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Abstract

Background: although diagnostic criteria for appendicitis are well- defined, the indications for performing appendectomy are still vague. This implies that the decision-making process differs between surgeons, hospitals and countries. Healthcare in China has developed over the last two decades, and is in many respects comparable to western countries, though there still exists room for improvement. To explore how medical decision-making works in China, and whether or not their medical results are applicable to the Western setting, we compared the indications for appendectomy in China with those in Sweden.

Objective: to investigate decision-making on appendectomy in Sweden and China.

Methods: a retrospective evaluation of all appendectomy procedures at the Karolinska Hospital in 2009 formed the basis of a questionnaire. Using this questionnaire, a prospective study was coinducted at Södersjukhuset and Karolinska University Hospital Stockholm in 2010 and at Taizhou hospital in 2013. The decision-making surgeon reported which factors were present at the time of treatment decision, and which factors had the greatest impact on their decision. 107 questionnaires were collected in China and compared to 117 collected in Sweden.

Results: the most frequently reported factors in Sweden and China were similar, but there were some differences. Tenderness in the right fossa had a great impact on the decision to operate in both countries, but an interesting difference was that there was a greater tendency to rely on image diagnostics in Sweden.

Limitations: further investigation is needed to evaluate how decision-making is related to evidence and how this affects outcome.

Conclusions: as regards appendicitis, the decision-making process in China is similar enough to allow results from China to be used in the Western setting.

1 Introduction

Appendectomy is one of the most commonly performed surgical procedures. The indications for performing appendectomy are, however, not clearly defined (1). This implies that indications may differ between surgeons, hospitals and countries. In surgery, the decision on whether to operate or not is of crucial importance (2). This makes it particularly important to understand how surgeons reach their decision to operate. The decision to perform an appendectomy is based on the clinical picture and evaluation of all diagnostic procedures. It also includes weighing the pros and cons of conservative management versus surgery in each case of probable appendicitis, and deciding on optimal timing (1). The integration of diagnostics and risk/benefit of management alternatives in every case, makes the decision-making process complex. Furthermore, decisions must be made without unnecessary delay. This usually means that the surgeon has to rely on evidence-based medicine as well as intuition, weighing all possible treatment outcomes together with the patient, in order to reach a trade-off between the risk of over-diagnosing and under-diagnosing as well as over-treatment and under-treatment (3).

It is generally believed that every clinician is capable of making correct decisions, as if this is something they learn during their medical education. Decision-making, however, is much more complex than that (4). Furthermore, diagnostic errors occur, which confirms that not every clinician is capable of *always* making adequate decisions (4). Humans are not as logical and rational as computers, but think in a more nuanced manner than computer algorithms, and can differentiate, on a higher level, between the various items in the data collection that lies behind a decision (5). Croskerry et al. (6) suggest that the decision-making process has been regarded, until quite recently, as a somewhat hidden process, and it has

therefore not been discussed as something that can be changed or improved. It has become evident, however, that making decisions need not be an invisible process. Many psychological processes and other factors play a part in the decision-making process. These processes and factors can be modified, and are indeed subjects for discussion. Decision-making can and must be improved (4-6).

According to Diener et al. (7), it is fairly easy to make a clinical decision based on evidence. The authors describe three steps in this process: 1. summarise all the facts; 2. translate this summary into clinical guidance; and 3. use it in the right time and place. However, it may be more difficult than it appears to carry out these three steps in every single patient. Systematic reviews were introduced several years ago in an attempt to make medical information easier to grasp and as a tool to help provide a solid basis of evidence for medical decisions (7). However it must be understood that studies rely on measurable variables. Some variables, such as clinical signs and indications for surgery, are difficult to measure or balance against other more easily computable objects. However, even if not quantifiable, these factors are of great importance in the decision to perform surgery. The term "evidence-based medicine" has been used for over 15 years, but it has only recently been introduced into the surgical field on a large scale. Surgery is only partly evidence-based and in many aspects still depends on traditions and experience (7).

1.1 Comparison with China

The trade-off between the risk of under-treatment and over-treatment is a process that should incorporate the risk of unnecessary suffering, prolonged hospital stay and loss of trust between surgeon responsible and patient. Even if the medical consequences of each decision may be similar worldwide, the consequences of adverse events following

an unnecessary surgical procedure or a delayed intervention depend on the economic system, traditions and numerous circumstances related to culture and family structure. By sharing experiences from these two different cultures and healthcare systems, and re-evaluation and benchmarking of the decision-making process, a better basis for effective decision-making may be achieved. Improvement in health care in both countries may be achieved through the mutual comparison of outcomes and shortcomings, leading to more accurate diagnoses and a reduction in complication rates. There are, to our knowledge, no previous studies in the literature comparing indications for appendectomy between different countries, and there is thus no study with which to compare ours. The aim of this study was to compare the decision-making process of appendectomy between Sweden and China by comparing indications for surgical treatment of acute appendicitis to see which are given highest priority.

