Clinical-pathological features and treatment of acute appendicitis in the very elderly: an interim analysis of the FRAILESEL Italian Multicentre Prospective Study

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Abstract

Background

emergency abdominal surgery in the elderly represents a global issue. Diagnosis of AA in old patients is often more difficult. Appendectomy remains the gold standard of treatment and, even though it is performed almost exclusively with a minimally invasive technique, it can still represent a great risk for the elderly patient, especially above 80 years of age. A careful selection of elderly patients to be directed to surgery is therefore fundamental. The primary aim was to critically appraise and compare the clinical-pathological characteristics and the outcomes between oldest old (≥ 80 years) and elderly (65–79 years) patients with Acute Appendicitis (AA).

Methods

The FRAILESEL is a large, nationwide, multicenter, prospective study investigating the perioperative outcomes of patients aged ≥ 65 years who underwent emergency abdominal surgery. Particular focus has been directed to the clinical and biochemical presentation as well as to the need for operative procedures, type of surgical approach, morbidity and mortality, and in-hospital length of stay. Two multivariate logistic regression analyses were performed to assess perioperative risk factors for morbidity and mortality.

Results

182 patients fulfilled the inclusions criteria. Mean age, ileocecal resection, OAD and ASA score ≥ 3 were related with both overall and major complication. The multivariate analysis showed that MPI and complicated appendicitis were independently factors associated with overall complications. OAD and ASA score ≥ 3 were independently factors for both overall and major complications.

Conclusions

age ≥ 80 years is not an independent risk factor for morbidities. POCUS is safe and effective for the diagnosis; however, a CECT is often needed. Having the oldest old a smaller functional organ reserve, an earlier intervention is needed, especially because they required greater rate of major resection.

Introduction

As the world population is aging rapidly, emergency abdominal surgery for acute abdomen in the elderly represents a global issue, both in developed and developing countries. (1–4) More than 20% of the Italian population is over the age of 65 and, by the year 2050, this percentage is expected to grow to 34%. Over the last 20 years, country's life expectancy has increased from 78 to 80 years for men and from 84 to 85 years for women. It is estimated that 21% of the total population older than 60 years will require surgery, compared with only 12% of people in the 45–60 age group. (5, 6) Demographic changes in the population have also modified the profile of emergency abdominal surgery, where typical causes of acute abdomen in the elderly include acute

cholecystitis, incarcerated hernia, bowel obstruction, acute diverticulitis and acute appendicitis (AA). (7, 8) AA is the most common general surgical emergency worldwide, but its diagnosis remains challenging. (9, 10) When compared to the general population, diagnosis of AA in old patients is often more difficult. (11) Older patients generally present later in the course of the disease and may have nonspecific symptoms. (12–13) To improve diagnosis of appendicitis, international guidelines recommend routine clinical risk scoring. (14, 15) Although the Appendicitis Inflammatory Response (AIRS) and Alvarado scores are recommended most frequently, no one of these score is widely used in clinical practice and none is specific for elderly patients. (16–19) In addition, their higher comorbidity rate and the less systemic reserve capacity may potentially lead to severe consequences in case of such an acute event. They often have other conditions such as diverticulitis or neoplasms that can mimic acute appendicitis. (20) Appendectomy remains the gold standard of treatment and, even though it is now performed almost exclusively with a minimally invasive technique, it can still represent a great risk for the elderly patient, especially above 80 years of age and in the event of multiple comorbidities. (14, 21, 22, 23) A careful selection of elderly patients to be directed to surgery versus those who can benefit only from antibiotic therapy is therefore fundamental, since if a “white” appendectomy rate is acceptable in young people, especially in women, this cannot be reproduced in the elderly because they have not the same ability to tolerate the stress induced by the surgical procedure. (1, 24) In this study, we focus our attention on the subgroup over 80 years old compared to the subgroup of elderly patient between 65–79 years old. The primary aim was to analyse the difference between the two groups in the clinical–pathological data, management strategies, and in the short-term outcomes after emergency surgery for Acute Appendicitis

Materials And Methods:

Study settings and protocol

This report originates from the FRAILESEL (Frailty and Emergency Surgery in the Elderly) study (ClinicalTrials.gov identifier: NCT02825082) (8, 23, 24). The FRAILESEL is a large, nationwide, multicenter, prospective study that investigated the perioperative outcomes of patients aged ≥ 65 years who underwent emergency abdominal surgery over a period of consecutive 18 months (January 2017 and June 2018). Data regarding elderly patients discharged from the participating centers were prospectively collected. Centres were included on a volunteer basis, and neither investigators nor participating hospitals were paid for their collaboration. Clinical decisions, including operative technique, were based on the criteria of individual centers and attending surgeons. The investigators were informed about the objectives of the study and asked for complete details about the surgical management of acute abdomen in the elderly following standard methods and collection protocols.

