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Abstracts

Scrubs (QUB Surgical Society) Medical Students' Academic Medicine Conference & Research Symposium

30th April 2022, Queen's University, Belfast

ENDOSCOPIC BALLOON DILATATION FOR PAEDIATRIC SUBGLOTTIC STENOSIS: SYSTEMATIC REVIEW AND META-ANALYSIS

Author: Gopika Sreejith

Aim: Subglottic stenosis (SGS) is a rare life-threatening condition that involves a narrowing of the airway. It may be congenital or acquired affecting children predominantly. Traditionally, it has been treated by surgical interventions, but in recent times a shift towards minimally invasive Endoscopic Balloon Dilatation (EBD) has been observed. This review aims to identify whether EBD is a safe approach as the primary mode of treatment of SGS in the paediatric population.

Methods: A systematic review was performed on EBD for paediatric SGS in compliance with the PRISMA guidelines. Studies published from 2000 onwards, with sample size greater than 5 and described EBD without adjuvant procedures were included. A meta-analysis of proportions was performed using the R software.

Results: 21 studies were included, with a total of 922 patients, of which 753 underwent EBD. The mean sample size of the studies is 43.90 ± 40.25, and the grand mean age is 2.91 ± 4.08 years. Primary outcome assessed was technical success. A high overall technical success rate (avoidance of tracheostomy/laryngotracheal reconstruction) was observed (84.30%, 95% CI [76.62%, 89.80%]). Similarly, low levels of mortality (2.13%, 95% CI [1.09%, 4.13%]), high rates of symptom improvement (77.42%, 95% CI [62.62%, 87.52%]) and low rates of reintervention (30.43%, 95% CI [18.88%, 45.12%]) were also observed.

Conclusion: EBD is a successful procedure in majority patients, with low levels of adverse events and marked symptom improvement. It is therefore a safe alternative to current procedures in the primary management of paediatric SGS.

A REVIEW OF LITERATURE ON ANATOMICAL VARIATION OF THE EXTRA-HEPATIC BILIARY TREE

Author: Grace Kettyle

Introduction: Knowledge of the notoriously variable anatomy of the extrahepatic biliary tree is crucial, given the increased occurrence and complexity of hepatobiliary surgeries where failure to recognise the variant anatomy may lead to inadvertent iatrogenic injury.

Aim: This review aimed to examine world literature to establish the types and frequencies of anatomical variants within the extrahepatic biliary tree, identified using cadaveric techniques and imaging modalities.

Methods: A database search of MEDLINE, EMBASE and PubMed conducted in June 2021 returned 3440 articles, of which 29 were deemed eligible for inclusion.

Results: A rare malposition, the left-sided gallbladder, was observed in 0.04-0.60% across five studies. The medially inserted cystic duct into the common hepatic duct had a reported prevalence ranging from 10-24.3%. Variant cystic artery origin was noted from the left hepatic artery (1-1.9%), gastroduodenal artery (1-7.5%) and the aberrant right hepatic artery (3-12.1%). It was also observed that in 3.6-32% of subjects the course of the cystic artery lay extraneous to Calot's triangle. Michels' and Hiatt's classification systems were used to define the anatomical variations of the hepatic arteries: studies using Michels' Type III reported a prevalence from 6.4-15%, Michels' Type VI from 0.6-7% and Hiatt's Type III recorded an incidence of 9.7-14.8%.

Conclusion: The anatomy of the extrahepatic biliary tract is *indeed* widely variable, as is the conflicting reported data from the different imaging modalities used. Surgeons should therefore anticipate such complexities and adapt techniques to avoid biliary and arterial injuries and associated intra- and postoperative complications.

IMPACT OF THE COVID-19 PANDEMIC ON PATIENTS WITH PAEDIATRIC CANCER IN LOW-INCOME, MIDDLE-INCOME, AND HIGH-INCOME COUNTRIES: A MULTICENTRE, INTERNATIONAL, OBSERVATIONAL COHORT STUDY.

