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Right Iliac Fossa Pain Treatment (RIFT) Study: Protocol for an international, multicentre, prospective observational study

The Right Iliac Fossa Pain Treatment (RIFT) Study Group on behalf of West Midlands Research Collaborative (WMRC)*

*Collaborating members are listed in the Appendix

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Abstract

Introduction

Patients presenting with right iliac fossa (RIF) pain are a common challenge for acute general surgical services. Given the range of potential pathologies, RIF pain creates diagnostic uncertainty and there is subsequent variation in investigation and management. Appendicitis is a diagnosis which must be considered in all patients with RIF pain, however over a fifth of patients undergoing appendicectomy, in the UK, have been proven to have a histologically normal appendix (negative appendicectomy). The primary aim of this study is to determine the contemporary negative appendicectomy rate. The study's secondary aims are to determine the rate of laparoscopy for appendicitis and to validate the Appendicitis Inflammatory Response (AIR) and Alvarado prediction scores.

Methods and Analysis

This multicentre, international prospective observational study will include all patients referred to surgical specialists with either RIF pain or suspected appendicitis. Consecutive patients presenting across four, two-week long data collection periods will be included. Data will be captured using a secure online data management system. A centre survey will profile local policy and service delivery for management of RIF pain.

Ethics and dissemination

Research ethics are not required for this study in the UK, as determined using the National Research Ethics Service decision tool. This study will be registered as a clinical audit in participating UK centres. National leads in countries outside the UK will oversee appropriate registration and study approval, which may include completing full ethical review. The study will be disseminated by trainee-led research collaboratives and through

social media. Peer-reviewed publications will be published under corporate authorship including 'RIFT Study Group' and 'West Midlands Research Collaborative'.

Strengths and limitations of this study

- This study will collect prospective, observational data on a large number of patients across Europe. A pre-planned validation process will verify case ascertainment and data accuracy.
- The study uses the UK National Research Collaborative model to capture high-quality data whilst minimising the burden on participating centres.
- Unlike previous studies, the clinical risk scores will be validated against a prospective cohort of patients presenting with undifferentiated right iliac fossa pain, rather than patients who have undergone appendicectomy.
- Within the remit of this observational study, it will not be possible track patient re-admissions to centres other than the index admitting hospital, or readmission rates beyond 30 days.
- This protocol is designed to be carried out alongside routine clinical practice. This limits the quantity and complexity of data it is feasible to collect. Specific data regarding antibiotic therapy for RIF pain and presenting symptoms outside of those included within risk scores will not be collected.

Introduction

Right iliac fossa (RIF) pain is one of the commonest presentations to acute general surgical services[1]. Causes include appendicitis, other gastrointestinal, urological, gynaecological, vascular, and musculoskeletal pathologies. Given this range of potential pathologies, variation in presentation and similarity to other conditions, particularly ovarian pathologies in women of reproductive age, diagnosing appendicitis can be a challenge. Traditionally, surgeons have relied upon clinical history, examination findings and basic laboratory investigations for diagnosis. Objective stratifiers such as the Appendicitis Inflammatory Response (AIR)[2] and Alvarado scores[3] have been developed to combat this diagnostic uncertainty; yet, these were derived from small retrospective cohorts, are poorly validated and not widely used[4].

Since delayed appendicectomy is associated with increased risk of complications, prompt diagnosis and treatment is essential[5]. Diagnostic uncertainty, coupled with the risks of diagnostic delay, has led to surgeons having a low threshold for operating on patients with equivocal symptoms resulting in high rates of negative appendicectomy: a national audit in 2012 found the UK's negative appendicectomy rate to be 20.6%[6].

Recent guidelines stipulate that appendicectomy should be performed laparoscopically unless this is contraindicated[7,8] (Table 1). However, in 2012 one third of patients underwent open appendicectomy[6]. Unlike laparoscopic surgery, open procedures typically commit the surgeon to proceed to appendicectomy even if the appendix is found to be macroscopically normal once visualised.

This study will test the hypothesis that, associated with increased take-up of laparoscopy, the negative appendicectomy rate will have decreased since 2012. In order to inform the implementation of recent guidelines which mandate risk stratification of patients with RIF pain, this study will also validate the AIR and Alvarado scores in a large, prospective, international cohort[7,8].

Methods and analysis

This prospective, observational, multicentre study will be coordinated by trainee-led research networks which have been described previously[9,10].

Aims and objectives

The primary aim of this study is to determine the negative appendicectomy rate. The secondary aims of this study are to determine the rate of laparoscopy for appendicectomy and to validate the AIRS and Alvarado scores for acute appendicitis. A centre survey will profile local policy and service delivery for management of patients presenting with RIF pain.

Patients and centres

Any hospital that offers acute general surgical services will be eligible to participate. Local collaborators at each centre will prospectively collect data during any of four, two-week long study periods, on consecutive patients referred to the general or paediatric surgery units with RIF pain or suspected appendicitis. Patients will be identified prospectively via hospital computer systems, handover lists, and by the clinical surgical team. Patients who are pregnant, have had abdominal surgery in the preceding 90 days, or have had previous appendicectomy, right hemi-colectomy, or total colectomy will be excluded (Figure 1). Variables required to calculate the AIRS and Alvarado scores will be collected at time of presentation to the surgical unit.

Follow up

Patients will be followed throughout their admission to determine their treatment pathway and length of stay. Data will also be collected on histology and readmission rates, for both

the operated and non-operated groups, within 30 days. Collaborators will access electronic records, emergency department and theatre systems, and patient notes to collect data. No patient identifiable information will be collected.

Centre survey

A consultant surgeon at each participating centre will complete a short questionnaire regarding the guidelines, protocols and resources available for the investigation and management of RIF pain in their hospital (Table 2).

Project management and recruitment

The RIFT steering committee will be responsible for protocol development, data collection and data analysis. A structured system of national, regional and local leadership has been created to coordinate the RIFT study. National leads will oversee participation in RIFT within their countries through networks including the West Midlands Research Collaborative (WMRC), UK National Surgical Research Collaborative (NRC) and Italian Surgical Research Group (ItSurg), as well as through social media platforms[11]. Regional leads will recruit, advise and ensure the correct approvals are in place for each hospital within their region. Local leads will oversee data collection in their hospital, ensuring adherence to local governance protocols and continuous data collection across the 2-week periods. Up to three collaborators per 2-week period, per hospital, will be recruited to participate. A secure server running the 'Research Electronic Data Capture' (REDCap, Boston, MA) web application hosted by the University of Birmingham, UK, will be used to collect and securely store data.

Sample size and statistical analysis

Based on pilot studies across four centres, we estimate that each centre will capture approximately 10 patients with RIF pain per week. The steering committee has received expressions of interest in participation from over 150 centres. It is estimated that around 75 centres will participate during each period. This would result in approximately 6000 patients being included in RIFT across the four data collection periods. It is anticipated that around 20% (1200 patients) will undergo appendicectomy.

Data will be reported in accordance with STROBE (Strengthening The Reporting of Observational studies in Epidemiology) guidelines for observational studies[12]. Differences between patient, disease and operative specific factors will be tested using Student's t-test for continuous data (p-value) and Chi-square for categorical data (reported as Chi-square, p-value). An ⟨-level of 0.05 will be accepted as significant.

Pre-planned analyses will include, and are not limited to: (1) variation in the negative appendicectomy and laparoscopy rates across participating centres and countries; (2) predictive value of AIR and Alvarado risk scores; (3) variation in management of RIF pain for patients with low-, medium- and high-risk of appendicitis, from both adult and paediatric populations; (4) delay to presentation and delay to surgery with relation to rates of complex appendicitis. Sensitivity, specificity, positive predictive value and negative predictive value will be calculated for clinical risk scores. A panelled multi-level, multivariate, binary logistic regression model, including centre as a random effect, will be used to assess the association of clinical risk scores with negative appendicectomy. A similar multilevel model will be used to assess the association between delay to surgery and complex appendicitis. The model fit will be tested with Area under the Curve analysis, using Somer's test to derive a C-statistic.