2 Methods

2.1 Retrospective part

In a retrospective examination, all appendectomy procedures conducted in 2009 at the Karolinska University Hospital were evaluated (8). The symptoms and signs documented in the patients' medical charts prior to appendectomy were registered in a standardised protocol. For each patient undergoing appendectomy, the two following patients not undergoing appendectomy when presenting with abdominal pain at the same emergency department, were used as controls. In this retrospective study, 15 symptoms, signs, and diagnostic procedures were identified. These factors had a significantly high odds ratio for appendectomy in patients seeking for general abdominal pain, compared to patients seeking for general abdominal pain but not undergoing an appendectomy. The 15 factors were: nausea; vomiting; loss of appetite; pain in right fossa, right hypochondrium, umbilical area and pain migration; tenderness in right fossa, right

hypochondrium, epigastrium and indirect tenderness; positive image diagnostics; elevated leucocyte count; and elevated and increasing c-reactive protein. These 15 factors, together with ten other factors that are commonly discussed in the literature on the diagnosis of acute appendicitis (1, 9-10), formed the basis for a questionnaire. This questionnaire was used in the prospective part of the study in Sweden in 2010. The same questionnaire translated into Chinese was used in China 2013,.

2.2 Prospective part

The prospective part of the study took three months during 2010 in Karolinska University Hospital, and Södersjukhuset, Stockholm, and two months in Taizhou Hospital, China. Surgeons responsible for the decision to perform an appendectomy were requested to answer the questionnaire. The surgeon was requested to specify which factors from the list of 25 were present at the time of treatment decision. They were also asked which three of the factors had the greatest impact on the decision to perform surgery.

2.3 Study group

117 questionnaires were collected from Karolinska University Hospital and Söder Hospital, Stockholm, (8), representing more than 80% of the appendectomies performed during the study period. 107 questionnaires were collected from Taizhou Hospital, which was 95% of all appendectomies performed during the study period. Two patients were not included in the study since the procedures were performed as elective procedures. Four patients were missed due to communication problems when starting the investigation.

2.4 Statistical analyses

2.4.1 Separate analyses

The data from China and Sweden were initially analysed separately. The percentage of patients reported with each factor, out of the total number of patients, was calculated. Factors reported among

more than 50% of the patients were considered to be frequently reported factors. The frequency of how often a factor had great impact on the treatment decision in relation to the number of patients reported with that factor, was also calculated.

2.4.2 Analyses of the factors' impact

The ratio of a factor having great impact on the treatment decision in relation to the total number of factors was calculated. This gave an estimate of how great the impact each factor had. The impact of each factor on the treatment decision was compared to the total average. This analysis was performed separately for China and Sweden.

2.4.3 Comparing analyses

The reported frequency of each factor in China was compared to the reported frequency in Sweden. These rates were

used to compare which factors were given greatest priority in each respective country. Statistical analyses were done with the chi-2 test using SPSS 17.0. Statistical significance was assumed at a p -value less than 0.05.

3 Results

3.1 Study groups

The study group in Sweden included 117 patients, of which 66 (56%) were women. Mean age was 37 years, standard deviation 16 years. The study group in China included 107 patients, of which 40 (36%) were women. The mean age was 31 years with a standard deviation of 20 years.

3.2 Symptoms, signs and diagnostic procedures in Sweden

The outcome of the Swedish prospective part of the study regarding symptoms, signs and diagnostic procedures recorded prior to surgery is presented in Table 1.

Table 1. Symptoms, signs, and diagnostic procedures prior to surgery in the Swedish study and their impact on treatment decision-making.