Author: Manasi Shirke

Aim: Paediatric cancer is a leading cause of death for children. Children in low-income and middle-income countries (LMICs) were four times more likely to die than children in high-income countries (HICs). This study aimed

to test the hypothesis that the COVID-19 pandemic had affected the delivery of healthcare services worldwide and exacerbated the disparity in paediatric cancer outcomes between LMICs and HICs.

Methods: A multicentre, international, collaborative cohort study. Patients recruited from 91 hospitals and cancer centres in 39 countries providing cancer treatment to paediatric patients between March and December 2020.

Results:1660 patients were recruited. 219 children had changes to their treatment due to the pandemic. Patients in LMICs were primarily affected (n=182/219, 83.1%). Relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 12.1 (95% CI 2.93 to 50.3) and 7.9 (95% CI 3.2 to 19.7) times the odds of death at 30 days and 90 days, respectively, after presentation during the COVID-19 pandemic ($p<0.001$). After adjusting for confounders, patients with paediatric cancer in LMICs had 15.6 (95% CI 3.7 to 65.8) times the odds of death at 30 days ($p<0.001$).

Conclusions: The COVID-19 pandemic has affected paediatric oncology service provision. It has disproportionately affected patients in LMICs, highlighting and compounding existing disparities in healthcare systems globally that need addressing urgently. However, many patients with paediatric cancer continued to receive their normal standard of care. This speaks to the adaptability and resilience of healthcare systems and healthcare workers globally.

PREOPERATIVE MEDIASTINAL STAGING IN RESECTABLE NON-SMALL CELL LUNG CANCER IN A SINGLE SURGICAL CENTRE

Author: Rachael Macaulay & Karolina Janus

Accurate preoperative staging of mediastinal lymph nodes in non-small cell lung cancer (NSCLC) aids selection of patients suitable for lung resection.

Guidelines released by the European Society of Thoracic Surgeons (ESTS) in 2014 outline that 100% patients with suspected cN1 or greater NSCLC require invasive mediastinal lymph node staging.

Aim: The aim of this audit was to collect and analyse data on the adherence to the ESTS guidelines for patients with TNM stage N1 or greater clinical lung cancer in a single surgical centre in Belfast.

Method: Data of all lung cancer resections between February 2019 and May 2021 were retrospectively reviewed using the Electronic Care record and the Dendrite operative database. 72 patients met the inclusion criteria.

Data collection included whether patient received EBUS and/or mediastinoscopy, along with pre-operative N stage (from PET) and post-operative N stage

Results: On analysis of the data:

- 34% of cN1 patients received staging
- 68% of cN2 patients received staging
- 4 patients were under staged (cN1 pre resection and pN2 post resection)

Conclusion: Our results fell short of the 100% standard set by ESTS.

It should be highlighted that our audit was during the height of the Covid-19 pandemic. During this time, system pressures in healthcare, particularly in Northern Ireland, were unprecedented. This is highly likely to have impacted these results, particularly in patients where confirmatory staging may not change the eventual treatment. Re-audit is recommended.

THORACOTOMY VS VIDEO-ASSISTED THORACOSCOPIC SURGERY IN THE TREATMENT OF VASCULAR RINGS

Author: Isabel Campbell

Aims: This review aims to investigate the surgical approach, post-operative complications, length of stay in hospital, symptom resolution, reoperation rates and mortality of both VATS procedures and thoracotomy procedures in the treatment of VRs. Then to assess the application of VATs in a modern surgical setting.

Methods: A literature search of the MEDLINE and SCOPUS databases were performed at the projects inception to present. From the 361 articles retrieved, 271 were excluded. After utilising the exclusion criteria and thorough manual screening, 14 studies were included in the review. 6 of these studies investigated the outcomes using thoracotomy, 3 case reports plus 2 studies that investigated the outcomes using VATS and 3 studies that directly compared the two procedures. Overall, 590 cases in this review focused on using thoracotomy operations and 190 cases used VATS.