Ethics

In the UK the online National Research Ethics Service (NRES) decision tool (http://www.hra-decisiontools.org.uk) confirmed that RIFT does not require research ethics approval in the UK. The RIFT study will be registered as a clinical audit in each participating UK centre. National leads in other countries will oversee appropriate registration and study approval, which may include completing full ethical review. Local investigators will be responsible for ensuring local approvals are in place, and will be required to demonstrate this in order to gain access to the online data collection tool.

Reporting and dissemination

A consultant surgeon will facilitate presentation of local study results at a governance meeting at each participating centre. Peer-reviewed publications will be published under corporate authorship including 'RIFT Study Group' and 'West Midlands Research Collaborative'.

Discussion

The RIFT study will be a large, multicentre, international, prospective observational study of undifferentiated patients presenting with RIF pain, and suspected appendicitis. By utilising a protocol driven, pre-planned data collection tool and analysis plan, this study will ensure high data quality, whilst minimising the burden on participating centres.

The 2012 national appendicectomy audit found a significant variation in management of appendicitis across the UK[6]. In light of recent guidelines stipulating that appendicectomy in adults should be performed laparoscopically unless contraindicated[7,8], the RIFT study offers the opportunity to examine health system-level quality improvement in the delivery of laparoscopic appendicectomy five years on from the 2012 study. By mapping real-life patient pathways for investigation and management of RIF pain, RIFT will importantly determine whether any increase in laparoscopy has been associated with a decrease in the rate of negative appendicectomy.

Validation of the AIR and Alvarado scores in a large international cohort will determine the suitability of using these to stratify patients in to low-, medium-, and high-risk groups for appendicitis, as envisaged by recent guidelines[7]. If these risk scores are found to have poor prognostic properties, it may be possible to develop and validate a new score based on the RIFT dataset. Risk scores may aid junior clinicians' decision making and may have a role in avoiding unnecessary operations, reducing the negative appendicectomy rate, and improving patient safety[4]. Furthermore, validated risk scores may be particularly useful in low resource settings with limited access to diagnostic investigations.

The UK National Surgical Research Collaborative's member groups have run trainee-led collaborative studies across 99% of the UK's surgical units[10], delivering large, prospective studies[6]. However, as trainees complete their training and become consultants, the sustainability of postgraduate trainee research collaboratives will be dependent on engaging new junior trainees each year. Whereas previous studies undertaken by surgical research collaboratives have been targeted at either senior trainees or medical students, RIFT is the first study aimed at junior specialty trainees. A surrogate marker for the

success of RIFT will therefore be successful engagement and mentoring of junior trainees in collaborative research.

Limitations

The RIFT Study Group has made specific efforts to minimise the risk of inherent bias in this observational study. Data will be collected prospectively and patient pathways followed proactively by collaborators, who will often be the frontline clinicians responsible for the patients' care. Unlike most previous studies which have focused specifically on patients who undergo appendicectomy, RIFT will include all patients presenting with RIF pain or suspected appendicitis, to general surgical services. Nonetheless, since these patients will have already been triaged by emergency department or general practice doctors, this is likely to be a selected group who are more likely to have appendicitis than patients with truly undifferentiated presentations.

Given the large volume of patients presenting with RIF pain and the short inpatient stays that most patients have, reliably identifying all eligible patients will be more challenging than in previous studies run by trainee collaboratives. However, pre-planned validation by an independent investigator will ensure that case ascertainment rates are monitored. This will also mitigate any risk of reporting bias from clinicians declining to submit details of patients that have been misdiagnosed at their centre.

Due to the pragmatic 'snap-shot' nature of this study, carried out by practicing clinicians, there is a limit to the depth and breadth of data points included. For instance, the study will not collect the length and nature of peri-operative antibiotic treatment (Table 1).

Furthermore, follow up is limited to 30 days after the index hospital admission. It is possible that a proportion of patients initially discharged having not undergone appendicectomy may subsequently be readmitted and undergo surgery either at other hospitals or beyond the 30 day follow up.

Conclusion

The RIFT study is a protocol-driven, international, multicentre prospective observational study using a 'snap-shot' methodology, in line with the UK surgical research collaborative model. The study aims to describe the current variation in investigation and management of right iliac fossa pain in several European countries, aligned to contemporaneous specialty guidelines.

Authors' contributions:

Conception and writing of protocol: Jacob H Matthews, Gabriella L Morley, Shivam Bhanderi, Sarus Jain, Imran Mohamed, Thuvarahan Amuthalingam, Robert Tyler, James C Glasbey, Richard Wilkin, Dmitri Nepogodiev, Aneel Bhangu

Participation in collaborator meeting, development of study concept, and editing of protocol: Jacob H Matthews, Gabriella L Morley, Shivam Bhanderi, Sarus Jain, Imran Mohamed, Thuvarahan Amuthalingam, Robert Tyler, James C Glasbey, Ewen Griffiths, Thomas Pinkney, Oliver Gee, Dion Morton, Francesco Pata, Gianluca Pellino, Valeria Farina, Laura Gavagna, Pietro Maria Naccari, Sandro Pasquali, Bruno Sensi, Alessandro Sgrò, Andrea Simioni, Ruth Blanco-Colino, Matteo Frasson, Antonio Sampaio Soares, Natalie Blencowe, Will Bolton, Stephen Chapman, Catherine Bradshaw, Grant Harris, James Haddow, Kapil Sahnan, John Mason, Scott McCain, David Milgrom, Saleem Noor Mohamed, James O'Brien, Jack Pearce, Mohammed Rabie, Gaël R. Nana, Panchali Sarmah, Nigel Jamieson, Richard Wilkin, Aneel Bhangu, Dmitri Nepogodiev.

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All authors read and approved the final manuscript.

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Data sharing statement: All data from this study will be available on request.

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Appendix 1

RIFT Study Group

Steering Committee: Jacob H Matthews[±], Gabriella L Morley, Shivam Bhanderi, Sarus Jain, Imran Mohamed, Thuvarahan Amuthalingam, Robert Tyler, James C Glasbey, Richard Wilkin, Dmitri Nepogodiev, Aneel Bhangu (senior author)

Advisory Group: Ewen Griffiths, Thomas Pinkney, Oliver Gee, Dion Morton

Italian Surgical Research Group: Francesco Pata, Gianluca Pellino, Valeria Farina, Laura Gavagna, Pietro Maria Naccari, Sandro Pasquali, Bruno Sensi, Alessandro Sgrò, Andrea Simioni

RIFT Spain and Portugal Leads: Ruth Blanco-Colino, Matteo Frasson, Antonio Sampaio Soares

RIFT UK Regional Leads: Natalie Blencowe (Severn & Peninsula Audit and Research Collaborative*); Will Bolton, Stephen Chapman (Yorkshire Surgical Research Collaborative*); Catherine Bradshaw (Paediatric Surgery Trainee Research Network*); Grant Harris (Northern Surgical Trainees Research Association*); James Haddow, Kapil Sahnan (London Surgical Research Group*); John Mason (Oxford Surgical Collaborative for Audit and Research*); Scott McCain (Northern Ireland Surgical Research Collaborative*); David Milgrom (North West Research Collaborative*); Saleem Noor Mohamed (West Midlands Research Collaborative*); James O'Brien (East of England Surgical Research Group*); Jack Pearce (Welsh Barbers Surgical Research Group*); Mohammed Rabie (Kent and Medway); Gaël R. Nana, Panchali Sarmah (East Midlands Surgical Academic Network*), Nigel Jamieson (Scotland).

[±]Steering Committee Chairman

*Corporate authorships of UK trainee surgical research collaboratives, also PUBMed citable.

Society	Statement	Guidance statement	Captured within

Table 1:
A complete compilation and comparison of the World Society of Emergency surgery's (WSES 2016) and the European Association of Endoscopic Surgery's (EAES 2016) guidance on the investigation and management of appendicitis. Those statements captured within the RIFT study's data collection have been highlighted. The EAES guidance is split into statements (S) and recommendations (R) under three sections; pre-operative care, operative managements and after care. The WSES guidance is numbered and listed under the sections described in the table.

