

the Wilson criteria is to detect disease that could be treated at an early stage. This audit aimed to measure the effectiveness of the upper age screening extension in Shropshire by comparing the cancer diagnosis rate to general screening population, size of cancer, and the ability to perform breast conservation.

Methods: Retrospective analysis of Breast Screening age extension of women invited to be screened aged 71 to 73 years old in Shropshire. Data included number of women invited, uptake rate, recall rate, cancer diagnosis and surgical treatment.

Results: 5517 older women were invited into Shropshire Breast Screening Programme as part of the AgeX trial by PHE since September 2014. 4801 women attended and were screened; 87% uptake rate, which exceeds BSP attendance rate of >80%. 104 women were recalled to assessment (2.1%) which is below BSP standard of <5% recall rate for incident screens. 46.1% (48) of women recalled to assessment were given a cancer diagnosis, this is compared to 30.5% in general screening population. 41.6% of the invasive cancer was <15mm. 95.8% of patients had surgery, with 70.8% of patients having breast and axillary conservation surgery.

Conclusion: BSP Standards uptake rate and recall rate have been exceeded by upper age extension. Our experience shows high cancer pick up rate of small cancers with the majority patients able to have breast conserving surgery.

61.

A COMPARATIVE STUDY OF MPNST ARISING SPORADICALLY AND IN PATIENTS WITH NF-1

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Background: Malignant peripheral nerve sheath tumours (MPNST) are a rare soft tissue sarcoma originating from the peripheral nerves. They can either arise sporadically or be associated with a germline mutation in the NF-1 gene. We wanted to analyse if there was a difference in outcome between these two groups of patients with this disease treatment.

Method: All patients treated at the Royal Marsden Hospital between 2010 – 2015 with MPNST were identified and analysed in this retrospective review. Kaplan Meier survival curves were constructed on patients with NF or sporadic MPNST.

39 patients were included in the analysis with a 2:1 male female ratio. The median age at diagnosis was 42 years and 46% of patients were NF positive. The site of tumour growth was equally distributed between trunk and limbs; 19 tumours were located in the trunk, 14 in the leg, 5 in the arm and 1 in the head/ neck.

Results: 29 patients were operable (74.3%), 3 had metastases at diagnosis and 7 had locally advanced disease. 28 patients underwent surgery with curative intent; 6 had neoadjuvant radiotherapy and 8 had radiotherapy post op.

75% of patients receiving surgery alone were alive at 4 years. Prognostic factors comparing both groups of patients are shown in table 1. Median OS in patients with NF 1 was 24.5 months compared with 48 months in non NF-1 tumours.

Conclusion: Despite similar standard prognostic features between the two cohorts, patients with NF-1 had much poorer survival suggesting an intrinsic negative effect on outcome.

86.

THE IMPACT OF PRE-OPERATIVE BILIARY DRAINAGE ON POSTOPERATIVE OUTCOMES IN PATIENTS UNDERGOING SURGERY FOR PANCREATIC CANCER, A RETROSPECTIVE SINGLE CENTRE STUDY

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Background: The optimum management of jaundice in patients with resectable pancreatic cancer remains controversial. Whilst pre-operative biliary drainage is often a helpful bridge to surgery, it reportedly increases the morbidity rate when compared to upfront surgery. This retrospective

study, evaluated postoperative outcomes in this cohort of patients with and without pre-operative biliary drainage.

Methods: All patients who underwent surgery for pancreatic cancer with a curative intent in a single tertiary centre over a 5-year period were included. Patients were stratified into those who underwent pre-operative biliary drainage (endoscopic retrograde cholangio-pancreatography or percutaneous transhepatic cholangiography) and those who received upfront surgery. Information collected included demographic data, biochemistry results and post-operative course. The main outcomes were post-operative complications, length of stay and mortality.

Results: A total of 113 patients undergoing surgery with curative intent met inclusion criteria. There was an equivalence of male and female patients with a mean age of 64 years. The mean Charlson comorbidity index was 4.7 and the mean ASA grade was 1.8. The mean serum bilirubin level was 127. Seventy-eight (69%) patients underwent pre-operative biliary drainage. Biliary drainage was associated with a significant increase in intra-operative blood loss ($P=0.005$). However, there was no significant difference in post-operative complications, length of stay or mortality.

Conclusion: Pre-operative biliary drainage was performed in two-thirds of patients in this cohort and was associated with a significant risk of intra-operative blood loss. However, it had no impact on the overall post-operative course including post-operative complications, prolonged length of stay or mortality.

BASO~ACS Prize Papers Monday 18th November 2019, 09:00 to 10:00

18.