Results: The main themes from the results demonstrated VATS had a reduced operating time, length of stay in hospital, reduced rates of post-operative complications in comparison to thoracotomy. Both procedures showed similar rates of reoperation, mortality and short-term symptom resolution.

Conclusion: This review provides insight into the encouraging outcomes in the use of VATS in comparison to thoracotomy in the treatment of VRs. VATs should be considered as an alternative to thoracotomy in the surgical treatment of vascular rings.

APPLICATION OF PHOTOGRAMMETRY IN MEDICAL EDUCATION

Author: Sofia Aliotta

Aims: It aims to offer the reader a better understanding of photogrammetry as a 3D reconstruction technique and to provide some guidance on how to choose the appropriate

photogrammetry approach for their research area (including single- versus multi-camera setups, structure-from-motion versus conventional photogrammetry and macro- versus microphotogrammetry) as well as guidance on how to obtain high-quality data.

Methods: This review introduces the photogrammetry approaches currently used for digital 3D reconstruction in anatomy teaching and discusses their suitability for different applications.

Results: This review highlights some key advantages of photogrammetry for a variety of applications in medical education, but it also discusses the limitations of this technique and the importance of taking steps to obtain high-quality images for accurate 3D reconstruction

Conclusion: Photogrammetry is an upcoming technology in medical education as it provides a non-invasive and cost-effective alternative to established 3D imaging techniques such as computed tomography.

PRIZE WINNERS

Ariana Axiaq (1st place, poster presentation)
Nidhruv Ravikumar (1st place, poster presentation)
Julia Slater (2nd place, poster presentation)
Michael Keenan (3rd place, poster presentation)

Gopika Sreejith (1st place, oral presentations)
Isabel Campbell (2nd place, oral presentation)
Sofia Aliotta (2nd place, oral presentation)
Manasi Mahesh Shirke (3rd place, oral presentation)

Defining the Rectosigmoid Junction in Clinical Practice.

Julia Slater, Department of Anatomy, Queens University Belfast

ABSTRACT

The differentiation between sigmoid and rectal cancers requires a precise, standardised definition of the rectosigmoid junction. This may maximise the benefits of adjuvant therapies and provide greater consistency between clinical trials, making the comparison and analysis of results more reliable. In current clinical practice, there is no single definition used to identify this point which may lead to the misclassification and suboptimal management of these patients.

Systematic reviews of Medline and Embase identified 19 articles defining the rectosigmoid junction; these descriptions were collated and categorised as endoscopic, radiological, and morphological, including both macroscopic and histological findings. Endoscopic and radiological markers are identified during preoperative investigations whilst morphological landmarks are useful in the intraoperative and postoperative analysis. A preoperative definition may be used to initially categorise a lesion as being rectal or sigmoid and if rectal, inform the decision as to whether neoadjuvant chemoradiotherapy may be required. From the endoscopic and radiological markers discussed, the visualisation of sigmoid take-off on MRI most consistently fulfils these criteria. A second postoperative definition may be used to definitively confirm the location of a lesion within the resected specimen. Currently, the coalescence of the taenia coli at the rectosigmoid junction appears to be an appropriate marker.

INTRODUCTION

The rectosigmoid junction (RSJ) represents the transition point between the distal sigmoid colon and proximal rectum, highlighted in Figure 1. This region may be identified by several anatomical landmarks. However, there is currently no single, universal definition used to accurately and consistently identify the RSJ, as evidenced in the most recent national guidelines (2,3). This can pose an issue when defining colorectal cancers as either sigmoid or rectal lesions. This decision is currently made by the individual clinician or multidisciplinary team which may lead to misclassification of cancers and possible suboptimal management. Furthermore, clinical trials comparing rectal and sigmoid tumours use a range of markers to define the RSJ, limiting the comparability and interpretation of these important studies. Therefore, a consistent definition of the RSJ is desirable to provide a universal method of classifying and treating colorectal cancers and to standardise study protocols of future clinical trials.