	Number		the RIFT Study
1) Diagnostic efficiency of clinical scoring systems			
EAES	Pre-Op R1	The combined variables of clinical assessment and biochemical testing in the Alvarado score should be used to determine the likelihood of appendicitis.	Yes
WSES	1.1	The Alvarado score (with cutoff score < 5) is sufficiently sensitive to exclude acute appendicitis.	Yes
WSES	1.2	The Alvarado score is not sufficiently specific in diagnosing acute appendicitis.	Yes
WSES	1.3	An ideal (high sensitivity and specificity), clinically applicable, diagnostic scoring system/clinical rule remains outstanding. This remains an area for future research	Yes
2) Role of imaging			
WSES	2.1	In patients with suspected appendicitis a tailored individualised approach is recommended, depending on disease probability, sex and age of the patient	Yes
WSES	2.2	Imaging should be linked to Risk Stratification such as AIR or Alvarado score	Yes
WSES	2.3	Low risk patients being admitted to hospital and not clinically improving or reassessed score could have appendicitis ruled-in or out by abdominal CT	Yes
WSES	2.4	Intermediate risk classification identifies patients likely to benefit from observation and systematic diagnostic imaging.	Yes
WSES	2.5	High risk patients (younger than 60 years old) may not require preoperative imaging.	Yes
EAES	Pre-Op R2	We recommend that ultrasound should be performed as a first level diagnostic imaging although it has lower diagnostic value in case radiological confirmation is desirable.	Yes
WSES	2.6	US Standard reporting templates for ultrasound and US three step sequential positioning may enhance over accuracy.	
EAES	Pre-Op R3	If after ultrasound the diagnosis of appendicitis is not confirmed nor ruled out we suggest that additional imaging studies (either a CT or MRI) should be performed.	Yes
EAES	Pre-Op R4	In obese patients, a CT or MRI is more accurate than ultrasonography; In case of diagnostic doubt we recommend a CT or MRI in these specific patients.	
EAES	Pre-Op R5	In pregnant patients radiation should be avoided; In case of diagnostic doubt we recommend an MRI in these specific patients.	
WSES	2.7	MRI is recommended in pregnant patients with suspected appendicitis, if this resource is available	
EAES	Pre-Op R6	In children radiation should be avoided; In case of diagnostic doubt we recommend an MRI in these specific patients.	Yes
3) Nonoperative treatment for uncomplicated appendicitis			
WSES	3.1	Antibiotic therapy can be successful in selected patients with uncomplicated appendicitis who wish to avoid surgery and accept the risk up to 38 % recurrence.	Yes
EAES	Pre-Op R7	Non-operative treatment (with antibiotics) of uncomplicated appendicitis in adults is not suggested as high quality evidence of superiority is still lacking.	Yes
WSES	3.2	Current evidence supports initial intravenous antibiotics with subsequent conversion to oral antibiotics.	
WSES	3.3	In patients with normal investigations and symptoms unlikely to be appendicitis but which do not settle; 1) Cross-sectional imaging is recommended before surgery; 2) Laparoscopy is the surgical approach of choice; and 3) There is inadequate evidence to recommend a routine approach at present	Yes
4) Timing of appendectomy and in-hospital delay			
WSES	4.1	Short, in-hospital surgical delay up to 12/24 h is safe in uncomplicated acute appendicitis and does not increase complications and/or perforation rate.	Yes
WSES	4.2	Surgery for uncomplicated appendicitis can be planned for next available list minimizing delay wherever possible (patient comfort etc.).	Yes
EAES	Operative R1	We recommend that surgery is performed as soon as feasible after diagnosis.	Yes
5) Surgical treatment			
WSES	5.1.1	Laparoscopic appendectomy should represent the first choice where laparoscopic equipment and skills are available, since it offers clear advantages in terms of less pain, lower incidence of SSI, decreased LOS, earlier return to work and overall costs.	Yes
EAES	Pre-Op	Laparoscopic appendectomy is recommended as the procedure of choice in adults with	Yes

	R8	uncomplicated acute appendicitis.	
WSES	5.1.2	Laparoscopy offers clear advantages and should be preferred in obese patients, older patients and patients with comorbidities	Yes
EAES	Pre-Op R11	Laparoscopic appendectomy is recommended as the procedure of choice in obese patients with acute appendicitis.	Yes
EAES	Pre-Op R14	Laparoscopic appendectomy is recommended as the procedure of choice in patients over 65 years of age.	Yes
WSES	5.1.3	Laparoscopy is feasible and safe in young male patients although no clear advantages can be demonstrated in such patients.	Yes
WSES	5.1.4	Laparoscopy should not be considered as a first choice over open appendectomy in pregnant patients	
EAES	Pre-Op R12	Laparoscopic appendectomy is suggested as the procedure of choice in pregnant patients with acute appendicitis. It should even be considered in the third trimester.	
WSES	5.1.5	No major benefits have also been observed in laparoscopic appendectomy in children, but it reduces hospital stay and overall morbidity	Yes
EAES	Pre-Op R13	Laparoscopic appendectomy is suggested as the procedure of choice in children with acute appendicitis and an indication for appendectomy.	Yes
WSES	5.1.6	In experienced hands, laparoscopy is more beneficial and cost-effective than open surgery for complicated appendicitis	Yes
EAES	Pre-Op R9	Laparoscopic appendectomy is suggested as the procedure of choice in patients with perforated appendicitis.	Yes
EAES	After Care R2	We suggest the use of local anesthetic for subcutaneous and muscular infiltration of incision sites prior to incision.	
EAES	Operative R6	Open: supine, one or both arms out, surgeon at the right side, assistant on the left side. Laparoscopic: supine, right arm out, left arm along the body, surgeon and assistant on the left side.	
EAES	Operative R7	The consensus held a preference for open access to the peritoneal cavity because of rare but serious complications associated with the Verees needle.	
EAES	Operative R8	Based upon the literature no recommendation can be made which trocars should be used and their placement. This should be left at the surgeon's discretion. Three-port technique should be standard. Single port approaches can be used by surgeons with sufficient experience.	
WSES	5.2	Peritoneal irrigation does not have any advantages over suction alone in complicated appendicitis	
WSES	5.3.1	There are no clinical differences in outcomes, LOS and complications rates between the different techniques described for mesentery dissection (monopolar electrocoagulation, bipolar energy, metal clips, endoloops, Ligasure, Harmonic Scalpel etc.).	
WSES	5.3.2	Monopolar electrocoagulation and bipolar energy are the most cost-effective techniques, even if more experience and technical skills is required to avoid potential complications (e.g. bleeding) and thermal injuries.	
WSES	5.4.1	There are no clinical advantages in the use of endostapler over endoloops for stump closure for both adults and children	
EAES	Operative R10	The use of stapler or suturing is recommended over clips or endoloops when the appendix base is inflamed, necrotic or perforated. The use of alternative measures to secure the appendiceal stump in this case may be insufficient.	
EAES	After Care R4	In order to prevent stump appendicitis, it is suggested that the appendiceal stump should be no longer than 0.5cm. Timely diagnosis allows laparoscopic stump resection. Delayed diagnosis may require extended bowel resection.	
WSES	5.4.2	Endoloops might be preferred for lowering the costs when appropriate skills/learning curve are available	
WSES	5.4.3	There are no advantages of stump inversion over simple ligation, either in open or laparoscopic surgery	
WSES	5.5.1	Drains are not recommended in complicated appendicitis in paediatric patients	
EAES	Operative R4	It is suggested that there is no indication for routine postoperative nasogastric tube placement in children or adults.	
EAES	Operative R11	It is recommended that extraction of the appendix should avoid direct contact of the appendix and the abdominal wall. There are several methods of achieving this and there is no evidence	

