PATEY PRIZE 2

O8   CHARACTERISATION OF PANCREATIC STELLATE CELL (PSC) EXOSOMES AND THEIR IMPACT ON PANCREATIC CANCER CELL PHENOTYPE

SM Robinson (1,2), DA Mann (1), J Mann (1), RM Charnley (2), SA White (1,2)
(1) Institute of Cellular Medicine, Newcastle University (2) Freeman Hospital, Newcastle upon Tyne

Introduction: Background Exosomes vesicles measuring up to 100nm in size and play key roles in cell-to-cell communication. They are particularly rich sources of miRNA and are therefore a means by which one cell can impact on the gene expression and phenotype of neighbouring cells. Pancreatic cancer has a dense stroma of which PSCs are a key component. The aim of this study is to characterise PSC exosomes and their impact on pancreatic cancer cell phenotype.

Method Exosomes were isolated from conditioned media of PSCs. Their RNA content was isolated and the miRNA cargo identified using the nanostring system. Pancreatic cancer cell lines MiaPACA2 and PANC1 were exposed to exosomes in 2D and 3D culture.

Result The top 15 miRNA's identified in exosomes were implicated in a variety of cancer associated KEGG pathways e.g. proteoglycans in cancer ($p<0.0001$), pancreatic cancer ($p<0.0001$), p53 signalling ($p<0.0001$), pathways in cancer ($p<0.0001$) involving over 620 genes. MiaPACA2 cells treated with exosomes demonstrate a 27% reduction in proliferation ($p<0.05$) whereas this is not seen in PANC1 cells. Exosome treatment reduced the sensitivity of PANC1 cells but not miaPACA2 cells to Gemcitabine. MiaPACA2 cells do not form spheroids in hanging drop culture however in the presence of exosomes do form 3D structures. PANC1 formed more compact spheroids in the presence of exosomes ($p<0.001$). This was associated with increased expression of cell adhesion genes e.g. CTGF ($p<0.01$), uPAR ($p<0.01$).

Conclusion PSC exosomes contain miRNA's implicated in a variety of cancer related cell signalling processes and impact on the phenotype of pancreatic cancer cells.

Take-home message:
PSC exosomes appear to have an impact on the phenotype of pancreatic cancer cells.

O9   DYSFUNCTIONAL TYROSINE METABOLISM IN OESOPHAGO-GASTRIC CANCER AND LINK TO PHENOL PRODUCTION

T Wiggins, S Antonowicz, S Kumar, Z Bodai, SR Markar, H Kudo, F Rosini, R Goldin. Z Takats, GB Hanna
Imperial College London

Introduction: Phenol has been identified as a potential marker of oesophago-gastric cancer in exhaled breath. The mechanism of origin is unknown but may be linked to dysfunctional tyrosine metabolism

Method: Dried blood spots from 33 oesophago-gastric cancer patients and 34 controls were analysed using nano-spray ionisation mass spectrometry and compounds relating to tyrosine breakdown were measured. Quantitative polymerase chain reaction (qPCR) was performed for pathway enzymes in 36 oesophageal and 16 gastric cancer cases. Immunohistochemistry was undertaken for these enzymes. Gas-chromatography mass spectrometry measured conversion of tyrosine to phenol within gastric content.

Result: Dried blood spot analysis demonstrated a significant reduction in median peak intensity for homogentisate in the cancer patients (Control cohort 1.03e-2; Cancer cohort 7.19e-3. Mann-Whitney U test (MWU) $p <0.001$). qPCR for oesophageal cancer patients demonstrated increased activity of the enzyme responsible for homogentisate breakdown (homogentisate 1,2-dioxygenase; fold change to matched healthy mucosa 62.96, MWU $p<0.0001$). In gastric cancer cases the enzyme responsible for homogentisate production was reduced (hydroxyphenylpyruvate dioxygenase, fold change 0.21, MWU 0.049). These findings were both validated with immunohistochemistry. Enrichment of gastric juice with tyrosine lead to phenol production.

Conclusion : This study has demonstrated that tyrosine metabolism is dysfunctional in oesophageal and gastric cancer with different areas of this biological pathway affected in each disease. This has been cross-validated with metabolic, biological and histological techniques. Tyrosine metabolism has been linked to phenol production within the stomach. Establishing the mechanism responsible for elevated phenol concentrations in oesophago-gastric cancer patients will help establish breath testing for early diagnosis of this disease.

Take-home message:
Tyrosine metabolism is dysfunctional in oesophago-gastric cancer and may be linked to increased phenol concentration in exhaled breath of these patients.