	Symptoms, signs and diagnostic procedures reported at treatment decision, per cent of all (n=117)		Symptoms, signs and diagnostic procedures with great impact on treatment decision (3 per patient), per cent of the left column		Impact on treatment decision <i>P-value</i>	Affirmed factors, difference between Sweden and China <i>P-value</i>	Factors with greatest impact, difference between Sweden and China <i>P-value</i>
	n	%	n	%			
Symptoms							
Nausea	66	56	0	0	<0.01	0.08	<0.01
Vomiting	39	33	2	5	<0.01	0.44	0.95
Loss of appetite	40	34	4	10	<0.01	0.25	0.65
Pain in the right fossa	110	94	27	25	0.05	0.66	<0.01
Pain in the left fossa	13	11	0	0	0.01	0.09	-
Pain in the right hypochondrium	12	10	0	0	0.01	0.03	-
Pain in the left hypochondrium	2	2	0	0	0.32	0.17	-
Pain in the epigastrium	12	10	0	0	0.01	0.50	-
Pain in the umbilical area	29	25	4	14	0.03	0.81	0.72
Pain migration	66	56	33	50	0.02	0.11	0.91
Occurrence of diffuse pain	58	50	4	7	<0.01	<0.01	0.80
Pain provoked by movement	55	47	10	19	0.02	<0.01	0.17
Signs							
Fever	38	32	8	21	0.11	0.13	0.53
Tenderness in the right fossa	106	91	81	76	<0.01	0.28	0.23
Tenderness in the left fossa	18	15	2	11	0.05	0.03	0.48
Tenderness in the right hypochondrium	7	6	1	14	0.29	0.12	0.57
Tenderness in the left hypochondrium	2	2	0	0	0.32	0.61	-
Tenderness in the epigastrium	2	2	0	0	0.32	0.07	-
Tenderness in the umbilical area	13	11	0	0	0.01	0.39	0.36
Indirect tenderness	51	44	18	35	0.72	0.01	0.01
Rigid abdomen	8	7	3	38	0.78	0.36	0.96
Diagnostic results							
Image diagnostics	78	67	70	90	<0.01	0.1	<0.01
Elevated leukocyte count	76	65	29	38	0.32	0.04	0.1
Elevated CRP	89	76	31	35	0.70	<0.01	0.06
Rising CRP	41	35	13	32	0.86	0.60	0.60

Abbreviations: CRP = C-reactive protein.

The most frequent symptoms, signs and diagnostic results reported at the time of treatment decision (percentage of total number of patients) were: pain in the right fossa (94%); tenderness in the right fossa (91%); elevated CRP (76%); results from

image diagnostics (67%); pain migration (56%); nausea (56%); and occurrence of diffuse pain (50%). The mean percentage of how great an impact all factors had on the surgical decision in Sweden was 33% (340/1031).

3.3 Symptoms, signs and diagnostic procedures in China

The outcome of this part of the study regarding symptoms, signs and diagnostic

procedures recorded prior to surgery is presented in Table 2.

	Symptoms, signs and diagnostic activities present at treatment decision, per cent of all (n=107)		Symptoms, signs and diagnostic activities of great impact on treatment decision (3 per patient), per cent of the most left column		Impact on treatment decision	Affirmed factors, divergence between Sweden and China	Factors of greatest impact, divergence between Sweden and China
	n	%	n	%	P-value	P-value	P-value
Symptoms							
Nausea	48	45	10	21	<0.01	0.08	<0.01
Vomiting	41	38	2	5	<0.01	0.44	0.95
Loss of appetite	29	27	2	7	<0.01	0.25	0.65
Pain in right fossa	99	93	80	80	<0.01	0.66	<0.01
Pain in left fossa	4	4	0	0	0.08	0.09	-
Pain in right hypochondrium	3	3	0	0	0.12	0.03	-
Pain in left hypochondrium	0	0	0	0	-	0.17	-
Pain in the epigastrium	13	12	0	0	0.01	0.50	-
Pain in umbilical area	28	26	3	11	<0.01	0.81	0.72
Pain migration	49	46	24	49	0.46	0.11	0.91
Diffuse occurrence of pain	11	10	1	9	0.02	<0.01	0.80
Pain provoked by movements	25	23	8	32	0.22	<0.01	0.17
Signs							
Fever	25	23	7	28	0.10	0.13	0.53
Tenderness in right fossa	101	94	84	83	<0.01	0.28	0.23
Tenderness in left fossa	4	4	0	0	0.08	0.03	0.48
Tenderness in right hypochondrium	2	2	0	0	0.21	0.12	0.57
Tenderness in left hypochondrium	1	1	0	0	0.38	0.61	-
Tenderness in the epigastrium	7	7	0	0	0.02	0.07	-
Tenderness in the umbilical area	16	15	1	6	<0.01	0.39	0.36
Indirect tenderness	25	23	2	8	<0.01	0.01	0.01
Rigid abdomen	11	10	4	36	0.61	0.36	0.96
Diagnostic activities							
Image diagnostic	82	77	44	54	0.06	0.1	<0.01
Elevated leukocyte levels	88	82	45	51	0.15	0.04	0.1
Elevated CRP	17	16	2	12	<0.01	<0.01	0.06
Increasing CRP	2	2	1	50	0.86	0.60	0.60

Table 2. Symptoms, signs, and diagnostic measures affirmed prior to surgery in the Chinese study and their impact on the treatment decision.