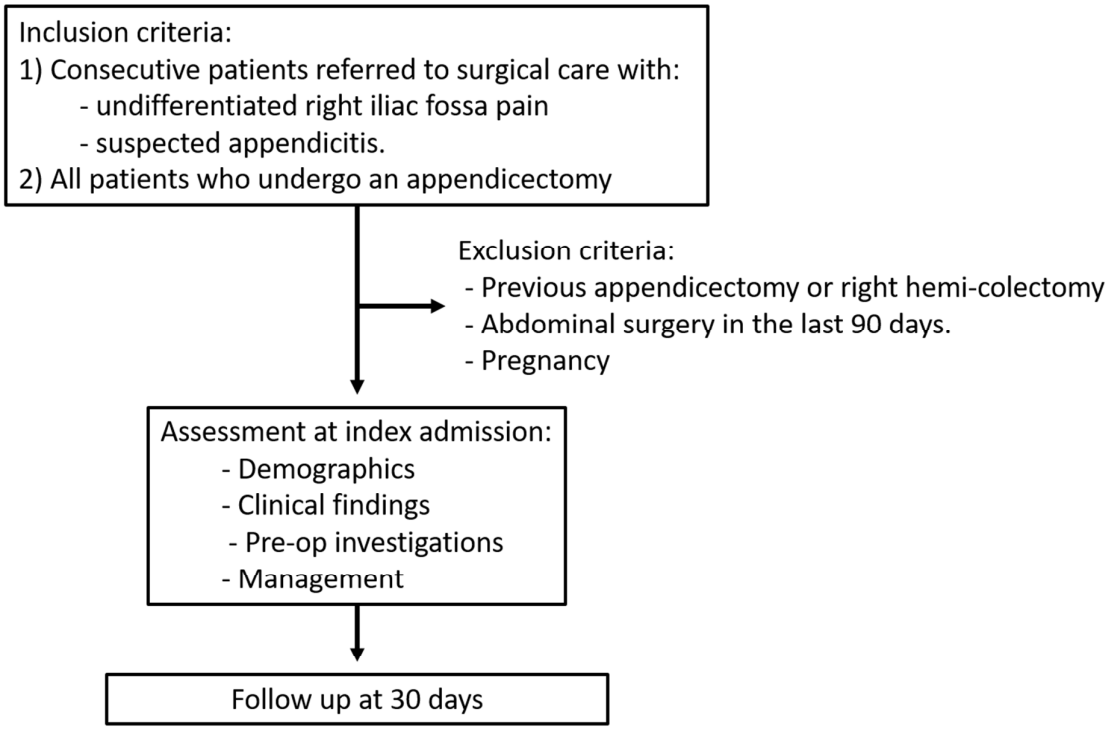
		supporting one above the other.	
EAES	Operative R5	It is suggested that there is no indication for routine postoperative catheter placement in children or adults.	
WSES	5.5.2	In adult patients, drain after appendectomy for perforated appendicitis and abscess/peritonitis should be used with judicious caution, given the absence of good evidence from the literature. Drains did not prove any efficacy in preventing intraabdominal abscess and seem to be associated with delayed hospital discharge.	
EAES	Operative R12	In general, meticulous suction of intra-peritoneal fluid or collections is suggested; the philosophy should be: “leave no pus behind”. Routine use of drains in appendectomy is not recommended.	
WSES	5.6	Delayed primary skin closure does not seem beneficial for reducing the risk of SSI and increase LOS in open appendectomies with contaminated/dirty wounds	
EAES	Operative R13	Primary wound closure is recommended for all cases of open appendectomy.	
EAES	Operative S1	Various reasons exist to convert LA. However, no recommendation about when to convert can be given. It should be stated that conversion to open surgery is not regarded as a complication.	Yes
EAES	After Care R3	There is no reason to restrict the postoperative diet after an uncomplicated appendectomy.	
		6) Scoring systems for intraoperative grading of appendicitis and their clinical usefulness	
WSES	6.1	The incidence of unexpected findings in appendectomy specimens is low but the intraoperative diagnosis alone is insufficient for identifying unexpected disease. From the current available evidence, routine histopathology is necessary	Yes
EAES	After Care R1	It is recommended to send all appendices to the pathology department routinely and the operated will review the results.	Yes
EAES	Operative R15	It is suggested that definitive treatment of a suspected malignancy will depend on final histological and staging information after initial treatment of the operative findings and may require further surgery or adjunct treatment.	
WSES	6.2	There is a lack of validated system for histological classification of acute appendicitis and controversies exist on this topic.	
WSES	6.3	Surgeon’s macroscopic judgement of early grades of acute appendicitis is inaccurate	Yes
WSES	6.4	If the appendix looks “normal” during surgery and no other disease is found in symptomatic patient, we recommend removal in any case.	Yes
EAES	Operative R9	It is suggested to remove the “normal” appearing appendix when operating for suspected appendicitis when no other pathology is identified.	Yes
WSES	6.5	We recommend adoption of a grading system for acute appendicitis based on clinical, imaging and operative findings, which can allow identification of homogeneous groups of patients, determining optimal grade disease management and comparing therapeutic modalities	
		7) Nonsurgical treatment for complicated appendicitis: abscess or phlegmone	
WSES	7.1	Percutaneous drainage of a peri-appendiceal abscess, if accessible, is an appropriate treatment in addition to antibiotics for complicated appendicitis.	Yes
WSES	7.2	Nonoperative management is a reasonable first line treatment for appendicitis with phlegmon or abscess	Yes
EAES	After Care R5	Initial treatment of intra-abdominal abscess (IAA) is conservative with antibiotics. In some patients, this may need to be combined with radiological or surgical drainage.	Yes
EAES	Pre-Op R10	Non-operative treatment is suggested as the procedure of choice for patients with an appendiceal mass in the absence of diffuse peritonitis. Data are lacking on the benefits of interval appendectomy.	Yes
WSES	7.3	Operative management of acute appendicitis with phlegmon or abscess is a safe alternative to nonoperative management in experienced hands	Yes
EAES	Operative R14	It is recommended to treat an inflammatory mass conservatively. We recommend that when encountered during laparoscopy, refrain from appendectomy. During follow-up: additional imaging is advised. Data are lacking on the benefits of interval appendectomy.	
WSES	7.4	Interval appendectomy is not routinely recommended both in adults and children.	Yes
WSES	7.5	Interval appendectomy is recommended for those patients with recurrent symptoms.	Yes
WSES	7.6	Colonic screening should be performed in those patients with appendicitis treated non-operatively if >40y/o	

8) Preoperative and Postoperative Antibiotics			
WSES	8.1	In patients with acute appendicitis preoperative broad-spectrum antibiotics are always recommended	
EAES	Operative R2	Prophylactic antibiotics are recommended in appendectomy in adults.	
EAES	Operative R3	Prophylactic antibiotics are recommended in appendectomy in children.	
WSES	8.2	For patients with uncomplicated appendicitis, postoperative antibiotics are not recommended	
EAES	After Care S1	Evidence for duration of administration of postoperative antibiotics is lacking.	
EAES	After Care S2	There is no evidence of routine use of postoperative antibiotics in uncomplicated appendicitis.	
EAES	After Care R6	In complicated appendicitis, postoperative antibiotics are recommended.	
WSES	8.3	In patients with complicated acute appendicitis, postoperative, broad-spectrum antibiotics are always recommended	
WSES	8.4	Although discontinuation of antimicrobial treatment should be based on clinical and laboratory criteria such as fever and leucocytosis, a period of 3–5 days for adult patients is generally recommended	

	Data Criteria	Options
Centre details		
1(a)	Does your unit care for?	▪ Adults only ▪ Children only ▪ Adults and children
2	Does your hospital have an on-site gynaecology service?	▪ Yes ▪ No
3	Does your centre have 'review clinic' slots for patients to return for further assessment/imaging the following day if a diagnosis is unclear?	▪ Yes – with ultrasound and clinical review ▪ Yes – clinical review only ▪ No
4(a)	How many **consultants** will be "on call" during the 2 week study period?	Number =
4(b)	How many consultant general surgeons work at your centre?	Number =
4 (c)	Is there a **dedicated** registrar based on SAU to review patients?	▪ Yes – 24/7 ▪ Yes – During the day ▪ No – One registrar splits time between theatre and SAU
5	At weekends, Is ultrasound available?	▪ Yes ▪ No
6(a)	At weekends, is CT available?	▪ Equivalent to weekday service ▪ Reduced service but available for urgent surgical requests ▪ Not available
6(b)	At night, is CT available?	▪ Equivalent to weekday service ▪ Reduced service but available for urgent surgical requests ▪ Not available
Does your centre have an agreed policy for:		
7	When to use appendicitis risk stratification scores?	▪ Yes – use of score recommended ▪ Yes – use of score discouraged ▪ No policy in place
8	Which patients should have a CT scan prior to appendicectomy? *(e.g. diagnosis unclear, age >50)*	▪ Yes – please detail ▪ No policy in place
9	Whether some patients with appendicitis may be managed non-operatively?	▪ Yes –conservative management recommended for some patients; please detail ▪ Yes – policy discourages conservative management ▪ No policy in place
10	Whether laparoscopic or open appendicectomy should be routinely performed?	▪ Yes – open surgery recommended ▪ Yes – laparoscopic surgery recommended ▪ No policy in place
11	Whether a macroscopically normal looking appendix should be removed or left in situ?	▪ Yes – removal recommended ▪ Yes – recommend it be left in situ ▪ No – no policy in place

