EAES Rapid Guideline: Appendicitis in the Elderly

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This rapid guideline addresses key questions on the diagnosis and management of acute appendicitis in elderly patients.

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Disclaimer

This clinical practice guideline has been developed under the auspice of the European Association for Endoscopic Surgery (EAES). It is intended to be used primarily by health professionals (e.g. surgeons, anaesthetists, physicians) and to assist in making informed clinical decisions on diagnostic measures and therapeutic management. It is also intended to inform individual practice of allied health professionals (e.g. surgical nurses, dieticians, physical rehabilitation therapists, psychologists); to inform strategic planning and resource management by health care authorities (e.g. regional and national authorities, health care institutions, hospital administration authorities); and to inform patients wishing to obtain an overview of the condition of interest and its management.
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1 - Protocol

ABSTRACT

Background

The proportion of elderly patients is expected to dramatically increase in the next 30 years. Acute appendicitis is a common disease in the elderly. No clinical practice guidelines have specifically addressed acute appendicitis in this population.

Methods and analysis

A rapid guideline will be developed in accordance with GRADE and AGREE II standards. The steering group will consist of general surgeons, members of the EAES Research Committee/Guideline Subcommittee with expertise and experience in guideline development, advanced medical statistics and evidence synthesis, biostatisticians, and a guideline methodologist. The guideline panel will consist of three general surgeons, an intensive care physician, a geriatrician and a patient advocate. Four PICO questions will address the diagnosis of acute appendicitis, the risks of appendectomy, and the efficacy of laparoscopic appendectomy in the elderly. Systematic reviews will be conducted and results of evidence synthesis will be summarized in summary of findings tables. Recommendations will be finalized through Delphi process of the guideline panel within an evidence-to-decision framework.

Ethics and dissemination

The funding body will not be involved in the development of this guideline. Conflicts of interest, if any, will be addressed by re-assigning functions or replacing participants with relevant conflicts.

Keywords

acute appendicitis; elderly; clinical practice guideline; rapid guideline; GRADE; AGREE II; EAES

INTRODUCTION

Background

The proportion of people over 60 years is expected to double from 12% to 22% between 2015 and 2050, according to the World Health Organization.*[1]* Consequently, the number of elderly recipients of health care services is expected to increase dramatically.

Healthcare providers, policy makers, and healthcare recipients need evidence-based information on the management of health problems in this patient population. Acute appendicitis is common in the elderly, with a risk of 5.2% between the age of 65 and 75.*[2]* Different patterns of co-morbidities, operative risks, and functional reserve of the elderly suggests that the management of acute appendicitis in this age group might be different from that in younger patients.

A survey of European surgeons by the EAES Research Committee/Guideline Subcommittee prioritized laparoscopic surgery in the elderly as a candidate topic to be addressed by a clinical practice guideline (46%) [EAES website]. No clinical practice guideline has specifically addressed laparoscopic surgery in the elderly, to the best of our knowledge. An update of guidelines by the World Society of Emergency Surgery published in 2020 did not conduct a statistical analysis of the available data and may thus fall short of providing the highest quality evidence when addressing the elderly population.*[3]*

Objective

The objective of this rapid guideline is to provide transparently developed, reliable, and evidence-informed recommendations on the the diagnosis of acute appendicitis in elderly patients and the use of laparoscopic appendectomy in this age group.

METHODS

The present protocol adheres to AGREE II and PRISMA reporting standards.*[4][5]* It will be available on the EAES website and on MAGICapp for access by healthcare professionals, and EAES members will be asked to comment on the content. Relevant comments will be considered by the steering group.

Funding

The project is funded by the European Association for Endoscopic Surgery. The funding bodies will not have any influence on the guideline development process.

Steering group

The steering group consists of general surgeons, members of the EAES Research Committee/Guideline Subcommittee, and experts in guideline development, medical statistics and evidence synthesis (SAA, POV, MM, FMC, GAA, DM).