The final FRAILESEL Study protocol was approved by the Ethics Committee of Sapienza University and of all the centers and by the boards of the involved societies. All parts of the study and the present manuscript have been checked and presented according to the checklist for (STROBE) (25).

Exclusion criteria and collected data confirmation

Exclusion criteria were the following: patients younger than 65 years old at the day of surgery; diagnostic laparoscopy/laparotomy with no further surgical procedures performed with the exception of intestinal ischemia; lack of informed consent for the study participation; endoscopic procedures and emergency

reoperations after elective surgery; patients already hospitalized and scheduled for the same procedure; patients participating in another trial. Submissions made by unconfirmed participants, duplicate submissions, record with more than 5% of missing data, and data submitted by residents from dual or more residency programs were excluded. Although demographic information was collected on the patients, all data were anonymized before analysis even for center identification. The FRAILESEL study encompassed the final enrollment of 2635 patients but 2563 with confirmed data.

Patients characteristics, preoperative variables and objectives of this study

The FRAILESEL study investigates over 130 variables, exploring five domains such as patient demographic and clinical data, preoperative risk factors and operative variables, frailty condition, and postoperative outcomes and follow-up. Data collected included patient demographic characteristics (age, gender, weight, height), medical and surgical history (comorbidities), common preoperative biochemical blood examination (including CRP, PCT and arterial blood gas analysis), pathological features, and operative details. Comorbidity was recorded if the condition was being medically treated at the time of admission, or if previous treatment for the condition was described in the admission report. Preoperative risk was assessed with anesthesiologist-assigned American Society of Anesthesiologists (ASA) class. Frailty was assessed by calculating the 5 modified Frailty Index (5-mFI) as described by Tracy et al. (26) The Mannheim Peritonitis Index (MPI) was also calculated. (27) Systemic inflammatory response syndrome (SIRS) and quick-Sofa (q-Sofa) were also evaluated. Postoperative complications have been reported and categorized according to the Clavien-Dindo (CD) classification system by the study leader in each of the participating centers. (28) Morbidity and mortality have been considered regardless of the time elapsed from the surgical procedure if reasonably related to it. With regard to the aims of the present study, patients were selected from the dataset using the International Classification of Diseases versions 9 (ICD-9™) (codes 540.xx to 543.xx). After the final revision, appendicitis due to neoplastic lesion and incidental appendectomy were excluded. Primary aim was to critically appraise and compare the clinical-pathological characteristics and the outcomes between oldest old (≥ 80 years) and elderly (65–79 years) patients with a diagnosis of AA. Particular focus has been directed to the clinical and biochemical presentation as well as to the need for operative procedures, type of surgical approach, morbidity and mortality rate, and length of in-hospital stay (LOS). An open conversion was defined as when a procedure was attempted via the minimally invasive approach but required an open incision to be completed. The decision for preoperative work-up was made by the attending surgeon and/or the attending emergency physician. Computerized tomography scan was performed with intravenous contrast material (CECT). Results of CECT scans and point-of-care-ultrasound (POCUS) were interpreted by a staff radiologist. Diagnosis of AA was made by the appearance of the appendiceal wall and by the presence of peri-cecal or peri-appendicular inflammation with or without intra-abdominal fluid collection. Complicated appendicitis was defined by the finding of a gangrenous or perforated appendix, as well as the presence of an intra-abdominal abscess. CECT was considered positive only when there could be no diagnostic doubts or differential diagnosis (e.g. pseudo-inflammatory tumours, abscess). Secondary aim was to determine the frequencies of elderly with acute appendicitis and the elderly to oldest old patient ratio. For this purpose, we randomly selected 19 centres and asked the principal investigator in each centre to select the total number of patients with acute appendicitis submitted to surgery in the study period. Eleven centres were able to provide the requested data.