The aims of this report were to identify and appraise the various markers of the RSJ, and to determine which of these markers may be used to differentiate between sigmoid and rectal lesions in the clinical setting.

METHODOLOGY

Systematic reviews of the literature were performed using the databases Medline and Embase; the keywords used were 'rectosigmoid junction' or 'colorectal junction'.

Inclusion criterion: a description of the RSJ in the abstract or a reference to a description made in the full text.

Exclusion criteria: Case reports and conference abstracts.

A total of 21 articles were identified from Medline and Embase; two of these articles were later recognised as commentaries of another review paper and were therefore excluded, leaving 19 papers to analyse.

RESULTS

Table 1, Categorisation of anatomical markers identifying the rectosigmoid junction.

Category	Description
Morphological	
• Macroscopic	Coalescence of the taenia coli
	Loss of epiploic appendices
	Level of the sacral promontory
	Level of the third sacral vertebra
	Sudeck's critical point
	Relation to the anterior peritoneal reflection
• Histological	Muscular sphincter
	Mesenteric waist
Endoscopic	
	Distance from the anal verge
	Distance from the dentate line
Radiological	
	Sacral promontory
	Anterior peritoneal reflection
	Sigmoid take-off

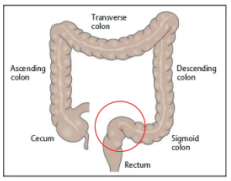


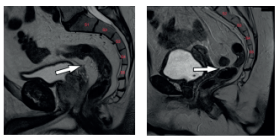
Figure 1, Anatomy of the Colon (1).

ANATOMICAL MARKERS

Histological / Macroscopic:
- Coalescence of taenia coli , shown as three distinct bands in Figure 2.
- May be disrupted by surrounding pathology.
- Does not inform preoperative diagnosis.

Endoscopic:
- RSJ typically measured from anal verge or dentate line.
- Variation in measurements possible between operators and instrumentation.

Radiological:
- Reproducible for preoperative diagnoses.
- Anterior peritoneal reflection, identified as 'definitively present' in 68% of MRI scans (5). Level varies between individuals as demonstrated in Figures 3 and 4.
- Sigmoid takeoff, demonstrated in Figure 5, describes the junction of mesorectum with mesosigmoid, level consistent in patients with and without colorectal cancer.



Figures 3 and 4, Sagittal MRI scans from a male and female respectively, white arrow indicates the levels of the anterior peritoneal reflection at S4 and below S5. Image courtesy of Radiology, Northumbria Healthcare Trust.

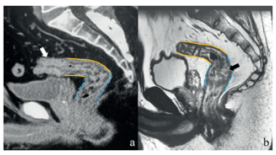


Figure 5, CT and MRI scans taken in the sagittal plane illustrating the rectosigmoid junction between the sigmoid colon, indicated by the solid yellow lines, and the rectum, indicated by the dashed blue line. White arrow - plane of the sigmoid take-off on CT. Black arrow – plane of the sigmoid take-off on MRI (6).

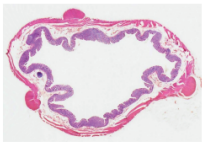


Figure 2, Histological specimen from the colon showing the three bands of the taenia coli (4).

CONCLUSION

The RSJ may be defined by a range of the morphological, endoscopic and radiological markers and it is of clinical importance in the characterisation of lesions as being rectal or sigmoid. The ideal preoperative marker for use in clinical practice would provide a consistent and reproducible means of distinguishing rectum from sigmoid, which also accounts for anatomical variations which may alter the length of the rectum. Of the endoscopic and radiological landmarks discussed, the sigmoid take-off appears to most accurately fulfils these criteria. The coalescence of the taenia coli is recommended as the postoperative definition of the RSJ, identified within a resected specimen. To further assess the suitability of these markers, a prospective study comparing the preoperative diagnoses of rectal and sigmoid lesions using the sigmoid take-off with postoperative identification of the taenia coli is recommended.