Abbreviations: CRP = C-reactive protein.

The most frequent symptoms, signs and diagnostic results reported at the time of treatment decision (percentage of total number of patients) were: tenderness in the right fossa (94%); pain in the right fossa (93%); elevated leukocyte count (82%); and results of image diagnostics (77%). The mean percentage of impact for all factors in China was 44% (321/731).

3.4 Factors having low impact

Factors in Sweden with a significantly lower value than 33% were: nausea; vomiting; loss of appetite; pain in the right fossa; pain in the left fossa; pain in the right hypochondrium; pain in the epigastrium; pain in the umbilical area; diffuse onset of pain; pain provoked by movement; tenderness in the left fossa; and tenderness in the umbilical area.

Factors in China with a significantly lower value than 44% were: nausea; vomiting; loss of appetite; pain in the epigastrium; pain in the umbilical area; occurrence of diffuse pain; tenderness in the epigastrium; tenderness in the umbilical area; indirect tenderness; and elevated C-reactive protein.

3.5 Factors having high impact

Factors in Sweden with a significantly higher value than 33% were factors that, when reported, were considered to have a higher impact on the surgical decision than all factors had in general. These factors were: the results of image diagnostics (90%); tenderness in the right fossa (76%); and pain migration (50%).

Factors in China with a significantly higher value than 44% were factors that, when reported, were considered to have a higher impact on the surgical decision than

all factors had in general. These factors were: tenderness in the right fossa (83%); and pain in the right fossa (80%). Results of image diagnostics were close to significant ($p=0.06$) with a great impact in 54% of the times they were reported. Elevated leucocyte count had a great impact in 51% of the times it was reported though not statistically significant ($p=0.15$).

3.6 Comparison between Sweden and China

3.6.1 Difference in frequencies

Symptoms, signs, and diagnostic procedures reported at the time of treatment decision are presented in Tables 1 and 2. Factors that differed significantly between China and Sweden were: pain in the right hypochondrium; diffuse onset of pain; pain provoked by movements; indirect tenderness; elevated leucocyte count; and elevated C-reactive protein.

3.6.2 Differences in impact

Symptoms, signs and diagnostic procedures with great impact are presented in Tables 1 and 2. The factors of greatest impact on treatment decision that differed significantly between China and Sweden were: nausea; pain in the right fossa; indirect tenderness; and image diagnostics.

4 Discussion

Although there were some differences in the assessment of patients with suspected appendicitis, the approach towards patients seeking healthcare for symptoms evoking suspicion of appendicitis was similar between the two countries. Pain in the right fossa, tenderness in the right fossa, the use of image diagnostics and laboratory results were the most frequently reported factors in both Sweden and China. This indicates that patients suffering from appendicitis in Sweden and

in China present and are assessed in a fairly similar fashion. Not all factors had the same impact on decision-making, probably due to differences in presenting symptoms. It could also be caused by differences in the surgeon's approach to the patient during clinical investigation; diffuse onset of pain, for example, was described in half of the Swedish patients compared to one in ten of the Chinese.

Differences regarding some of the variables were not large enough to indicate substantial differences in the management of patients with acute abdominal pain between the two countries. Even in the absence of accurate diagnostic evidence and well-defined indications for surgery, the way in which this patient group was gathered conforms enough to support the external validity of data obtained in either of the two countries. The suspicion that local traditions and resources renders experience obtained in China invalid in the Western world was not supported in this study.

Pain in the right hypochondrium, pain provoked by movement, tenderness in the left fossa, and indirect tenderness are factors that are significantly more often reported in Swedish cases than in Chinese. This could mean that these signs and symptoms are less frequent in Chinese patients with suspected appendicitis than in Swedish. Inaccurate translation could also be the cause in some of the cases; diffuse onset of pain, for example, which did not translate as well as other factors in the questionnaire, might have been neglected simply because of misinterpretation. Moreover, the Swedish surgeons generally reported more factors on each questionnaire, than the Chinese. This could imply that surgical examination of a patient with suspected appendicitis in a Swedish hospital focuses more on the abdominal status than it does in a Chinese hospital. To elicit all symptoms and signs associated with appendicitis is safe healthcare practice, but if time is limited, perhaps only the findings considered most

relevant are sought after. According to Arora et al. (12), stress impairs both the technical and the non-technical skills of a surgeon, especially surgeons under training. Since it is often surgeons under training who perform appendectomy, perhaps decision-making in suspected appendicitis is performed more often in a stressful environment, than in many other surgical conditions.