Statistical analysis

Statistical analysis was performed with SPSS software, version 21 (IBM, New York, NY - USA) for MacOSX. Dichotomous data and counts were presented in frequencies, whereas continuous data were presented as mean values $\pm$ standard deviations and/or median with Interquartile Range (IQR). Differences between means were compared using the independent sample Student's t-test or the Mann–Whitney U test when indicated. Fisher's exact test or χ^2 test, with or without Yates correction, were implemented to compare differences in frequencies. Two further multivariate logistic regression analyses were performed in order to assess perioperative risk factors for morbidity and mortality. All variables with p value < 0.20 at univariate analysis were entered into a multivariate model. A p value ≤ 0.05 was considered statistically significant.

Results

During the study period, 182 patients underwent emergency surgery procedure for acute appendicitis, fulfilled the inclusion criteria for this study. Table 1 reports patients' characteristics in detail. The overall median age was 74.5 ± 7.3 years and there was a male predominance (141 male patients, 77.5%). Of these, 41 (22,5%) were aged ≥ 80 years and constituted the oldest old Group (OOG); the remaining 141 (77,9%) patients had an age between 65 and 79 years and represented the Control Elderly Group (CEG). Table 1 shows also the comparison between the OOG and the CEG group. In the oldest old, 75.6% were male, and we observed the same male/female ratio in CEG with 78.0% of male. The survey revealed that the overall mean rate of elderly patients with acute appendicitis was 10.7% (range: 4.6–14.2%), while the mean rate of oldest old patients was 23.8% (range: 19.4–26.3%). Overall severe frailty rate was 50.5%; although slightly higher in the OOG, frailty rates were not statistically different between the two groups, being present as severe in 61.0% in the oldest old group, and 47.5% in the control elderly group.

Table 1
Patients clinical features

		Total	%	Oldest old	%	Elderly < 80	%	P value
Number of Patients		182		41		141		
Age Mean (SD)		74.5 ± 7.3		85.5 ± 4.3		71.3 ± 4.0		< 0.001
Median (IQR)		74 (65–95)		84 (80–95)		71 (65–79)		
Sex	Female	41	22.5%	10	24.4%	31	22.0%	0.91
	Male	141	77.5%	31	75.6%	110	78.0%	
BMI		26.13 ± 4.7		24.9 ± 4.2		26.5 ± 4.8		0.98
Frailty								0.18
5-mFI 0/0.2 (not or moderate frailty)		90	49.5%	16	39.0%	74	52.5%	
5-mFI ≥ 0.4 (severe frailty)		92	50.5%	25	61.0%	67	47.5%	
Temperature		37.3 ± 0.8		37.2 ± 0.9		37.3 ± 0.8		0.40
WBC		13.2 ± 4.4		11.3 ± 3.2		13.7 ± 4.6		0.35
PCR		7.4 ± 8.2		8.6 ± 8.6		7.0 ± 8.0		0.50
Creatinine		1.15 ± 0.8		1.5 ± 1.2		1.0 0.5		< 0.05
Glicemia		134.6 ± 61.3		138.3 ± 97.3		133.5 ± 46.3		0.18
Lactate		0.9 ± 1.7	31.3%	2.0 ± 3.9		0.6 ± 0.8		< 0.05
SIRS	Yes	41	22.5%	7	17.1%	34	24.1%	0.46
	No	141	77.5%	34	82.9%	107	75.9%	
Mannheim Peritonitis Index		10.5 ± 5.0		10.8 ± 5.9		10.4 ± 4.8		0.082
Comorbidity	Yes	153	84.1%	35	85.4%	118	83.7%	0.98
	No	29	15.9%	6	14.6%	23	16.3%	
Diabetes	Yes	43	23.6%	13	31.7%	30	21.3%	0.32
	No	139	76.4%	28	68.3%	111	78.7%	

		Total	%	Oldest old	%	Elderly < 80	%	P value
Oral anticoagulant drugs	Yes	46	25.3%	11	26.8%	35	24.8%	0.79
	No	136	74.7%	30	73.2%	106	75.2%	
ASA	1	11	6.0%	1	2.4%	10	7.1%	0.35
	2	65	35.7%	13	31.7%	52	36.9%	
	3	99	54.4%	24	58.5%	75	53.2%	
	4	6	3.3%	3	7.3%	3	2.1%	
	5	1	0.5%	0	0.0%	1	0.7%	