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The Impact of Ionising Radiation on Endothelial Cell Physiology

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Research conducted as part of MSc project in Cancer Medicine

ScruOs

Introduction

Aim:
To investigate the pathophysiology induced in endothelial cells following exposure to ionising radiation (IR).
An estimated 50-60% of patients with cancer receive some form of radiotherapy, which may be curative, palliative or an adjunct to surgery[1]. **It works by killing cancer cells preferentially compared to normal cells.**

However, normal tissues are unavoidably exposed to IR, leading to adverse effects including a triphasic inflammatory response. In the acute phase, rapidly dividing tissues (e.g. mucosae) fail to proliferate leading to ulceration. In the months following, fibrotic changes take place. This can lead to a loss of organ functionality[2].

In addition, the endothelium has been shown to exhibit a **pro-inflammatory change in phenotype**[3]. IR may be responsible for prolonged endothelial activation, along with endothelial cell loss. The endothelium is responsible for the delivery of O_2 and nutrients to surrounding cells[4]. Endothelial dysfunction induced by IR may therefore play a role in the chronic adverse effects of IR[5]. Therefore it is important to understand the underlying pathophysiological changes leading to this dysfunction.

Methods

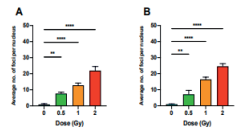
Cell culture:
Cardiac microvascular endothelial cells (CMEC) and bEnd.3 (Brain endothelial.3) cells were incubated at 37 in recommended media conditions.
Irradiation: Samples were irradiated with an X-RAD 225 (PRECISION X-RAY INC.)
Immunofluorescence: DNA damage was assessed using an antibody to 53BP1 (Table 2.1), a DNA damage repair protein which specifically localises to DNA double strand breaks (DSBs), described here as foci. Cells were fixed in paraformaldehyde 4%.

Calcium Imaging
Dishes were irradiated at 2 Gy and loaded with Fluo-4 AM/probenecid one hour post irradiation and compared to a non-irradiated control dish. Fluo-4AM is an indicator of Ca2+.
Cells were visualized using a 10X water dipping objective lens (CFI Plan Fluor 10X/0.30W).

Excitation of Fluo-4 AM was performed with a mercury lamp through the use of excitation/emission filters . WinFluor software (v4.1.6) was for acquisition and data analysis
Fluorescence intensity (F) was determined from 50 cells for each recording by placing a ROI on a randomly selected individual cell. The change (Δ) in fluorescence ΔF/F0 was plotted against time (s) for each recording where ΔF/F0 = F(t)-F0/F0, where F(t) is the fluorescent value at a given time. Data was exported to Microsoft excel where maximum fluorescence values were calculated
Cell Proliferation
2 x 96 well plates were seeded per timepoint. A control plate was compared to a treatment (2 Gy) plate.
Plates were read at 24, 48 and 72 hour timepoints. (FLUOstar Omega Plate Reader). 10 µl cell proliferation reagent PrestoBlue™ Cell Viability reagent was added to each well. Absorbance values were read 1.5 hourspost-addition (Excitation/emission: 560/590nm).

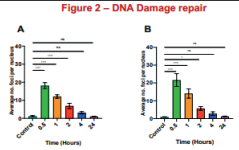
Results

Figure 1 – Dose response relationship



Dose response relationship indicating a linear increase in the number of DNA Double Strand Breaks (DSBs) with dose up to 2 Gy compared to unirradiated control. DSBs were labelled with anti-53BP1 with the average foci per nucleus found across 50 EC nuclei per cell line.
1A - CMEC
1B - bEnd.3
Key for statistical significance:
One star (*) P<0.05, two stars (**) P<0.01, three stars (***) P<0.001, four stars P<0.0001(****)

Figure 2 – DNA Damage repair

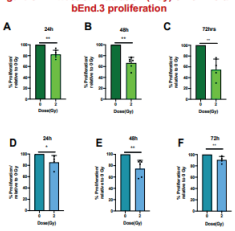


2A – CMEC
The number of DSBs significantly increased at T=0.5h (P<0.0001) The number of DSBs then gradually decreased back to non-significant levels (P>0.05) by T=4h, continuing this decline up to 24 hrs post-irradiation. One-way ANOVA was performed to test for statistical significance where P<0.0001(****).

