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The significant impact of age on the clinical outcomes of laparoscopic appendectomy

Results from the Polish Laparoscopic Appendectomy multicenter large cohort study

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Abstract

Acute appendicitis (AA) is the most common surgical emergency and can occur at any age. Nearly all of the studies comparing outcomes of appendectomy between younger and older patients set cut-off point at 65 years. In this multicenter observational study, we aimed to compare laparoscopic appendectomy for AA in various groups of patients with particular interest in the elderly and very elderly in comparison to younger adults.

Our multicenter observational study of 18 surgical units assessed the outcomes of 4618 laparoscopic appendectomies for AA. Patients were divided in 4 groups according to their age: Group 1—<40 years old; Group 2—between 40 and 64 years old; Group 3—between 65 and 74 years old; and Group 4—75 years old or older. Groups were compared in terms of peri- and postoperative outcomes.

The ratio of complicated appendicitis grew with age (20.97% vs 37.50% vs 43.97% vs 56.84%, $P<.001$). Similarly, elderly patients more frequently suffered from perioperative complications (5.06% vs 9.3% vs 10.88% vs 13.68%, $P<.001$) and had the longest median length of stay (3 [Interquartile Range (IQR) 2–4] vs 3 [IQR 3–5], vs 4 [IQR 3–5], vs 5 [IQR 3–6], $P<.001$) as well as the rate of patients with prolonged length of hospital stay (LOS) >8 days. Logistic regression models comparing perioperative results of each of

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the 3 oldest groups compared with the youngest one showed significant differences in odds ratios of symptoms lasting >48 hours, presence of complicated appendicitis, perioperative morbidity, conversion rate, prolonged LOS (>8 days).

The findings of this study confirm that the outcomes of laparoscopic approach to AA in different age groups are not the same regarding outcomes and the clinical picture. Older patients are at high risk both in the preoperative, intraoperative, and postoperative period. The differences are visible already at the age of 40 years old. Since delayed diagnosis and postponed surgery result in the development of complicated appendicitis, more effort should be placed in improving treatment patterns for the elderly and their clinical outcome.

Abbreviations: ASA score = American Society of Anesthesiologists score, BMI = body mass index, CRP = C-reactive protein level, IAA = intraabdominal abscess, LA = laparoscopic appendectomy, LOS = length of hospital stay, STROBE = Strengthening the Reporting of Observational Studies in Epidemiology, WBC = white blood cell count.

Keywords: acute appendicitis, elderly, laparoscopic appendectomy

1. Introduction

Acute appendicitis is the most common surgical emergency with the reported lifetime incidence of 8%.[1,2] The incidence of AA is highest in the second to forth decade of life, but this condition can occur at any age.[1] As world demographics trend towards an increasing number of the elderly, the absolute number of elderly requiring treatment for AA will also increase. Unlike in younger patients, diagnosing AA in the elderly may be challenging—only one-quarter present with typical symptoms of AA and more than one-third are diagnosed after significant delay in seeking medical attention. Moreover, only half are correctly diagnosed on admission.[3] This as well as high incidence of frailty reaching even almost 80% in elderly patients undergoing emergency abdominal surgery obviously leads to inferior outcomes[4] and introducing of proper reconditioning program can be beneficial for these patients.[5]

Although nonoperative management of AA is feasible, appendectomy remains a gold standard of treatment.[6] Previous studies have confirmed that the laparoscopic approach for appendectomies is beneficial for the elderly.[7] For the minimally invasive approach it is typically associated with faster recovery and a shorter hospital stay comparing to open access and can be performed even in ambulatory setting.[8–10] Registry studies underline the reduction in overall morbidity. However, the major morbidity and mortality was not confirmed in all of these analyses.[11–13] Interestingly, the majority of studies compare the laparoscopic and the open approach to AA, while the data comparing clinical outcomes of laparoscopic appendectomy between younger and older patients is sparse. In addition, nearly all of the studies were designed to compare only 2 age groups (younger vs older) and set a cut-off point at 65 years. This underrepresents populations nowadays, especially in developed countries where life expectancy exceeds 80 years.[14,15] Such study design does not allow a full analysis of outcomes of the very elderly individuals.

1.1. Aim

In this multicenter observational study, we aimed to compare LA for AA in various groups of patients with particular interest in the elderly and very elderly in comparison to younger adults.