ORTHOTOPIC LIVER TRANSPLANTATION FOR INTRAHEPATIC CHOLANGIOCARCINOMA: A SYSTEMATIC REVIEW & PROPORTIONAL META-ANALYSIS

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Background: Prognosis for intrahepatic cholangiocarcinoma (iCCA) has improved little in recent decades, despite increasing incidence. Initially hypothesised as an ideal treatment option for iCCA, orthotopic liver transplantation (OLT) has been largely abandoned due to the extremely poor survival rates reported by early studies. Recent studies have however reignited the discussion surrounding OLT for iCCA, especially in the setting of 'early' iCCA & when treated with neoadjuvant chemoradiation.

Methods: A search of the MEDLINE, EMBASE, Scopus and Web of Science databases was conducted and data were extracted from relevant studies. A proportional meta-analysis was performed to pool the 1, 3- and 5-year survival and disease recurrence rates, reported following OLT for iCCA.

Results: Eleven studies comprising 215 patients were eligible for final analysis. The pooled 1, 3- and 5-year overall survival rates following OLT were 69.1% (95% CI 56.5 – 79.5), 46.3% (95% CI 34.7 – 58.4) and 37.2% (95% CI 26.6 – 49.3). The pooled recurrence rate post-OLT was 43.3% (95% CI 33.9 – 53.2). Treatment with neoadjuvant chemoradiation prior to OLT resulted in increased long-term survival, whilst finding of iCCA incidentally on explant specimen had no effect on long-term outcomes.

Conclusions: Long term survival outcomes following OLT for iCCA are poor, and disease recurrences rates are high. Although recent studies have shown improved survival when OLT is combined with neoadjuvant therapy, these are limited in scope and number. Superior outcomes have been reported following OLT for 'early' iCCA, these outcomes could potentially be improved further with incorporation of a neoadjuvant treatment protocol.

27.

THE MATRIX METALLOPROTEINASE SYSTEM IN COLORECTAL CANCER PROGRESSION AND 15-YEAR SURVIVAL

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Background: The matrix metalloproteinase (MMP) system is involved in tumour invasion and metastasis in colorectal and other cancers. The MMP

system consists of the MMPs and specific tissue inhibitors of metalloproteinases (TIMPs). Synthetic MMP inhibitors have been trialled with limited success. The study will determine the expression of MMP system components in colorectal tumour and pre-operative plasma samples and correlate these with tumour pathology and 15-year survival.

Methods: 100 paired tumour and normal tissue samples and 76 pre-operative plasma samples were analysed by ELISA for MMPs (-1, -2, -3, -7 and -9) and tissue inhibitors (TIMP-1, -2; ng/mg protein for tissue and ng/ml for plasma samples). Tissue and plasma levels were correlated with tumour pathology ($P < 0.05$; Spearman's correlation coefficient) and 15-year survival analysis was performed (overall and disease-free; Kaplan Meier, $P < 0.05$). The study had ethics committee approval.

Results: The levels of MMPs and TIMP-1 were all significantly greater in colorectal tumour tissue than the corresponding normal mucosa. Tumour tissue levels of all MMPs correlated with Dukes stage and TIMP-1 with tumour depth. Preoperative plasma levels of TIMP-2 demonstrated a negative correlation with tumour differentiation.

Results of Kaplan Meier survival analysis found levels of active MMP-2 and MMP-9 in tumour tissue and MMP-7 in plasma samples significantly correlated with both overall and disease-free 15-year survival, with higher levels associated with poorer survival.

Conclusions: Tissue and pre-operative plasma levels of some MMP system components significantly correlated with the tumour histopathology, disease-free and overall 15-year survival.

35.

PHARMACOLOGICAL INHIBITION OF ACID CERAMIDASE; A NOVEL RADIOSENSITISER IN A 3D RECTAL CANCER MODEL

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Background: We have previously utilized proteomic and immuno-histochemical data to validate that high levels of acid ceramidase (AC) expression confers poorer neoadjuvant chemoradiotherapy response in rectal cancer. Biological (siRNA, plasmid) and pharmacological (Carmofur) AC manipulation validated altered responses of radiosensitivity in-vitro. LCL521, a novel small molecular inhibitor, specifically targets AC.

Methods: Optimal LCL521 dosing using standard ELISA activity assays with DMSO control was established in multiple colorectal cancer cell lines (HCT116, HT29, LIM1215). Western blotting confirmed altered expression of AC. Standard clonogenic assays assessed cell survival following increasing x-ray irradiation and change in spheroid volume to assess growth.