2B – bEnd.3
The increase in DSBs is statistically significant at T=0.5h, the timepoint at which the maximum number of DNA DSBs were counted (P(0.0001). The number of DSBs decreased back to non-significant levels (P>0.05) by T=4h, continuing this decline up to 24 hrs post-irradiation. One-way ANOVA was performed to test for statistical significance where P<0.0001(****).

Results

Figure 3 – Effect of irradiation (2Gy) on CMEC and bEnd.3 proliferation

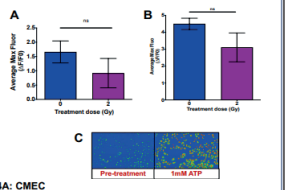


3A - Relative reduction in CMEC proliferation post-irradiation (2Gy) compared to non-irradiated controls at 24 hours. Proliferation was reduced by 17.83% following 2Gy irradiation, relative to 0Gy. (p<0.01, N=5).
3B - At 48 hours, the mean percentage proliferation of irradiated cells was 66.66%. The reduction was statistically significant (P<0.01, N=5).
3C - At 72 hours, the percentage proliferation was reduced to 54.59% in irradiated (2Gy) CMEC cells, relative to 0Gy.The percentage difference was statistically significant (P<0.01, N=4).
3D - Relative reduction in bEnd.3 proliferation to a mean of 85.5% relative to 0 Gy following exposure to 2 Gy at 24 hours. This was found to be a statistically significant reduction (P<0.005, N=4).
3E - Further reduction compared to control observed, where proliferation fell by 25.38%. The reduction was also found to be statistically significant (P<0.01, N=5).
3F - Recovery in % proliferation relative to 0Gy. Mean percentage proliferation relative to 0 Gy rose to 90.51%. The reduction in proliferation was still found to be was found to be statistically significant (P<0.05, N=4).

Statistical data was analysed using a Mann-Whitney U test

Results

Figure 4 - The effect of radiation on cell physiology as assessed by Ca^{2+} transients evoked by ATP bEnd.3 and CMEC cells



4A: CMEC
Bar graph shows the average maximum fluorescence (Ca^{2+} influx). The 2 Gy treatment plate demonstrated a reduction in mean average maximum fluorescence (0.9174 DF/F0) compared to 0 Gy control (1.659 DF/F0) – however this difference was not statistically significant following analysis with unpaired t-test (P>0.05).

4B: bEnd.3
Bar graph shows the average maximum fluorescence. The 2 Gy treatment plate demonstrated a reduction in mean average maximum fluorescence (3.106 DF/F0) compared to 0 Gy control (4.494 DF/F0) – however this difference was not statistically significant following analysis with unpaired t-test (P>0.05, N=5).
4C: Live cell Ca^{2+} imaging

Conclusions

- The data obtained indicate that IR is capable of inflicting significant pathophysiological damage to ECs.
- ECs are capable of fixing DNA damage as shown and preserve physiological Ca^{2+} signalling is at clinical doses of radiation (2 Gy).
- However, EC proliferative capabilities are reduced following exposure to IR. Their inability to fully recover in 2 cell lines warrant further investigation into disrupted underlying cell signalling mechanisms.

Further research and future work

- Further work (not shown) completed as part of this MSc project investigated the impact of the endothelial inflammatory activators **Nigericin** and **lipopolysaccharide** on EC proliferation. An analysis of the **fibrotic changes** induced in mouse bladders at 20 Gy was also conducted.
- Future work would harness **western blot** analysis to understand the cell signalling pathways involved in EC inflammatory activation, and **ex vivo Ca2+ imaging**

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