We evidenced no differences between the two groups in terms of comorbidities, diabetes and use of Oral Anticoagulant Drugs (OAD), Body Mass Index (BMI), Body Temperature (BT). Regarding pre-operative biochemical values, the OOG show higher creatinine levels (1.5 ± 1.2 vs 1.0 ± 0.5 , $p < 0.05$) and higher lactate level (2.0 ± 3.9 vs 0.6 ± 0.8 $p < 0.05$) compared to the CEG. However, no differences were evidenced between the two groups in terms of SIRS (7 patients, 17.1% vs 34 patients, 24.1% in the OOG compared to CEG, respectively; $p = 0.46$) and q-SOFA (9 patients 21,9% % vs 37 26,2% patients in the OOG compared to CEG, respectively; $p = 0.51$) According to the Mannheim Peritonitis Index, the oldest old showed a slightly more severe peritonitis but not statistically significant (10.8 ± 5.9 vs 10.4 ± 4.8 , in the OOG compared to CEG, respectively; $p = 0,082$). The overall mean American Society of Anaesthesiology (ASA) score was ASA 3 (99 patients, 54.4%) followed by ASA 2 (66 patients, 35.7%). The same distribution of patients according to the ASA score was observed in the two groups, with no statistically significant differences ($p = 0,35$). Under the clinical point of view, a POCUS was performed in 106 patients (58,2%) and a CECT of the abdomen was performed in 149 patients (81,9%). Of note POCUS was positive for acute appendicitis in 66% of the cases with no difference between the two groups while CT scan was positive in almost all the patients (85,9%). A clinical picture of complicated appendicitis was highlighted in the 34.6%patients with a slightly higher rate in the CEG (46 patients, 32,6% vs 17 patients, 4155, in the CEG compared to OOG, respectively; $p = 0.3$). Table 2 summarized the pre-operative data and outcomes. All but seven patients underwent surgical procedure (175 patients, 96.7%) with just one negative exploration (0.5%). Of these seven patients, 6 (3,3%) underwent a pure non-operative management with only antibiotic therapy and one (0,5%) underwent percutaneous drainage associated with antibiotic therapy. Even if it is not possible to make a statistical comparison, we want to underline how 6 out of the 7 conservative treatments belonged to the Oldest Old Group. Appendectomy was performed in 129 (91.5%) of the CEG patients while it was performed in 75,6% of the OOG. The difference was statistically significant ($p < 0,05$), even if most of the ileocecal resection were performed in the CEG without statistical significance (9.8% vs 7,1. % in the OOG compared to CEG respectively $p = 0,39$). More specifically, a laparoscopic approach was most commonly adopted in the CEG group (100 patients – 70,9%) as compared to the OOG (13 patients – 31,7%) ($p < 0.05$). However, there was no statistically significant difference regarding the conversion rate between the two groups (4 patients, 30,8% vs 16 patients, 15,8. % in the OOG compared to CEG, respectively, $p = 0,39$). There was no difference in terms of morbidity, Surgical Site Infections (SSI), intra-abdominal abscess and mortality, with an overall morbidity and mortality rate of 64 patients, 35.2% and 2 patients, 1,1% respectively. The univariate and multivariate analysis for overall and major complications are showed in Table 3. At univariate analysis, factors related to both overall

and major complication were mean age, ileocecal resection, OAD and ASA score ≥ 3 . The multivariate analysis showed that MPI and complicated appendicitis were independently factors associated with overall complications while higher INR value was independently associated with major complications. Moreover, OAD and ASA score ≥ 3 were independently factors associated with both overall and major complications.

