.4% and sensitivity 17.1% for large clot load. Many of the other ECG changes that have been described in PE occur too infrequently to be of predictive value or are as likely to occur in patients with cardiorespiratory disease suspected of having PE whose CTPAs are negative.

References

1. Zhan Z, Wang C, Wang Z, Nikus K, Baranchuk A, Yuan R, et al. Significance of ST-segment deviation in patients with acute pulmonary embolism and negative T waves. *Cardiol J* 2015;22(5):583-589.
2. Icli A, Kayrak M, Akilli H, Aribas A, Coskun M, Ozer S, et al. Prognostic value of Tpeak-Tend interval in patients with acute pulmonary embolism. *BMC Cardiovasc Disord* 2015;15(1):99-99.
3. Zhang J, Liu G, Wang S, Du W, Lv P, Guo H, et al. The electrocardiographic characteristics of an acute embolism in the pulmonary trunk and the main pulmonary arteries. *Am J Emerg Med* 2016;34(2):212-217.
4. Nobes J, Messow C-M, Khan M, et al. Age-adjusted D-dimer excludes pulmonary embolism and reduces unnecessary radiation exposure in older adults: retrospective study. *Postgrad Med J* 2016.