Table 2: Centre Survey

Figure 1: study flowchart



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Right Iliac Fossa Pain Treatment (RIFT) Study: Protocol for an international, multicentre, prospective observational study

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Right Iliac Fossa Pain Treatment (RIFT) Study: Protocol for an international, multicentre, prospective observational study

The Right Iliac Fossa Pain Treatment (RIFT) Study Group on behalf of West Midlands Research Collaborative (WMRC)*

*Collaborating members are listed in the Appendix 1

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Abstract

Introduction

Patients presenting with right iliac fossa (RIF) pain are a common challenge for acute general surgical services. Given the range of potential pathologies, RIF pain creates diagnostic uncertainty and there is subsequent variation in investigation and management. Appendicitis is a diagnosis which must be considered in all patients with RIF pain, however over a fifth of patients undergoing appendicectomy, in the UK, have been proven to have a histologically normal appendix (negative appendicectomy). The primary aim of this study is to determine the contemporary negative appendicectomy rate. The study's secondary aims are to determine the rate of laparoscopy for appendicitis and to validate the Appendicitis Inflammatory Response (AIR) and Alvarado prediction scores.

Methods and Analysis

This multicentre, international prospective observational study will include all patients referred to surgical specialists with either RIF pain or suspected appendicitis. Consecutive patients presenting within two-week long data collection periods will be included. Centres will be invited to participate in up to 4 data collection periods between February and August 2017. Data will be captured using a secure online data management system. A centre survey will profile local policy and service delivery for management of RIF pain.

Ethics and dissemination

Research ethics are not required for this study in the UK, as determined using the National Research Ethics Service decision tool. This study will be registered as a clinical audit in participating UK centres. National leads in countries outside the UK will oversee appropriate registration and study approval, which may include completing full ethical review. The study will be disseminated by trainee-led research collaboratives and through social media. Peer-

reviewed publications will be published under corporate authorship including 'RIFT Study Group' and 'West Midlands Research Collaborative'.

Strengths and limitations of this study

- This study will collect prospective, observational data on a large number of patients across Europe. A pre-planned validation process will verify case ascertainment and data accuracy.
- The study uses the UK National Research Collaborative model to capture high-quality data whilst minimising the burden on participating centres.
- Unlike previous studies, the clinical risk scores will be validated against a prospective cohort of patients presenting with undifferentiated right iliac fossa pain, rather than patients who have undergone appendicectomy.
- Within the remit of this observational study, it will not be possible track patient re-admissions to centres other than the index admitting hospital, or readmission rates beyond 30 days.
- This protocol is designed to be carried out alongside routine clinical practice. This limits the quantity and complexity of data it is feasible to collect. Specific data regarding antibiotic therapy for RIF pain and presenting symptoms outside of those included within risk scores will not be collected.

Introduction

Right iliac fossa (RIF) pain is one of the commonest presentations to acute general surgical services [1]. Causes include appendicitis, other gastrointestinal, urological, gynaecological, vascular, and musculoskeletal pathologies. Given this range of potential pathologies, variation in presentation and similarity to other conditions, particularly ovarian pathologies in women of reproductive age, diagnosing appendicitis can be a challenge [2]. Traditionally, surgeons have relied upon clinical history, examination findings and basic laboratory investigations for diagnosis. Objective stratifiers such as the Appendicitis Inflammatory Response (AIR) [3] and Alvarado scores [4] have been developed to combat this diagnostic uncertainty; yet, these were derived from small retrospective cohorts, are poorly validated and not widely used [5].

Since delayed appendicectomy is associated with increased risk of complications, prompt diagnosis and treatment is essential [6]. Diagnostic uncertainty, coupled with the risks of diagnostic delay, has led to surgeons having a low threshold for operating on patients with equivocal symptoms resulting in high rates of negative appendicectomy: a national audit in 2012 found the UK's negative appendicectomy rate to be 20.6% [7, 8].

Recent guidelines stipulate that appendicectomy should be performed laparoscopically unless this is contraindicated [9, 10] (Table 1). However, in 2012 one third of patients underwent open appendicectomy [7]. Unlike laparoscopic surgery, open procedures typically commit the surgeon to proceed to appendicectomy even if the appendix is found to be macroscopically normal once visualised [8].

This study will test the hypothesis that, associated with increased take-up of laparoscopy, the negative appendicectomy rate will have decreased since 2012 [8]. In order to inform the implementation of recent guidelines which mandate risk stratification of patients with RIF pain,

this study will also validate the AIR and Alvarado scores in a large, prospective, international cohort [9,10].

Methods and analysis

This prospective, observational, multicentre study will be coordinated by trainee-led research networks which have been described previously [11, 12].

Aims and objectives

The primary aim of this study is to determine the negative appendicectomy rate. The secondary aims of this study are to determine the rate of laparoscopy for appendicectomy and to validate the AIRS and Alvarado scores for acute appendicitis. A centre survey will profile local policy and service delivery for management of patients presenting with RIF pain.

Patients and centres

Any hospital that offers acute general surgical services will be eligible to participate. Local collaborators at each centre will prospectively collect data during two-week long study periods, on consecutive patients referred to the general or paediatric surgery units with RIF pain or suspected appendicitis. Each centre will be able to submit data from up to 4 study periods between February and August 2017. Patients will be identified prospectively via hospital computer systems, handover lists, and by the clinical surgical team. Patients who are pregnant, have had abdominal surgery in the preceding 90 days, or have had previous appendicectomy, right hemi-colectomy, or total colectomy will be excluded (Figure 1). Variables required to calculate the AIRS and Alvarado scores will be collected at time of presentation to the surgical unit.

Follow up

Patients will be followed throughout their admission to determine their treatment pathway and length of stay. Data will also be collected on histology and readmission rates, for both the operated and non-operated groups, within 30 days. Collaborators will access electronic records, emergency department and theatre systems, and patient notes to collect data. The group who undergo an operation will be followed up to determined the negative appendicectomy rate, and the non-operative group will be followed up to allow for the validation of the AIR and Alvarado scores low risk prediction for this group. The non-operative group will also include those patients diagnosed as simple appendicitis and treated non-operatively and will require follow up to assess whether they then require a subsequent operation. No patient identifiable information will be collected.

Centre survey

A consultant surgeon at each participating centre will complete a short questionnaire regarding the guidelines, protocols and resources available for the investigation and management of RIF pain in their hospital (Table 2).

Project management and recruitment

The RIFT steering committee (Appendix 1) will be responsible for protocol development, data collection and data analysis. A structured system of national, regional and local leadership has been created to coordinate the RIFT study. National leads will oversee participation in RIFT within their countries through networks including the West Midlands Research Collaborative (WMRC), UK National Surgical Research Collaborative (NRC) and Italian Surgical Research Group (ItSurg), as well as through social media platforms [13]. Regional leads will recruit, advise and ensure the correct approvals are in place for each hospital within their region. Local leads will oversee data collection in their hospital, ensuring adherence to local governance protocols

and continuous data collection across the 2-week periods. Up to three collaborators per 2-week period, per hospital, will be recruited to participate. A secure server running the 'Research Electronic Data Capture' (REDCap, Boston, MA) web application hosted by the University of Birmingham, UK, will be used to collect and securely store data.