Table 2
perioperative variable and outcomes

		Total	%	Oldest old	%	Elderly < 80	%	P value
Preoperative abdominal US		106	58.2%	19	46.3%	87	61.7%	0.08
	Positive preoperative abdominal US	70 / 106	66%	10 / 19	52.6%	60 / 87	69.0%	0.17
Preoperative abdominal CT		149	81.9%	38	92.7%	111	78.7%	< 0.05
	Positive preoperative abdominal CT	128 / 149	85.9%	35 / 38	92.1%	93 / 111	83.8%	0.28
Complicated appendicitis		63	34.6%	17	41.5%	46	32.6%	0.30
Time to surgery		15.2 ± 1.6		12.9 ± 2.1		15.9 ± 1.9		0.44
Appendectomy		160	87.9%	31	75.6%	129	91.5%	< 0.05
Ileo-cecal resection		14	7.7%	4	9.8%	10	7.1%	0.39
Negative exploration		1	0.5%	-		1		na
Non-Operative Management		6		5		1		na
Percutaneous Drainage		1		1		-	-	na
Surgical approach	Open	69	37.9%	28	68.3%	41	29.1%	< 0.05
	Laparoscopic	113	62.1%	13	31.7%	100	70.9%	
Conversion rate		20	17.5%	4	30.8%	16	15.8%	0.17
Morbidity	Yes	64	35.2%	10	24.4%	54	38.3%	0.10
	No	118	64.8%	31	75.6%	87	61.7%	
Infective complications	Yes	32	17.6%	6	14.6%	26	18.4%	0.74
	No	150	82.4%	35	85.4%	115	81.6%	
			21.4%		14.6%		23.4%	0.32
Clavien-Dindo 2–4	Yes	39		6		33		
	No	143	78.6%	35	85.4%	108	76.6%	

		Total	%	Oldest old	%	Elderly < 80	%	P value
Mortality	Yes	2	1.1%	1	2.4%	1	0.7%	0.40
	No	180	98.9%	40	97.6%	140	99.3%	

Table 3

Univariate and multivariate analysis for Overall complications and Major complications (Clavien-Dindo II-IV)

	Overall Complications (C-D II-IV)				Major complications (C-D II-IV)			
	OR (95%CI) univariate	p	OR (95%CI) multivariate	p	OR (95%CI) univariate	p	OR (95%CI) multivariate	p
Age (mean)	0,952 (0,910- 0,995)	0,031			0,928 (0,875- 0,983)	0,012		
MMPI	1,075 (1,010 – 1,145)	0,050	1,058 (1,009 – 1,108)	0,019		> 0,200		
INR		> 0,200			2,410 (1,158- 5,028)	0,019	2,126 (1,154- 3,917)	0,016
Ileo.cecal resection	3,698 (1,183 – 11,560)	0,037			8,280 (2,590- 3,360)	< 0,001	0,213 (0,087 – 0,519)	0,001
Complicated appendicitis	2,047 (1,087 – 3,856)	0,025	0,529 (0,296- 0,945)	0,031	1,629 (0,790- 3,856)	0,184		
Oral anticoagulants	2,317 (1,169- 4,593)	0,015	0,483 (0,252- 0,927)	0,029	3,038 (1,431- 6,958)	0,003	0,048 (0,202- 0,992)	0,048
Kidney disease	2,667 (0,882- 8,060)	0,133			2,190 (0,689- 8,060)	0,184		
COPD	1,684 (0,878- 3,230)	0,115				> 0,200		
ASA ≥ 3	1,730 (0,916- 3,265)	0,015	0,502 (0,225- 0,990)	0,047	4,263 (1,766 – 10,288)	0,001	0,337 (0,135- 0,844)	0,020
Age < 80	2,09 (1,138- 3,867)	0,101				> 0,200		
Hypertension		> 0,200			1,739 (0,890- 3,397)	0,103		
Diabetes (Y/N)		> 0,200			2,083 (1,002– 4,333)	0,042		

Discussion

Life expectancy is increasing and consequently there is an increasing elderly population with multiple concomitant and more severe co-morbidities. (5, 6) With this increase of the lifespan, a growing incidence of acute appendicitis has been registered in the elderly (≥ 65 years old) population and also in the oldest old (> 80 years old). (9, 29) Moreover, emergency surgery in the elderly is challenging in terms of decision-making, managing co-morbidity and post-operative rehabilitation with high morbidity and mortality rate. (2, 3, 7) On the light of this, it is pivotal to define the possible clinical-pathological features and treatment of such disease in a well-known frailer portion of the population.

New pathophysiology acknowledgement and improved surgical and anaesthetic skills allowed the surgeon to achieve better results in treating these high-risk patients. (3), However, diagnosis and treatment of acute appendicitis in elderly patients still remain a challenge. (12–15).

We particularly focused on the age-related clinical differences and investigated the role of age as independent risk factor for the main clinical course and outcomes.