2. Methods

2.1. Study design

This multicenter study was performed across 18 surgical centers in both Poland and Germany over a 6-month period. An internet-based database collected data from patients admitted for laparoscopic appendectomies including both retrospective and prospective data from patients operated on during the study period. The coordinating surgeon and the local team of nurses, anesthesiologists, and assistants acquired data in each participating surgical unit. The database recorded the following variables from each center: annual number of laparoscopic appendectomies performed, patient characteristics (sex, age, body mass index [BMI], American Society of Anesthesiologists [ASA] score, history of smoking, diabetes mellitus, timing from onset of symptoms to surgery, Alvarado score), white blood cell count (WBC), C-reactive protein level (CRP), operative parameters (operative time, type of surgeon performing the appendectomy [resident/specialist], type of AA [uncomplicated/complicated], intraoperative adverse events), and postoperative outcomes (postoperative morbidity, need for surgical reintervention, length of hospital stay [LOS], need for readmission). Morbidity was defined as any deviation from the normal postoperative course, requiring additional pharmacological or interventional treatment that occurred within 30 days postoperatively. It was ranked according to Clavien-Dindo classification.[16] Prolonged LOS was defined as longer than 2*upper quartile of the entire cohort (8 days). The design and implementation of this study followed the guidelines of The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Patients were divided in 4 groups according to their age: Group 1—<40 years old; Group 2—between 40 and 64 years old; Group 3—between 65 and 74 years old; and Group 4—75 years old or older.

The project was supported by the Polish Videosurgery Society—chapter of the Association of Polish Surgeons. This study did not implement any changes in patient treatment. A primary investigator monitored this study. He processed and verified any missing or unclear data submitted to the database. The data collected was anonymized and had no identifying patient information. The only hospital data included was the number of laparoscopic appendectomies performed annually. Approval by the local ethics committee of Jagiellonian University, Krakow, Poland has been obtained for conducting this study.

2.2. Statistical analysis

Statistical analyses were done using Statsoft STATISTICA 13.0 PL (Statsoft Inc., Tulsa, OK). Continuous variables were presented using means with standard deviations (SD) or medians with inter-quartile ranges (IQR) for skewed variables. Then, comparisons between groups were done using t student tests for normally distributed variables and Mann–Whitney U tests for skewed variables. Dichotomous variables were included in chisquared Pearson, Yate, and Fisher exact tests, depending on the quantities in the subgroups. Groups were compared using Kruskal–Walli analysis of variance test with multiple comparison of ranges. Logistic regression models were built to determine odds ratios depending on each age group. Finally, in order to establish whether age is an independent risk factor for complications and prolonged LOS, multivariate logistic regression models using Rosenbrock and quasi-Newton test were built. Results were considered statistically significant when P-values were $<.05$. In the case of missing data, pairwise deletion was used.

3. Results

Data of 4618 patients who underwent laparoscopic appendectomy were inputted into the database. Table 1 shows basic characteristics of the groups. Most patients (3004 [65.05%]) belonged to the youngest group (<40 years old). The least patients (95) (2.06%) were in the oldest group (≥75 years old). The number of women in groups rose with the age of population in the groups starting with 47% in group 1 up to 61% in group 4. ASA class was correlated with age as well. ASA dominated in group 1 was ASA I while as much as 40% of patients were ASA III in group 4. The rate of patients with diabetes mellitus increased with the patient's age. Similarly, the ratio of patients with symptom onset >48 hours increased with age (27.6% vs 37.27% vs 44.77% vs 45.26%, $P<.001$). Differences in median CRP and WBC were also observed and their increase correlated with age.

The perioperative outcomes are presented in Table 2. The median operative time was shortest in the youngest group (50 minutes [IQR 40–70]) and longest among the elderly. The ratio of complicated appendicitis grew with age (20.97% vs 37.50% vs 43.97% vs 56.84%, $P<.001$). Similarly, elderly patients more frequently suffered from perioperative complications (5.06% vs 9.3% vs 10.88% vs 13.68%, $P<.001$) and had the longest median length of stay (3 [IQR 2–4] vs 3 [IQR 3–5], vs 4 [IQR 3–5], vs 5 [IQR 3–6], $P<.001$) as well as the rate of patients with prolonged LOS >8 days.

Table 3 shows the details of univariate logistic regression models comparing perioperative results of each of the 3 oldest groups compared with the youngest one. Significant differences in odds ratios of symptoms lasting >48 hours, presence of complicated appendicitis, perioperative morbidity, conversion rate, prolonged LOS (>8 days) were noted. Multivariate logistic regression models confirmed that age is an independent risk factor for postoperative morbidity (65–74 years old—OR: 1.38 [95% CI 1.05–1.83], 65–74 years old—3.45 [95% CI 1.90–6.26], and ≥75 years old 2.56 [95% CI: 1.12–5.82] in comparison with patients <40 years old) and prolonged LOS (65–74 years old—OR: 1.87 [95% CI 1.40–2.49], 65–74 years old—1.89 [95% CI 1.03–3.45] and ≥75 years old 2.84 [95% CI: 1.39–5.82] in comparison with patients <40 years old).