Sample size and statistical analysis

Based on pilot studies across four centres, we estimate that each centre will capture approximately 10 patients with RIF pain per week. The steering committee has received expressions of interest in participation from over 150 centres. It is estimated that around 75 centres will participate during each period. This would result in approximately 6000 patients being included in RIFT across the four data collection periods. It is anticipated that around 20% (1200 patients) will undergo appendicectomy.

Data will be reported in accordance with STROBE (Strengthening The Reporting of Observational studies in Epidemiology) guidelines for observational studies [14]. Differences between patient, disease and operative specific factors will be tested using Student's t-test for continuous data (p-value) and Chi-square for categorical data (reported as Chi-square, p-value). An á-level of 0.05 will be accepted as significant.

Pre-planned analyses will include, and are not limited to: (1) variation in the negative appendicectomy and laparoscopy rates across participating centres and countries; (2) predictive value of AIR and Alvarado risk scores. Sensitivity, specificity, positive predictive value and negative predictive value will be calculated for clinical risk scores. A panelled multi-level, multivariate, binary logistic regression model, including centre as a random effect, will be used to assess the association of clinical risk scores with negative appendicectomy. The model fit will be tested with Area under the Curve analysis, using Somer's test to derive a C-statistic.

Ethics

In the UK the online National Research Ethics Service (NRES) decision tool (http://www.hra-decisiontools.org.uk) confirmed that RIFT does not require research ethics approval in the UK. The RIFT study will be registered as a clinical audit in each participating UK centre. National leads in other countries will oversee appropriate registration and study approval, which may include completing full ethical review. Local investigators will be responsible for ensuring local approvals are in place, and will be required to demonstrate this in order to gain access to the online data collection tool.

Reporting and dissemination

A consultant surgeon will facilitate presentation of local study results at a governance meeting at each participating centre. Peer-reviewed publications will be published under corporate authorship including 'RIFT Study Group' and 'West Midlands Research Collaborative'.

Discussion

The RIFT study will be a large, multicentre, international, prospective observational study of undifferentiated patients presenting with RIF pain, and suspected appendicitis. By utilising a protocol driven, pre-planned data collection tool and analysis plan, this study will ensure high data quality, whilst minimising the burden on participating centres.

The 2012 national appendicectomy audit found a significant variation in management of appendicitis across the UK [7]. In light of recent guidelines stipulating that appendicectomy in adults should be performed laparoscopically unless contraindicated [9,10], the RIFT study offers the opportunity to examine health system-level quality improvement in the delivery of laparoscopic appendicectomy five years on from the 2012 study. By mapping real-life patient

pathways for investigation and management of RIF pain, RIFT will indicate whether any increased use of modern technologies, including CT scanning and laparoscopy, have been associated with a decrease in the rate of negative appendicectomy.

Validation of the AIR and Alvarado scores in a large international cohort will determine the suitability of using these to stratify patients in to low-, medium-, and high-risk groups for appendicitis, as envisaged by recent guidelines [9]. If these risk scores are found to have poor prognostic properties, it may be possible to develop and validate a new score based on the RIFT dataset. Risk scores may aid junior clinicians' decision making and may have a role in avoiding unnecessary operations, reducing the negative appendicectomy rate, and improving patient safety [5]. Furthermore, validated risk scores may be particularly useful in low resource settings with limited access to diagnostic investigations.

The UK National Surgical Research Collaborative's member groups have run trainee-led collaborative studies across 99% of the UK's surgical units [12], delivering large, prospective studies [7]. However, as trainees complete their training and become consultants, the sustainability of postgraduate trainee research collaboratives will be dependent on engaging new junior trainees each year. Whereas previous studies undertaken by surgical research collaboratives have been targeted at either senior trainees or medical students, RIFT is the first study aimed at junior specialty trainees (recent graduates). A surrogate marker for the success of RIFT will therefore be successful engagement and mentoring of junior trainees in collaborative research.

Limitations

The RIFT Study Group has made specific efforts to minimise the risk of inherent bias in this observational study. Data will be collected prospectively and patient pathways followed

proactively by collaborators, who will often be the frontline clinicians responsible for the patients' care. Unlike most previous studies which have focused specifically on patients who undergo appendicectomy, RIFT will include all patients presenting with RIF pain or suspected appendicitis, to general surgical services. Nonetheless, since these patients will have already been triaged by emergency department or general practice doctors, this is likely to be a selected group who are more likely to have appendicitis than patients with truly undifferentiated presentations.

Given the large volume of patients presenting with RIF pain and the short inpatient stays that most patients have, reliably identifying all eligible patients will be more challenging than in previous studies run by trainee collaboratives. However, pre-planned validation by an independent investigator will ensure that case ascertainment rates are monitored. This will also mitigate any risk of reporting bias from clinicians declining to submit details of patients that have been misdiagnosed at their centre.

A centre survey has been developed to determine details about participating centres resources and policies (Table 2). Due to the large number of centres involved in this study from different countries and health systems, it is anticipated that there may be variation in the resources available, such as CT scanning and review clinics. By asking for details of this resource variation in advance we aim to control for this in our statistical analysis.

Due to the pragmatic 'snap-shot' nature of this study, carried out by practicing clinicians, there is a limit to the depth and breadth of data points included. For instance, the study will not collect the length and nature of peri-operative antibiotic treatment (Table 1). Furthermore, follow up is limited to 30 days after the index hospital admission. It is possible that a proportion of patients

initially discharged having not undergone appendicectomy may subsequently be readmitted and undergo surgery either at other hospitals or beyond the 30 day follow up.

In summary, the RIFT study is a protocol-driven, international, multicentre prospective observational study using a 'snap-shot' methodology, in line with the UK surgical research collaborative model. The study aims to describe the current variation in investigation and management of right iliac fossa pain in several European countries, aligned to contemporaneous specialty guidelines.

Authors' contributions:

Conception and writing of protocol: Jacob H Matthews, Gabriella L Morley, Shivam Bhanderi, Sarus Jain, Imran Mohamed, Thuvarahan Amuthalingam, Robert Tyler, James C Glasbey, Richard Wilkin, Dmitri Nepogodiev, Aneel Bhangu

Participation in collaborator meeting, development of study concept, and editing of protocol: Jacob H Matthews, Gabriella L Morley, Shivam Bhanderi, Sarus Jain, Imran Mohamed, Thuvarahan Amuthalingam, Robert Tyler, James C Glasbey, Ewen Griffiths, Thomas Pinkney, Oliver Gee, Dion Morton, Francesco Pata, Gianluca Pellino, Valeria Farina, Laura Gavagna, Pietro Maria Naccari, Sandro Pasquali, Bruno Sensi, Alessandro Sgrò, Andrea Simioni, Ruth Blanco-Colino, Matteo Frasson, Antonio Sampaio Soares, Natalie Blencowe, Will Bolton, Stephen Chapman, Catherine Bradshaw, Grant Harris, James Haddow, Kapil Sahnan, John Mason, Scott McCain, David Milgrom, Saleem Noor Mohamed, James O'Brien, Jack Pearce, Mohammed Rabie, Gaël R. Nana, Panchali Sarmah, Nigel Jamieson, Richard Wilkin, Aneel Bhangu, Dmitri Nepogodiev.

Guarantor: Aneel Bhangu,

All authors read and approved the final manuscript.

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Competing interests: None to declare.

Data sharing statement: All data from this study will be available on request.

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Table 1:

A complete compilation and comparison of the World Society of Emergency surgery's (WSES 2016) and the European Association of Endoscopic Surgery's (EAES 2016) guidance on the investigation and management of appendicitis. Those statements captured within the RIFT study's data collection have been highlighted. The EAES guidance is split into statements (S) and recommendations (R) under three sections; pre-operative care, operative managements and after care. The WSES guidance is numbered and listed under the sections described in the table.