Guideline methodologist

The primary author (SAA) fulfills the criteria of a GRADE methodologist,*[6]* has participated in the development of more than 10 clinical practice guidelines, has experience in evidence synthesis, and will serve as a guideline methodologist in this guideline.

Guideline panel

The guideline panel will consist of three general surgeons, an intensive care physician, a geriatrician, and a patient advocate. The guideline panel's contribution will be acknowledged by authorship in the resulting journal publication of this guideline.

PICO questions

The PICO questions have been formulated by the steering group and thresholds for clinical importance will be proposed to the guideline panel.

PICO questions will be the following:

1. Which is the best score for diagnosis of acute appendicitis in elderly patients?
2. What are the risks of appendectomy in elderly patients?
3. Should antibiotic treatment be preferred over appendectomy in elderly patients?
4. Should laparoscopic appendectomy be preferred over open appendectomy in elderly patients?

Thematic breakdown of questions and methodology to address these are presented in the **Table 1**.

Question	Method for obtaining effect sizes	Patient	Intervention	Comparator	Outcomes	Minimal clinically important difference
1. Which is the best score for diagnosis of acute appendicitis in elderly patients?	Diagnostic test accuracy pairwise meta-analyses	Patients with pain in the right lower abdomen and age >65 years	Alvarado score RIPASA score AIR score	CT/MRI	Diagnosis of acute appendicitis	N/A
1a. Subgroup analysis	Diagnostic test accuracy pairwise meta-analyses	>75 years				
1b. Subgroup analysis	Diagnostic test accuracy pairwise meta-analyses	>80 years				
2. What are the risks of appendectomy in elderly patients?	Proportion meta-analysis	Patients with acute appendicitis	Appendectomy	N/A	Mortality	OR/RR 1.2
					Major morbidity	OR/RR 1.3
					Minor morbidity	OR/RR 1.5
2a. Subgroup analysis	Proportion meta-analysis	>75 years				
2b. Subgroup analysis	Proportion meta-analysis	>80 years				
2c. Subgroup analysis	Proportion meta-analysis	ASA score ≥3				
3. Should antibiotic treatment be preferred over appendectomy in elderly patients?	Pairwise meta-analysis				Mortality	OR/RR 1.2
					Major morbidity	OR/RR 1.3
					Minor morbidity	OR/RR 1.3
					Quality of life	SMD 1.5
					Hospital stay	WMD 3 days
					ICU stay	WMD 1 day
3a. Subgroup analysis	Pairwise meta-analysis	>75 years				

3b. Subgroup analysis	Pairwise meta-analysis	>80 years					
3c. Subgroup analysis	Pairwise meta-analysis	ASA score ≥3					
3d. Subgroup analysis	Meta-regression analysis	Laparoscopic versus open appendectomy					
4. Should laparoscopic appendectomy be preferred over open appendectomy in elderly patients?	Pairwise meta-analysis	Patients with acute appendicitis and age >65 years	Laparoscopic appendectomy	Open appendectomy	Mortality	OR/RR 1.2	
					Major morbidity	OR/RR 1.3	
					Minor morbidity	OR/RR 1.3	
					Quality of life	SMD 1.5	
					Hospital stay	WMD 3 days	
					ICU stay	WMD 1 day	
4a. Subgroup analysis	Pairwise meta-analysis	>75 years					
4b. Subgroup analysis	Pairwise meta-analysis	>80 years					
4c. Subgroup analysis	Pairwise meta-analysis	ASA score ≥3					
4c. Subgroup analysis	Pairwise meta-analysis	Frail patients*					

* As defined by study authors
RIPASA: Raja Isteri Pengiran Anak Saleha Appendicitis
AIR: Appendicitis Inflammatory Response
CT: computed tomography
MRI: magnetic resonance imaging
SMD: standardized mean difference
WMD: weighted mean difference
N/A: not applicable
OR/RR: odds ratio/risk ratio
ASA: American Society of Anesthesiologists

Guideline development methodology

An outline of the guideline development methodology is presented in **Fig. 1**. The guideline development process will adhere to AGREE II and GRADE guideline development standards, and methodology parameters of rapid recommendations.*[7]* The guideline panel will comment on PICO questions, subgroup analyses and minimal clinically important differences, and rate the importance of outcomes on a 9-point scale proposed by GRADE. Any additional outcomes proposed by the panel will be considered for inclusion.