4. Discussion

This study evaluates the characteristics of AA and its outcomes in different age groups. Generally, compared with younger, cases, older patients were more often operated on when symptoms lasted longer than 48 hours and were more likely to develop complicated AA. Moreover, the differences were observed already at the age >40 years and were even more pronounced with older patients. The morbidity rate was significantly higher in every group; however, severe complications and readmissions did not differ. In addition, when we excluded patients with conversion, we noticed a significant increase in complication rates in analyzed groups. As a result, a longer LOS and higher rates of prolonged hospitalizations were observed in older groups.

The proportion of the elderly requiring emergency surgery reflects changes in life expectancy in the 21st century. Major surgical interventions among octogenarians and older are not uncommon and are no longer contraindication to surgery.[17,18] Although the incidence of AA varies with age with the highest in younger individuals, it still occurs in later decades of life.[19–21] In our cohort, advanced age resulted in increasing rate of complicated appendicitis. Several analyses previously confirmed

Table 1

Basics characteristics.

Age group	<40 years old	40–64 years old	65–74 years old	≥75 years old	*P*-value
Number (%)	3004 (65.05%)	1280 (27.72%)	239 (5.17%)	95 (2.06%)	n/a
Males/Females (%)	1592/1411 (53%/47%)	668/612 (52%/48%)	112/127 (47%/53%)	37/58 (39%/61%)	**.017**
Median BMI, kg/m^2 (IQR)	23.93 (21.3–26.8)	26.87 (24.03–30.4)	27.7 (22.7–30.5)	27.37 (24.2–31.6)	**<.001**
Obesity	365 (12.15%)	343 (26.80%)	90 (37.66%)	24 (25.26%)	**<.001**
ASA class					
IV	1 (0.03%)	0	4 (1.67%)	1 (1.05%)	**<.001**
III	17 (0.57%)	80 (6.25%)	61 (25.52%)	38 (40%)	
II	420 (13.98%)	637 (49.77%)	144 (60.25%)	46 (48.42%)	
I	2566 (85.42%)	563 (43.98%)	30 (12.55%)	10 (10.53%)	
Smoking	477 (15.88%)	273 (21.33%)	39 (16.32%)	4 (4.21%)	**<.001**
DM	22 (0.73%)	66 (5.16%)	40 (16.74%)	18 (18.95%)	**<.001**
Symptoms >48 h vs <48 h	829 (27.60%)	477 (37.27%)	107 (44.77%)	43 (45.26%)	**<.001**
Median Alvarado score (IQR)	6 (4–9)	6 (5–8)	6 (5–8)	6 (4–7)	.093
Alvarado ≥7	1268 (42.21%)	605 (47.27%)	105 (43.93%)	38 (40%)	.093
Median leukocytosis, *1000 per mm^3 (IQR)	13.15 (10–16.19)	13.16 (10.26–16.17)	12.8 (10.27–16.1)	11.71 (9.5–14.05)	**.014**
Leukocytosis >20 tys.	266 (8.85%)	125 (9.77%)	20 (8.36%)	9 (9.47%)	.807
Median CRP, mg/L (IQR)	20.6 (4.6–55)	42 (11.6–95.78)	62.25 (19.6–113.6)	85.3 (35.3–179)	**<.001**
CRP >100	385 (12.82%)	316 (24.69%)	76 (31.8%)	38 (40%)	**<.001**

ASA = American Society of Anesthesiologists, BMI = body mass index CRP = C-reactive protein level
Bold values indicate statistical significance.

Table 2

Perioperative outcomes.