Society	Statement Number	Guidance statement	Captured within the RIFT Study
1) Diagnostic efficiency of clinical scoring systems			
EAES	Pre-Op R1	The combined variables of clinical assessment and biochemical testing in the Alvarado score should be used to determine the likelihood of appendicitis.	Yes
WSES	1.1	The Alvarado score (with cutoff score < 5) is sufficiently sensitive to exclude acute appendicitis.	Yes
WSES	1.2	The Alvarado score is not sufficiently specific in diagnosing acute appendicitis.	Yes
WSES	1.3	An ideal (high sensitivity and specificity), clinically applicable, diagnostic scoring system/clinical rule remains outstanding. This remains an area for future research	Yes
2) Role of imaging			
WSES	2.1	In patients with suspected appendicitis a tailored individualised approach is recommended, depending on disease probability, sex and age of the patient	Yes
WSES	2.2	Imaging should be linked to Risk Stratification such as AIR or Alvarado score	Yes
WSES	2.3	Low risk patients being admitted to hospital and not clinically improving or reassessed score could have appendicitis ruled-in or out by abdominal CT	Yes
WSES	2.4	Intermediate risk classification identifies patients likely to benefit from observation and systematic diagnostic imaging.	Yes
WSES	2.5	High risk patients (younger than 60 years old) may not require preoperative imaging.	Yes
EAES	Pre-Op R2	We recommend that ultrasound should be performed as a first level diagnostic imaging although it has lower diagnostic value in case radiological confirmation is desirable.	Yes
WSES	2.6	US Standard reporting templates for ultrasound and US three step sequential positioning may enhance over accuracy.	
EAES	Pre-Op R3	If after ultrasound the diagnosis of appendicitis is not confirmed nor ruled out we suggest that additional imaging studies (either a CT or MRI) should be performed.	Yes
EAES	Pre-Op R4	In obese patients, a CT or MRI is more accurate than ultrasonography; In case of diagnostic doubt we recommend a CT or MRI in these specific patients.	
EAES	Pre-Op R5	In pregnant patients radiation should be avoided; In case of diagnostic doubt we recommend an MRI in these specific patients.	
WSES	2.7	MRI is recommended in pregnant patients with suspected appendicitis, if this resource is available	
EAES	Pre-Op R6	In children radiation should be avoided; In case of diagnostic doubt we recommend an MRI in these specific patients.	Yes
3) Nonoperative treatment for uncomplicated appendicitis			
WSES	3.1	Antibiotic therapy can be successful in selected patients with uncomplicated appendicitis who wish to avoid surgery and accept the risk up to 38 % recurrence.	Yes
EAES	Pre-Op R7	Non-operative treatment (with antibiotics) of uncomplicated appendicitis in adults is not suggested as high quality evidence of superiority is still lacking.	Yes
WSES	3.2	Current evidence supports initial intravenous antibiotics with subsequent conversion to oral antibiotics.	
WSES	3.3	In patients with normal investigations and symptoms unlikely to be appendicitis but which do not settle; 1) Cross-sectional imaging is recommended before surgery; 2) Laparoscopy is the surgical approach of choice; and 3) There is inadequate evidence to recommend a routine approach at present	Yes
4) Timing of appendectomy and in-hospital delay			
WSES	4.1	Short, in-hospital surgical delay up to 12/24 h is safe in uncomplicated acute appendicitis and does not increase complications and/or perforation rate.	Yes
WSES	4.2	Surgery for uncomplicated appendicitis can be planned for next available list minimizing delay wherever possible (patient comfort etc.).	Yes

EAES	Operative R1	We recommend that surgery is performed as soon as feasible after diagnosis.	Yes
		5) Surgical treatment	
WSES	5.1.1	Laparoscopic appendectomy should represent the first choice where laparoscopic equipment and skills are available, since it offers clear advantages in terms of less pain, lower incidence of SSI, decreased LOS, earlier return to work and overall costs.	Yes
EAES	Pre-Op R8	Laparoscopic appendectomy is recommended as the procedure of choice in adults with uncomplicated acute appendicitis.	Yes
WSES	5.1.2	Laparoscopy offers clear advantages and should be preferred in obese patients, older patients and patients with comorbidities	Yes
EAES	Pre-Op R11	Laparoscopic appendectomy is recommended as the procedure of choice in obese patients with acute appendicitis.	Yes
EAES	Pre-Op R14	Laparoscopic appendectomy is recommended as the procedure of choice in patients over 65 years of age.	Yes
WSES	5.1.3	Laparoscopy is feasible and safe in young male patients although no clear advantages can be demonstrated in such patients.	Yes
WSES	5.1.4	Laparoscopy should not be considered as a first choice over open appendectomy in pregnant patients	
EAES	Pre-Op R12	Laparoscopic appendectomy is suggested as the procedure of choice in pregnant patients with acute appendicitis. It should even be considered in the third trimester.	
WSES	5.1.5	No major benefits have also been observed in laparoscopic appendectomy in children, but it reduces hospital stay and overall morbidity	Yes
EAES	Pre-Op R13	Laparoscopic appendectomy is suggested as the procedure of choice in children with acute appendicitis and an indication for appendectomy.	Yes
WSES	5.1.6	In experienced hands, laparoscopy is more beneficial and cost-effective than open surgery for complicated appendicitis	Yes
EAES	Pre-Op R9	Laparoscopic appendectomy is suggested as the procedure of choice in patients with perforated appendicitis.	Yes
EAES	After Care R2	We suggest the use of local anesthetic for subcutaneous and muscular infiltration of incision sites prior to incision.	
EAES	Operative R6	Open: supine, one or both arms out, surgeon at the right side, assistant on the left side. Laparoscopic: supine, right arm out, left arm along the body, surgeon and assistant on the left side.	
EAES	Operative R7	The consensus held a preference for open access to the peritoneal cavity because of rare but serious complications associated with the Verees needle.	
EAES	Operative R8	Based upon the literature no recommendation can be made which trocars should be used and their placement. This should be left at the surgeon's discretion. Three-port technique should be standard. Single port approaches can be used by surgeons with sufficient experience.	
WSES	5.2	Peritoneal irrigation does not have any advantages over suction alone in complicated appendicitis	
WSES	5.3.1	There are no clinical differences in outcomes, LOS and complications rates between the different techniques described for mesentery dissection (monopolar electrocoagulation, bipolar energy, metal clips, endoloops, Ligasure, Harmonic Scalpel etc.).	
WSES	5.3.2	Monopolar electrocoagulation and bipolar energy are the most cost-effective techniques, even if more experience and technical skills is required to avoid potential complications (e.g. bleeding) and thermal injuries.	
WSES	5.4.1	There are no clinical advantages in the use of endostapler over endoloops for stump closure for both adults and children	
EAES	Operative R10	The use of stapler or suturing is recommended over clips or endoloops when the appendix base is inflamed, necrotic or perforated. The use of alternative measures to secure the appendiceal stump in this case may be	