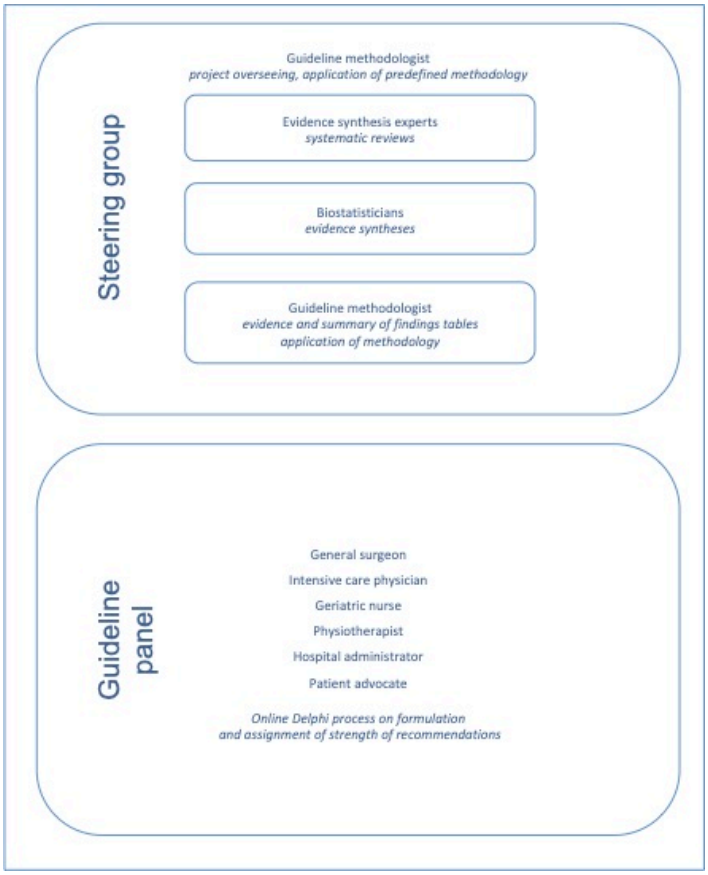

Fig. 1: Flow of guideline development, composition and functions of steering group members and guideline panel. There may be overlap in the roles and tasks of the group members.

The literature search strategy will be developed by a member of the steering group with experience in outreach, knowledge, and evidence search. The Healthcare Databases Advanced Search (HDAS) interface developed by the National Institute for Health and Care Excellence (NICE) will be used to interrogate Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica database (EMBASE), and Cochrane Controlled Register of Trials (CENTRAL). The grey literature will be searched through OpenGrey (Exalead). Relevant terms will be selected to identify eligible reports. Thesaurus headings, search operators, and search limits in each of the above databases will be adapted accordingly.
Risk of bias of eligible studies will be assessed using RoB 2 for randomized trials,*[8]* ROBINS-I for observational studies,*[9]* QUADAS-2 for diagnostic test accuracy studies,*[10]* and the NIH Quality Assessment Tool for case series.*[11]* Study selection, risk of bias assessment and data extraction will be performed by one investigator and independently cross-checked by a collaborator; disagreements will be resolved by discussion. Statistical analyses as outlined in Table 1 will be performed by biostatisticians using the methodology reported below.
GRADE evidence tables and summary of findings tables will be constructed and presented to the guideline panel in a web-based meeting. Draft recommendations will be formulated and strength of recommendations will be defined. The recommendations will be refined and their strength will be assessed and revised as judged by the guideline panel through an online Delphi process. Comments by the Delphi panel must be in accordance with the GRADE methodology in order to be considered. Formulation of recommendations will be informed by GRADE and AGREE-REX.*[12][13]*

Evidence synthesis methodology

1. Diagnostic test accuracy meta-analysis
To evaluate the performance of the test in correctly identifying those with appendicitis (sensitivity) and those without appendicitis (specificity), we will extract the following information of the eligible studies; true positives, false positives, true negatives, false negatives. We will employ a random effects model and derive pooled estimates for sensitivity and specificity and produce relevant forest plots using RevMan/R.