	<40 years old	40–64 years old	65–74 years old	≥75 years old	*P*-value
Number (%)	3004 (65.05%)	1280 (27.72%)	239 (5.17%)	95 (2.06%)	n/a
Number of appendectomies/year in department					
>50	2092 (69.64%)	924 (72.19%)	184 (76.99%)	69 (72.63%)	.052
<50	912 (30.36%)	356 (27.81%)	55 (23.01%)	26 (27.37%)	
Residents vs specialists	1345/1659 (44.77%/55.26%)	542/738 (42.34%/57.66%)	110/129 (46.03%/53.97%)	33/62 (34.74%/65.26%)	.123
Median operative time, min (IQR)	50 (40–70)	55 (40–75)	60 (45–80)	60 (40–85)	**<.001**
Technique of appendix stump closure					
Clipping	1869 (62.22%)	796 (62.19%)	130 (54.39%)	51 (53.68%)	
Suturing/Ligature	250 (8.32%)	156 (12.19%)	32 (13.39%)	15 (15.79%)	
Stapling	233 (7.76%)	70 (5.47%)	5 (2.09%)	3 (3.16%)	**<.001**
Endoloop	382 (12.72%)	156 (12.19%)	48 (20.08%)	20 (21.05%)	
Roeder loop	270 (8.99%)	102 (7.97%)	24 (10.04%)	6 (6.32%)	
Introperative diagnosis					
Unchanged appendix	248 (8.26%)	96 (7.5%)	16 (6.69%)	12 (12.63%)	
Purulent appendicitis	2231 (74.27%)	766 (59.84%)	136 (56.90%)	35 (36.84%)	
Gangrenous appendicitis	445 (14.81%)	323 (25.23%)	63 (26.36%)	37 (38.95%)	**<.001**
Perforated/autoamputated appnedix	80 (2.66%)	95 (7.42%)	24 (10.04%)	11 (11.58%)	
Complicated appendicitis	630 (20.97%)	480 (37.50%)	105 (43.93%)	54 (56.84%)	**<.001**
Postoperative drainage	2266 (75.43%)	1021 (79.76%)	208 (87.03%)	84 (88.42%)	**<.001**
Perioperative morbidity	152 (5.06%)	119 (9.30%)	26 (10.88%)	13 (13.68%)	**<.001**
Perioperative major morbidity III–V (Clavien-Dindo)	36 (1.20%)	36 (2.81%)	9 (3.77%)	3 (3.16%)	**<.001**
Perioperative morbidity in patients without conversion	130 (4.52%)	93 (8.00%)	17 (8.17%)	8 (9.88%)	**<.001**
Perioperative major morbidity in patients without conversion	29 (0.59%)	29 (2.50%)	4 (1.92%)	3 (3.70%)	**.003**
Clavien-Dindo classification of surgical complications					
V	0	2	0	1	
IV	1	1	1	1	
III	35	33	8	1	**.038**
II	34	34	7	5	
I	82	49	10	5	
Conversions	129 (4.29%)	118 (9.22%)	31 (12.97%)	14 (14.74%)	**<.001**
Reinterventions	45 (1.50%)	38 (2.97%)	14 (5.86%)	1 (1.05%)	**<.001**
Median LOS (IQR)	3 (2–4)	3 (3–5)	4 (3–5)	5 (3–6)	**<.001**
LOS >8	96 (3.20%)	87 (6.80%)	27 (11.30%)	17 (17.89%)	**<.001**
Readmissions	74 (2.46%)	34 (2.66%)	9 (3.78%)	1 (1.05%)	.466

Bold values indicate statistical significance.

this finding.[3,22–24] We also observed that the rate of patients with symptoms lasting >48 hours in the last group was 20% higher than in the youngest patients. Segev et al[25] observed that the interval from symptoms onset to admission for the octogenarians was nearly doubled compared with younger patients confirming our observations. Appropriate clinical diagnosis in the older patients is often complicated by many factors leading to an untypical clinical picture of the disease. They include diminished immune function, vague symptoms, multiple comorbidities, and normal senescent anatomic alterations. This is attributed to atypical presentations leading to frequent misdiagnoses.[26] Therefore, computed tomography should be considered as the first line option in the diagnostics of the older patients with suspected acute appendicitis. Unfortunately, we did not include

Table 3

Univariate logistic regression models (in comparison with patients <40 years old).