We have herein reported, to the best of our knowledge, the largest series of comparison of clinical features and outcomes between patients aged 80 years and older and elderly patients with an age comprised between 65 and 79 years presenting with AA, since no series with similar design were found in the current literature. The elderly account for approximately 10% of the population and between them about a quarter is represented by patient > 80 years old. Several studies evidenced significant differences in terms of AA clinical course between patients older and younger than 65 years with an increased morbidity and length of stay in the elderly. (12–15) Interestingly enough, in our study population, age ≥ 80 years was not an independent risk factor for both major and overall morbidities as well as for frailty which surprisingly is not statistically associated with postoperative complications. Focusing on the clinical presentation of AA, we found no difference in terms of pre-operative variables such as sex, BMI, BT, MPI and presence of comorbidities between the two groups. Regarding laboratories value, only few studies have investigated the predictive role of preoperative laboratory parameters. (30, 31). According to the literature, the age of the patient is one of the most important factor affecting the degree of elevation in inflammatory markers. Although there are many studies that have evaluated the benefits of using WBC, consensus has not yet been reached. (32, 33) Moreover, elderly patients have generally less remarkable inflammatory factors, due to decreased immune system response ability. (34, 35). At this regard, our study shows no difference in terms of WBC, PCR and glycaemia between the two groups and we evidenced also a similar rate of SIRS and q-SOFA. On the contrary, we reported a significant higher level of lactate and creatinine in the oldest old group. A possible explanation could be linked to the long-terms pre-existing comorbidities in the oldest old group that negatively influence the already reduced physiological functions of elderly patients, leading to an insufficient organ reserve to cope with an inflammatory insult such as AA.

Several studies have shown a higher rate of complicated AA in the elderly group. (24, 36, 37) This finding may be explained by the fact that elderly patients with perforated appendix would show poor exacerbation of pain as well as more generalized lower abdominal tenderness and guarding leading to a delay in presentation to the hospital. (38, 39) This is in line with other studies who report a reduction of pain in oldest old patients, probably linked to a greater capacity to endure or to report it. (40, 41)

However, our series did not show a significant increase rate of complicated AA in the oldest group, but nevertheless perforation or abscess at presentation are independent risk factors for overall morbidities.

Based on this premise, we can assume that it is absolutely necessary to consider all clinical and laboratory findings, as well as the radiological methods for diagnosing acute appendicitis, above all in the oldest old. According to the recent literature, the role of diagnostic imaging, such as POCUS and CECT is another major controversy. (14, 42) In our series, more than half of the patients underwent preoperative POCUS with no difference in terms of positive findings between the elderly and the oldest old group. However, an abdomen CECT scan was done in the 81% of the patients, reaching a rate of 92,7% in the oldest-old group. This finding is consistent with the number of ileocolic resection performed, since in the presence of a not clear diagnosis of appendicitis only at CECT (e.i. ileocecal abscess or pseudo inflammatory tumour) a major resection was carried out. The recently published Cochrane systematic review on CECT scan for diagnosis of AA in adults identified 64 studies including 71 separate study populations with a total of 10280 participants (4583 with and 5697 without AA). Summary sensitivity of CECT scan was 0.95, and summary specificity was 0.94. At the median prevalence of AA (0.43), the probability of having AA following a positive CECT result was 0.92, and the probability of having AA following a negative CECT result was 0.04. (43). According to the last World Society of Emergency Surgery guidelines (WSES), we agree that POCUS is the most appropriate first-line diagnostic tool, however as the elderly have often not typical laboratories values and symptoms unlikely to be acute appendicitis, cross-sectional imaging such as CECT scan is recommended before surgery. (14). Delay in presentation was found by many authors to be the reason behind the higher rate of perforation seen in the elderly population while in a meta-analysis of van Dijk a delaying appendectomy for up to 24 hours after admission does not appear to be a risk factor for complicated appendicitis, SSI or other morbidities. (44, 45)

Our research showed a slight lower time to surgery in the OOG. This can be interposed in light of the fact that when facing with oldest old, having them a smaller functional reserve, a more timely intervention is needed, and it also run with the greater rate of major resection carried out in this group. However, time to surgery was not a risk factor for overall and major complications. Regarding treatment strategies, even if over the last few years, several reports have been published describing non-operative-management (NOM) of AA, in our series all but seven patients underwent surgical procedure. (46–49) However 6 out of 7 of NOM patients were > 80 years old. Such findings, reflects the tendency of avoiding surgical procedures in patients generally defined as not fit for surgery.