O10   IS AUTONOMIC NERVOUS ACTIVITY ALTERED IN PRIMARY HYPERHIDROSIS?

M Desai, T Tidswell, DM Baker
Royal Free London NHS Foundation Trust

Introduction: Hyperhidrosis, the production of sweat greater than physiological demands, is successfully managed by disturbing autonomic nervous activity (e.g. thoracoscopic sympathectomy, Botox injections, topical or systemic anticholinergic drug therapy). This study determines if patients with hyperhidrosis have an altered autonomic nervous activity.

Method: 17 consecutive patients with primary hyperhidrosis (mean age 27±7 years; female: male

13:4) affecting various regions (axilla 5, palmarplantar 8, and generalised 4) and Hyperhidrosis Disease Severity Scores of 4/4, underwent neurophysiology tests prior to commencing treatment. Studies included sural sensory nerve large fibre conduction testing, sympathetic skin response testing (change in skin voltage associated with sympathetic activity, usually measured in response to loud noise or electrical stimulation of a different limb); cardiac RR interval variability testing (mainly a balance between sympathetic and parasympathetic activity), tested with normal and deep breathing.

Result: In all cases the sural nerve sensory amplitude was within the normal range (24 μV: range 12-38). There was a normal sympathetic skin responses in 16/17 patients (one patient who had previously had a sympathectomy had an absent response from the hand, but a normal response from the foot). The RR interval increase from normal to deep breathing was a mean of 2.8 seconds (range 1.2 to 4.0) which are all with in the normal range.

Conclusion : Hyperhidrosis is associated with no significant autonomic dysfunction. The precipitating factors are most likely to be arising from a central nervous system cause.

Take-home message:
Hyperhidrosis is associated with no significant autonomic dysfunction.

O11   DEVELOPMENT AND VALIDATION OF A PANCREATIC INJURY MORTALITY SCORE (PIMS) BASED ON 473 CONSECUTIVE PATIENTS TREATED AT A LEVEL 1 TRAUMA CENTRE

RT Spence, A Nicol, PH Navsaria, JEJ Krige
HPB Surgical Unit, Department of Surgery University of Cape Town Health Sciences Faculty Anzio Road, Observatory, 7925

Introduction: At present there is no consensus regarding which specific risk factors predict mortality after a major pancreatic injury. Our objective was to develop a pancreatic injury mortality score (PIMS).

Method All consecutive patients who had sustained pancreatic injuries and were treated at Groote Schuur Hospital, South Africa, between January 1990 and December 2015 were included. Two thirds of the patients were assigned to the derivation cohort and one third to the validation cohort. Variables with a univariate correlation with mortality in the derivation cohort were considered in stepwise logistic regression analyses that identified the factors included in the risk index. The PIMS discriminative ability was assessed using receiver operating characteristic (ROC) analysis.

Result During the study period, 473 patients were treated for pancreatic injuries with a mortality rate of 15.4%. The resultant PIMS relies on age, presence or absence of shock, presence or absence of a vascular injury, number of associated injuries and the pancreatic AAST. The ROC of the score in the derivation dataset was 0.84 (95% CI 0.79 – 0.89) and in the validation dataset was 0.91 (95% CI 0.84 – 0.97), (p= 0.1). Finally, cut-off scores were used to generate three risk groups and the rate of mortality in the low (PIMS 0-4), medium (PIMS 5-9), and high-risk (PIMS 10–20) groups was 0.52%, 14.36% and 51.19%, and 0.81%, 16.94% and 47.76% in the derivation and validation datasets, respectively.

Conclusion: We have derived and validated the PIMS, a novel risk prediction score for in-hospital mortality following major pancreatic trauma.

Take-home message:
At present there is no consensus regarding which specific risk factors predict mortality after a major pancreatic injury.We have derived and validated the PIMS, a novel risk prediction score for in-hospital mortality following major pancreatic trauma.

O12   THE EFFECT OF PERFUSATE TEMPERATURE ON RENAL FUNCTION DURING EX-VIVO KIDNEY PERFUSION

TD Adams (1), M Patel (2), SA Hosgood (1), ML Nicholson (1)
(1) Division of Transplantation, Department of Surgery, University of Cambridge, Department of Surgery, (2) Department Infection, Immunity and Inflammation, Transplant Group, University of Leicester

Introduction: Reducing the temperature of the perfusate to sub-normothermia may be beneficial during ex-vivo perfusion (EVP) and early graft function. The aim of this study was to investigate whether sub-normothermia would influence the conditioning effect of EVP when compared to normothermic perfusion, and standard cold static storage (CS).