Results: ELISA revealed reduced expression of AC to 18% with 10 μ m LCL in HCT116, 12% HT29 and 30% LIM1215. 2-hour pre-treated clonogenic assays demonstrated reduced colony formation efficiency (colonies/number of cells plated–CFE) and improved radiosensitivity across cell lines. HT29 showed 0.758(CFE) control v 0.317(CFE) LCL at 1Gy, 0.441(CFE) control v 0.260(CFE) at 2Gy and 0.0250(CFE) control v 0.0119(CFE) LCL at 4Gy (p value=0.024). LCL521 dosing of spheroids improved radiosensitivity across cell lines (HCT116 spheroid volume day 15 post-LCL521 2.36x10⁻⁵mm v control 4.15x10⁻⁵mm).

Conclusions: Initial work demonstrates that pharmacological inhibition of AC with LCL521 produces comparative radiosensitizing effects in-vitro with these cell lines. This work further solidifies acid ceramidase as a potential therapeutic biomarker, however further work is needed to recapitulate these findings in more complex organoid models and ultimately in-vivo to establish a translatable clinical role in this setting.

36.

ACID CERAMIDASE AS A POTENTIAL BIOMARKER FOR LOCALLY ADVANCED RECTAL CANCER; IS APOPTOSIS THE MECHANISM?

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Background: We have previously utilized proteomic and immuno-histochemical data to validate that high levels of acid ceramidase (AC) expression confers poorer neoadjuvant chemoradiotherapy response in rectal cancer. Biological (siRNA knockdown, plasmid over-expression) and pharmacological (Carmofur, LCL521) AC manipulation validated altered responses of radiosensitivity in-vitro; further solidifying the potential of AC as a therapeutic biomarker through unknown mechanism.

Methods: siRNA AC knockdown was achieved in multiple colorectal cancer cell lines (HCT116, HT29, LIM1215), with non-targeting siRNA control, prior to irradiation. Cleaved PARP-1 fragments were detected and quantified using western blotting. Cell cycle analysis was performed using Attune NxT Flow Cytometry and propidium iodide staining (PI). Progressive apoptosis stage detection was achieved combining a PI and Annexin V stain.

Results: Western blotting confirmed increased PARP-1 cleavage fragments for siRNA AC across radiation doses compared to control (4.8-8.2fold increase ($p < 0.05$)). These findings were reproduced with treatment with AC inhibitor Carmofur. Cell cycle analysis demonstrated a pre-G0/1 spike compared to control; also potentially indicative of apoptosis. Annexin V staining showed a significant increase in cells of all stages of apoptosis at both 8 and 24hours post-irradiation.

Conclusions: Initial work suggests that AC expression may be linked to cell apoptosis post-irradiation. With much needed potential predictive or therapeutic biomarkers for rectal cancer, AC may be able to act as a target to improve response to neoadjuvant chemoradiotherapy and allow tailored treatment. Further work to fully understand the underlying mechanism is required to establish a clinical role.

75.

IS ONCOPLASTIC BREAST CONSERVING SURGERY ONCOLOGICALLY SAFE? A META-ANALYSIS OF 18,163 PATIENTS

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Background: The role of oncoplastic breast conserving surgery (OBCS) is that of a middle ground between standard breast conserving surgery (SBCS) and mastectomy - it allows adequate resection margins of tumours unsuitable for traditional breast conserving surgery whilst allowing for a better cosmetic outcome and a reduced morbidity rate when compared to a traditional mastectomy. However, due to this being a relatively new type of procedure, there is limited evidence on its oncological safety.

Methods: This study aims to compare oncological safety of OBCS with SBCS and mastectomy by examining the relative risk of cancer recurrence and re-operation rates. Literature search of Pubmed and Web of Science databases was conducted. Meta-Analysis was performed using R Statistical Software (www.r-project.org).

Results: 19 studies including 18,163 patients were included in the analysis. For the primary outcome measure of recurrence there was found to be no significant difference between the OBCS and SBCS or mastectomy (RR 0.861; 95% CI 0.640-1.160; $p < 0.296$). The secondary outcome measure of re-operation was initially found to be significant in favour of OBCS (RR 0.64; 95% CI 0.46-0.89; $p < 0.01$), however after adjustment for publication bias this was attenuated to an insignificant difference between the two study groups (RR 0.86; 95% CI 0.56-1.31; $p > 0.05$).

Conclusions: For both recurrence of cancer and re-operation rate, there was not found to be a significant difference between OBCS and techniques that are more traditional. This would suggest that OBCS is of comparable oncological safety to more established operations and a useful option in suitable patients.

79.

ROLE OF BONE SCINTIGRAPHY IN ADDITION TO CT SCAN IN THE DETECTION OF BONE METASTASIS IN ADVANCED BREAST CANCER

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Background: The NICE guidelines (CG 81: 1.1.2& 1.1.3) updated in 2017; in spite of the above guidance, the current policy for detection of bone metastatic is not uniform in the entire country (UK), some centres count on staging CT of the chest, abdomen and pelvis (CT CAP) only but many still