2. Proportion meta-analysis
Pooled proportions and 95% confidence intervals will be calculated using back transformation of the weighted mean of the transformed proportions via the Freeman-Tukey double arcsine method. Conceptual heterogeneity related to patient-intervention-outcome parameters and the study design will be assessed, and statistical heterogeneity will be tested for using the I2 statistic. Both a fixed effect and a random effects model in sensitivity analyses will be used, whereas results of the latter will not be taken into account in the presence of substantial funnel plot asymmetry. Small-study effects, a proxy for publication bias, will be assessed by visually evaluating the symmetry of the funnel plots if >10 studies are included in the analysis. Statistical analyses will be performed using R and the library meta.

3. Pairwise meta-analysis
Mantel-Haenszel pooled odds ratios will be calculated for binary outcomes (adding 0.5 in the case of zero events in a single arm) and the standardized mean difference for continuous outcomes, with corresponding 95% confidence intervals. Conceptual heterogeneity related to the PICO parameters and the study design will be assessed, and statistical heterogeneity will be tested for using the I2 statistic. A fixed effect and a random effects model will be applied, and the likelihood of publication bias will be investigated using the methodology described above. Statistical analyses will be performed using RevMan (Review Manager 5.4, The Nordic Cochrane Centre, Copenhagen, Denmark).
Where means and p-values will be given, the standard error and the standard deviation will be estimated by calculating the standard error and t-value using the given degrees of freedom. The standard error and the standard deviation will be obtained from confidence intervals by using the formula suggested by the Cochrane Collaboration.*[14]*

Target users
This guideline is intented to be used by general surgeons, general practicioners, emergency and intensive care physicians, geriatric nurses, physiotherapists, hospital administrators, policy makers, and patients. The guideline publication will contain a short abstract in plain language to be used by patients.

Publication and dissemination strategy
As a EAES Research Committee/Guideline Subcommittee project, this guideline will be submitted for publication in Surgical Endoscopy, official journal of the Association and streamlined through the social media, email newsletters and congress presentations. The full guideline will be available on MAGICapp.

Feedback
The steering group will consider constructive feedback received during the conduct of the project via various routes and sources such as letters to the editor and social media. Such feedback will be taken into account in the guideline development process or a future update of the guideline.

Monitoring, update and future steps
Use of the guideline by EAES members will be monitored through an online survey 2 years after publication. The timing of the update of the guideline will be decided by the steering group on the basis of new research evidence on this topic.

DISCUSSION

Implications for practice and research
Stringent criteria defined by GRADE and AGREE II will be applied to collate, appraise and analyze the available evidence. The guideline is expected to inform decision making, and guide clinical practice and health policy. Guidance will be provided on direction and implications for future research in light of identified evidence gaps.

Strengths and limitations
The strengths and limitations of rapid guidelines have been previously reported.*[7][15][16]* The merits of rapid guidelines, including trustworthiness, credibility, and time efficiency have to outweigh the shortcomings, such as the narrow scope and possible missing of resources due to the rapid review process.

Research ethics
EAES, as the funder, will not be involved in the development of this guideline. Research Ethics Committee approval is not necessary as this project does not involve any identifiable patient data. Conflicts of interest statements will be collected by all participants before and upon completion of the project. Participants with substantial conflicts will be either re-assigned functions or replaced. Authors of studies considered for development of evidence summaries will not be involved in risk of bias appraisal of these studies and discussion of the relevant evidence to decision framework.

CONCLUSION
This rapid guideline will address the diagnosis and management of acute appendicitis in elderly patients and aspires to provide a useful information source for key stakeholders.

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