		insufficient.	
EAES	After Care R4	In order to prevent stump appendicitis, it is suggested that the appendiceal stump should be no longer than 0.5cm. Timely diagnosis allows laparoscopic stump resection. Delayed diagnosis may require extended bowel resection.	
WSES	5.4.2	Endoloops might be preferred for lowering the costs when appropriate skills/learning curve are available	
WSES	5.4.3	There are no advantages of stump inversion over simple ligation, either in open or laparoscopic surgery	
WSES	5.5.1	Drains are not recommended in complicated appendicitis in paediatric patients	
EAES	Operative R4	It is suggested that there is no indication for routine postoperative nasogastric tube placement in children or adults.	
EAES	Operative R11	It is recommended that extraction of the appendix should avoid direct contact of the appendix and the abdominal wall. There are several methods of achieving this and there is no evidence supporting one above the other.	
EAES	Operative R5	It is suggested that there is no indication for routine postoperative catheter placement in children or adults.	
WSES	5.5.2	In adult patients, drain after appendectomy for perforated appendicitis and abscess/peritonitis should be used with judicious caution, given the absence of good evidence from the literature. Drains did not prove any efficacy in preventing intraabdominal abscess and seem to be associated with delayed hospital discharge.	
EAES	Operative R12	In general, meticulous suction of intra-peritoneal fluid or collections is suggested; the philosophy should be: “leave no pus behind”. Routine use of drains in appendectomy is not recommended.	
WSES	5.6	Delayed primary skin closure does not seem beneficial for reducing the risk of SSI and increase LOS in open appendectomies with contaminated/dirty wounds	
EAES	Operative R13	Primary wound closure is recommended for all cases of open appendectomy.	
EAES	Operative S1	Various reasons exist to convert LA. However, no recommendation about when to convert can be given. It should be stated that conversion to open surgery is not regarded as a complication.	Yes
EAES	After Care R3	There is no reason to restrict the postoperative diet after an uncomplicated appendectomy.	
6) Scoring systems for intraoperative grading of appendicitis and their clinical usefulness			
WSES	6.1	The incidence of unexpected findings in appendectomy specimens is low but the intraoperative diagnosis alone is insufficient for identifying unexpected disease. From the current available evidence, routine histopathology is necessary	Yes
EAES	After Care R1	It is recommended to send all appendices to the pathology department routinely and the operated will review the results.	Yes
EAES	Operative R15	It is suggested that definitive treatment of a suspected malignancy will depend on final histological and staging information after initial treatment of the operative findings and may require further surgery or adjunct treatment.	
WSES	6.2	There is a lack of validated system for histological classification of acute appendicitis and controversies exist on this topic.	
WSES	6.3	Surgeon’s macroscopic judgement of early grades of acute appendicitis is inaccurate	Yes
WSES	6.4	If the appendix looks “normal” during surgery and no other disease is found in symptomatic patient, we recommend removal in any case.	Yes
EAES	Operative R9	It is suggested to remove the “normal” appearing appendix when operating for suspected appendicitis when no other pathology is identified.	Yes
WSES	6.5	We recommend adoption of a grading system for acute appendicitis based on clinical, imaging and operative findings, which can allow identification of homogeneous groups of patients, determining optimal grade disease management and comparing therapeutic modalities	

7) Nonsurgical treatment for complicated appendicitis: abscess or phlegmone			
WSES	7.1	Percutaneous drainage of a peri-appendiceal abscess, if accessible, is an appropriate treatment in addition to antibiotics for complicated appendicitis.	Yes
WSES	7.2	Nonoperative management is a reasonable first line treatment for appendicitis with phlegmon or abscess	Yes
EAES	After Care R5	Initial treatment of intra-abdominal abscess (IAA) is conservative with antibiotics. In some patients, this may need to be combined with radiological or surgical drainage.	Yes
EAES	Pre-Op R10	Non-operative treatment is suggested as the procedure of choice for patients with an appendiceal mass in the absence of diffuse peritonitis. Data are lacking on the benefits of interval appendectomy.	Yes
WSES	7.3	Operative management of acute appendicitis with phlegmon or abscess is a safe alternative to nonoperative management in experienced hands	Yes
EAES	Operative R14	It is recommended to treat an inflammatory mass conservatively. We recommend that when encountered during laparoscopy, refrain from appendectomy. During follow-up: additional imaging is advised. Data are lacking on the benefits of interval appendectomy.	
WSES	7.4	Interval appendectomy is not routinely recommended both in adults and children.	Yes
WSES	7.5	Interval appendectomy is recommended for those patients with recurrent symptoms.	Yes
WSES	7.6	Colonic screening should be performed in those patients with appendicitis treated non-operatively if >40y/o	
8) Preoperative and Postoperative Antibiotics			
WSES	8.1	In patients with acute appendicitis preoperative broad-spectrum antibiotics are always recommended	
EAES	Operative R2	Prophylactic antibiotics are recommended in appendectomy in adults.	
EAES	Operative R3	Prophylactic antibiotics are recommended in appendectomy in children.	
WSES	8.2	For patients with uncomplicated appendicitis, postoperative antibiotics are not recommended	
EAES	After Care S1	Evidence for duration of administration of postoperative antibiotics is lacking.	
EAES	After Care S2	There is no evidence of routine use of postoperative antibiotics in uncomplicated appendicitis.	
EAES	After Care R6	In complicated appendicitis, postoperative antibiotics are recommended.	
WSES	8.3	In patients with complicated acute appendicitis, postoperative, broad-spectrum antibiotics are always recommended	
WSES	8.4	Although discontinuation of antimicrobial treatment should be based on clinical and laboratory criteria such as fever and leucocytosis, a period of 3–5 days for adult patients is generally recommended	

Table 2: Centre Survey

	Data Criteria	Options
Centre details		
1(a)	Does your unit care for?	▪ Adults only ▪ Children only ▪ Adults and children
2	Does your hospital have an on-site gynaecology service?	▪ Yes ▪ No
3	Does your centre have 'review clinic' slots for patients to return for further assessment/imaging the following day if a diagnosis is unclear?	▪ Yes – with ultrasound and clinical review ▪ Yes – clinical review only ▪ No
4(a)	How many **consultants** will be "on call" during the 2 week study period?	Number =
4(b)	How many consultant general surgeons work at your centre?	Number =
4 (c)	Is there a **dedicated** registrar based on SAU to review patients?	▪ Yes – 24/7 ▪ Yes – During the day ▪ No – One registrar splits time between theatre and SAU
5	At weekends, Is ultrasound available?	▪ Yes ▪ No
6(a)	At weekends, is CT available?	▪ Equivalent to weekday service ▪ Reduced service but available for urgent surgical requests ▪ Not available
6(b)	At night, is CT available?	▪ Equivalent to weekday service ▪ Reduced service but available for urgent surgical requests ▪ Not available
Does your centre have an agreed policy for:		
7	When to use appendicitis risk stratification scores?	▪ Yes – use of score recommended ▪ Yes – use of score discouraged ▪ No policy in place
8	Which patients should have a CT scan prior to appendicectomy? *(e.g. diagnosis unclear, age >50)*	▪ Yes – please detail ▪ No policy in place
9	Whether some patients with appendicitis may be managed non-operatively?	▪ Yes –conservative management recommended for some patients; please detail ▪ Yes – policy discourages conservative management ▪ No policy in place
10	Whether laparoscopic or open appendicectomy should be routinely performed?	▪ Yes – open surgery recommended ▪ Yes – laparoscopic surgery recommended

		▪ No policy in place
11	Whether a macroscopically normal looking appendix should be removed or left in situ?	▪ Yes – removal recommended ▪ Yes – recommend it be left in situ ▪ No – no policy in place

Figure 1: study flowchart

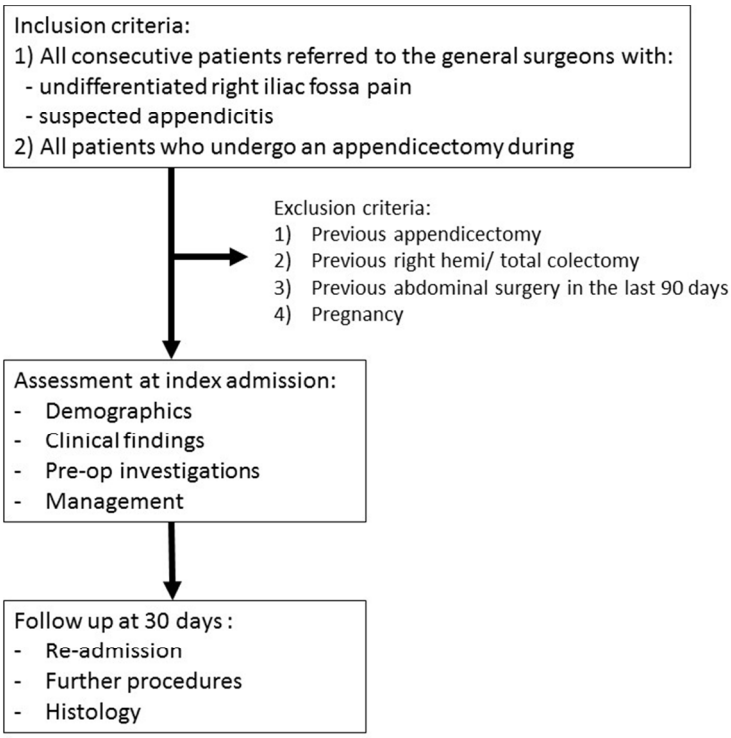

Figure 1: study flowchart

81x60mm (300 x 300 DPI)

Appendix 1

RIFT Study Group

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*Corporate authorships of UK trainee surgical research collaboratives, also PUBMed citable.