	40–64 years old			65–74 years old			≥75 years old		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Symptoms >48 h	1.56	1.33–1.82	**<.001**	2.13	1.59–2.86	**<.001**	2.18	1.37–3.46	**.001**
Complicated appendicitis	2.26	1.96–2.61	**<.001**	2.95	2.25–3.87	**<.001**	4.96	3.28–7.52	**<.001**
Perioperative morbidity	1.92	1.50–2.47	**<.001**	2.29	1.48–3.55	**<.001**	2.97	1.62–5.46	**<.001**
Perioperative major morbidity III–V (Clavien-Dindo)	2.39	1.50–3.81	**<.001**	3.23	1.53–6.78	**.002**	2.69	0.81–8.89	.105
Perioperative morbidity in patients without conversion	1.78	1.35–2.34	**<.001**	1.33	1.02–1.73	**.035**	1.29	1.01–1.66	**.043**
Perioperative major morbidity in patients without conversion	2.44	1.45–4.10	**.001**	1.35	0.79–2.28	.272	1.53	1.02–2.28	**.040**
Conversions	2.26	1.73–2.94	**<.001**	3.33	2.19–5.07	**<.001**	3.86	2.13–7.01	**<.001**
Reinterventions after primary procedure	2.01	1.30–3.11	**.002**	4.09	2.21–7.57	**<.001**	0.70	0.10–5.14	.725
Prolonged LOS (>8 d)	2.21	1.64–2.98	**<.001**	3.86	2.46–6.05	**<.001**	6.60	3.76–11.59	**<.001**
Readmissions	1.08	0.69–1.68	.748	1.60	0.79–3.26	.192	0.44	0.06–3.22	.419

Bold values indicate statistical significance.

questions regarding preoperative imaging in our database and therefore, we are not able to establish whether there are differences among groups in the use of preoperative computed tomography compared with diagnostic laparoscopy for diagnosis.

Although conversion and reintervention rates were greater among older patients, we do not believe it is related to age but rather to the clinical state of AA. Not surprisingly, complicated appendicitis, for example, periappendiceal abscess, perforation, and difficult appendix stump for obvious reasons are risk factors for conversion.[27,28] It should be emphasized that conversion is usually inevitable and should not be considered an inferior treatment. In a previous analysis by Kim et al,[29] conversion after attempted laparoscopic appendectomy was associated with a longer operative time but it did not affect postoperative morbidity and length of stay when compared with an initially open surgery. However, taking into consideration benefits of laparoscopic approach in the elderly, it seems obvious that is should be attempted whenever possible, since it decreases mortality and the rate of bedridden patients.[9] Moreover, to keep the conversion rate as low as possible, an experienced surgeon should operate on or take over when a resident is not able to move forward with the procedure. It is particularly important in older patients with delayed diagnosis and/or complicated appendicitis. In our older study population, we did not observe the difference in complications between the residents and specialists. However, the oldest population was too small to draw definitive conclusions regarding this factor.

An interesting finding in this cohort is that odds ratios for postoperative morbidity was increasing in every group in comparison to baseline (<40 years old). However, when patients with conversion were excluded these trends were not observed both for overall and for major morbidity. This also speaks for benefits of laparoscopic approach among the elderly. Obviously higher complications rates observed in the older population can be explained not only by delay in the appropriate diagnosis, more advanced disease, and operative technique but also by higher number of comorbidities complicating the recovery (including cognitive impairment and functional dependence).[30] In our study we did not used any dedicated comorbidity scale apart from routinely used ASA score, which significantly raised with advanced age. Similarly, the longer LOS in the older group is not only the effect of more demanding treatment but also often caused by social reasons. Therefore, early identification of social issues and prompt discharge planning should be done to minimalize this effect. With prolonged hospitalization, older patients are more prone to hospitalization-related complications and functional deterioration, which can be a direct way to disability and increased risk of death in the longer follow-up.[31]

This study has several limitations. The majority of patients were included retrospectively, and we did not analyze perioperative protocols (antibiotics, postoperative care). However, we believe this had little impact on final outcomes. Due to the lack of detailed data we were not able to analyze the relationship between existing comorbidities and treatment results. The only comorbidity included in our database was diabetes mellitus, which differed in age groups (highest among elderly) and is a well-known risk factor for postoperative complications.[32] In addition, when analyzing postoperative morbidity and readmissions, the timeframe included 30 days. Although sufficient for younger patients, we are uncertain this was enough in older patients. Moreover, we were able to provide data on readmissions only for patients readmitted to participating centers, possibly biasing our results to some extent. Nevertheless, we are certain that the large number of participating centers allow for comprehensive results that are generally applicable to other hospitals. Lastly, since our database only includes patients undergoing surgery for AA, we did not include those managed conservatively. This modality is becoming an increasingly used and valid treatment option in uncomplicated appendicitis.[33,34] This factor has to be considered when analyzing results of our study in terms of the general treatment of AA.

5. Conclusion

The findings of this study confirm that the outcomes of laparoscopic approach to AA in different age groups are not the same regarding outcomes and the clinical picture. Older patients are at high risk both in the preoperative, intraoperative, and postoperative period. The differences are visible already at the age of 40 years old. Since delayed diagnosis and postponed surgery result in the development of complicated appendicitis, more effort should be placed in improving treatment patterns for the elderly and their clinical outcome.

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