Method: Porcine kidneys underwent static CS for 23hrs followed by 1h of EVP using leukocyte-depleted blood at a mean temperature of 32°C or 37°C (both n= 6). Following this, kidneys were reperfused with whole autologous blood at 37°C for 3h to assess renal function and injury. These were compared to a control group that underwent 24h CS (n=6). Continuous functional measurements were taken; urine output, blood and cortical wedge biopsies were taken at hourly intervals.

Result: During EVP, kidneys perfused at 37°C had a higher level of renal blood flow (246±61 vs. 90±23 ml/min/100g, p=0.001) and oxygen consumption (53.7±19.0 vs. 27.5±3.9 ml/min/g, p=0.002) compared to EVP at 32°C. During reperfusion, 32°C EVP kidneys had lower creatinine clearance (p=0.023) and urine output than control (0.2±0.2 vs 0.8± 0.5 ml/min/100g, p=0.011) and a higher fractional excretion of sodium (p=0.01), lower serum potassium (p=0.023) and lower serum aspartate transaminase than 37°C EVP kidneys (156±50 vs. 823±412 mmol/L, p=0.009).

Conclusion: Near-physiological temperatures of 37°C better preserved tubular and renal function during 1h of EVP, when compared to EVP at 32°C or cold storage.

Take-home message:
Ex-Vivo Perfusion improves the condition of transplant kidneys. Near-physiological temperatures of 37°C better preserved tubular and renal function during 1h of EVP, when compared to EVP at 32°C or cold storage.

O13   THE STUDY OF VISUAL COMPONENTS OF 2 DIMENSIONAL VS 3 DIMENSIONAL LAPAROSCOPIC IMAGES

M El Boghdady, G Ramakrishnan, B Tang, A Alijani
Cuschieri Skills Centre, Ninewells Hospital and Medical School, University of Dundee

Introduction: There is strong evidence to suggest that 3D imaging improves the laparoscopic task performance when compared against 2D. However, to date no study has explained why that might be. We identified 6 generic visual components during laparoscopic imaging and aimed to study each component in both 2D and 3D environments for comparison.
Method: Twenty four consented laparoscopic novices performed specific isolated tasks in a laparoscopic endo trainer in 2D and 3D separately. The six endpoints were the accuracy in detecting changes in the following components: area, distance, curvature, angle, volume and spatial coordinates. All the components except the spatial coordinates were assessed by: creation, measurement and comparison. Each component was analysed between 2D and 3D groups, and within each group at different values. Tests of Spatial coordinates were video recorded and analysed for error number and error types by Human Reliability Analysis technique. Errors types included past-pointing, not reaching the object, and touching the wrong object. The results were statistically analysed with independent T-test.
Result: There was no statistically significant difference between 2D and 3D accuracy of measurement in the angle, area, distance and curvature. 3D performed more accurately in comparing volumes ($p=0.05$). In spatial coordinates, there was a statistically significant higher number of errors in 2D as compared to the 3D ($p<0.001$). Past-pointing and touching the wrong objects were significantly higher in 2D ($p<0.05$).
Conclusion : Between all the visual components, detecting change in volume and the spatial coordinates showed significant improvement in 3D environment when compared to 2D.
Take-home message:
3D laparoscopy improves the task performance by better detection in changes in volume of shapes and the spatial coordinates.

O14   ACCURACY OF STANDARD METHODS USED TO ESTIMATE BURN SIZE COMPARED TO DIFFERENT SMARTPHONE APPLICATIONS.

K. Smith, S Southern, S Jivan
Pinderfields Hospital

Introduction: Accurate estimation of burn size is essential to ensure appropriate treatment is given to the patient especially with respect to resuscitations burns. Under estimation can lead to delayed treatment and overestimation can lead to unnecessary fluid resuscitation.
Method: We drew a known area onto the back of a model to represent a burn injury, then using the Du Bois formula we calculated this as a percentage of the total body surface area. We then transferred this onto a Lund and Browder Chat and a rule of nines chart and estimated the burn surface area using these standard methods. Next we used the Mersey Burns application and BurnCase3D application, and drew out the same area to see what percentage these methods gave us.
Result: We found that the 2D images used on the paper charts and the 2D Mersey Burns app all overestimated burn size when compared to the calculated one from the DuBois formula. The 3D model used in the BurnCase 3D app gave a much more accurate percentage.
Conclusion: There was an overestimation of burn size on all 2D methods, which may be attributed to the fact that none of these methods include the flanks of the body. We propose an adaptation of the Lund and Browder chart to include a side view of the images where flanks of the body are also given a percentage surface area.
Take-home message:
Current 2D methods of estimating burn size need to be improved, as flanks of the body are not included which results in an overestimation of percentage burn size.