Appendectomy was the overall most common surgical procedure, the rate of major surgery such as ileocecal resection was similar in both groups and it was an independent risk factor for major post-operative complication at both univariate and multivariate analysis. This could be linked with another evidence emerged from our study which shows how the presence of complicated appendicitis is an independent risk factor for overall and major complications both at univariate and multivariate analysis.

Regarding the surgical approach, several systematic reviews of randomized control trials comparing laparoscopic appendectomy (LA) versus open appendectomy (OA), conclude that LA leads to less postoperative pain, lower overall hospital stays, and significantly decreases postoperative complications, in particular SSI. (14, 51) From our experience, the laparoscopic approach was statistically more frequent in the elderly group. This could be linked to the fact that being the oldest old often less autonomous and often more bedridden, the advantages of laparoscopy are less important.

Of note, according to our analysis, there was no difference regarding the conversion rate in both groups and it was not a risk factor for post-operative morbidity. On the other side, an ASA ≥ 3 score was an independent

factor for overall and major complications both at univariate and multivariate analysis, so we can assume that concomitant comorbidities might contribute the most to higher morbidity rate in aged patients.

Focusing on major complications, another important finding of our study is that there was an inverse relationship between increasing age and AA related major complications, highlighted how oldest patients in their frailty, achieve a more stable physiologic status compared to elderly patient with equal comorbidity rate. Moreover, comorbidities such as hypertension, diabetes, use of OAD and kidney dysfunction are independent risk factors for major comorbidity regardless patient age.

Although our study represents, to the best of our knowledge, the largest case series that specifically focuses on the AA clinical course in the over 80-year population, some limitations should be outlined. The observational multicenter cohort design, without a control population to compare is the most important. Another limitation concerns the epidemiological data, that are limited by the number responder centres

However, the prospective data collection and “*a priori*” definition of criteria to identify postoperative complications might mitigate these limitations. Moreover, a wide multicenter study allows more variables and reproducible results than a single center, while the large series of patients allowed excluding confounders by multiple logistic analyses.

Conclusion

Our study suggests that age ≥ 80 years is not an independent risk factor for morbidities. Moreover, no difference in terms of pre-operative variables such as sex, BMI, BT, MPI and presence of comorbidities in the OOG were found. POCUS is safe and effective for the diagnosis of appendicitis in the elderly; however, a CECT is often needed to exclude other age-related diseases such as tumours. Having the oldest old a smaller functional organ reserve, an earlier intervention is needed, especially because they required greater rate of major resection.

Abbreviations

FraileseI

Frailty and Emergency Surgery in the Elderly

AA

acute appendicitis

AIRS

Appendicitis Inflammatory Response

STROBE

Strengthening the Reporting of Observational Studies in Epidemiology

CRP

C-Reactive Protein

PCT

procalcitonin

ASA

American Society of Anesthesiologists

MPI

Mannheim Peritonitis Index
CD
Clavien-Dindo
SIRS
Systemic Inflammatory Response Syndrome
q-Sofa
quick- Sequential Organ Failure Assessment
ICD-9™
International Classification of Diseases versions 9
LOS
Length of in-hospital Stay
CECT
Contrast Enhancement Computerized Tomography
POCUS
Point-of-Care-Ultrasound
IQR
Interquartile Range
OOG
Oldest Old Group
CEG
Control Elderly Group
OAD
Oral Anticoagulant Drugs
BMI
Body Mass Index
BT
Body Temperature
WBC
White Blood Cells Count

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no potential financial conflict of interest related to this manuscript.

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Authors' contributions

PF: Study conception and design, literature search, acquisition, interpretation and analysis of data, drafting and critically revising the article for important intellectual content and final approval of the version to be published. VF: literature search, acquisition, interpretation and analysis of data VC: literature search, acquisition, interpretation and analysis of data GC: acquisition, interpretation and analysis of data, drafting and critically revising the article for important intellectual content and final approval of the version to be published LP: acquisition, interpretation and analysis of data PM: acquisition, interpretation and analysis of data ALG: drafting and critically revising the article for important intellectual content and final approval of the version to be published GS: drafting and critically revising the article for important intellectual content and final approval of the version to be published

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