There seems to be difference regarding which laboratory result is paid most attention to in Sweden compared to in China. Elevated leucocyte count was reported more frequently in Chinese patients than in Swedish, and elevated C-reactive protein was reported more frequently in Swedish patients than in Chinese. Both white blood cell count and C-reactive protein are biomarkers for inflammation, sharing a low sensitivity but a fairly high specificity in the diagnosis of acute appendicitis. According to recent studies, both biomarkers are equally as accurate when used in diagnosing acute appendicitis (13,14). The reason for this difference in focus on laboratory results to cannot be explained by this study.

Tenderness in the right fossa was an important factor in treatment decision-making in both Sweden and China. Pain migration, image diagnostics and laboratory results also have a great impact on treatment decision in both countries. There was a significant difference in the impact of image diagnostics on decision-making between Sweden and China. Imaging was performed frequently in both countries, but in Sweden there seems to be a greater tendency to rely on imaging than in China, as the Swedish surgeons reported imaging to have a great impact on their decision in nine out of ten patients, whereas in China, the number was five of ten. The reason for this cannot be explained by this study. The image modality was not defined in the questionnaire and there is thus no information about the difference in impact on treatment decision between computer

tomography and ultrasound. Further evaluation may possibly reveal how the level of experience of the doctor performing the ultrasound affects the impact of the result, since the accuracy of ultrasound is strongly dependent on the skills of the performer (15).

Another factor that had a different impact on the treatment decision between the countries was nausea. Nausea had a great impact on the treatment decision in one out of five patients with suspected appendicitis in China, whereas for the surgeons in Sweden nausea had no great impact in any of the cases. This difference is remarkable bearing in mind that most patients suffering from appendicitis present with nausea in the first hours of the disease. Nevertheless, it is a non-specific symptom that occurs in many other disorders presenting with abdominal pain (1, 16, 17).

Divergences between the two countries may also be explained by access to laparoscopy as a method of diagnosis as well as treatment of acute appendicitis. Laparoscopy has been shown to have numerous advantages in terms of patient safety, accuracy of diagnosis and postoperative recovery. Nevertheless, it is more costly than clinical diagnosis and open appendectomy. Laparoscopic appendectomy has been established as clinical routine in China (18), but differences in the economic systems between Sweden and China may influence the diffusion of the technique.

Our results raised some new questions. If the study had been started at an earlier stage in the management algorithm, we perhaps could have gained further information on what factors that cause surgeons to decide not to operate; a negative radiology result or only slight increases in inflammatory parameters for example. Starting the study earlier in the algorithm may have provided information on how the healthcare system in China, where many patients lack fully covering

health insurance, affects the decision to operate. It would also have been of interest to compare these results with the final outcome of surgery. This could possibly have given further information about differences in indications when dealing with uncomplicated appendicitis, complicated appendicitis (perforation and abscess), and non-specific abdominal pain.

4.1 Conclusions

Our study shows that there are more similarities than differences regarding the impact of symptoms and signs on the decision to operate for appendicitis between Swedish surgeons and their Chinese counterparts. This would suggest that experience reported from China on appendicitis is valid for clinical decision making in Sweden – and probably throughout the Western world. The factors having greatest impact on treatment decision-making differed in some ways between Sweden and China. However, tenderness in the right fossa had a great impact when deciding whether or not to operate in suspected appendicitis in both Sweden and China. Furthermore, the use of image diagnostics and laboratory results were important in both countries as well. However there was a significantly greater tendency to rely on image diagnostics in Sweden. To guarantee the clinical relevance of these statistically significant results, we believe that further investigations would benefit from improved study design and larger study groups.

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References

1. Wagner JM, McKinney WP, Carpenter JL. Does this patient have appendicitis? *JAMA*. 1996;276(19):1589-94.
2. Ansaloni L, Catena F, Coccolini F, Ercolani G, Gazzotti F, Pasqualini E, et al. Surgery versus conservative antibiotic treatment in acute appendicitis: a systematic review and meta-analysis of randomized controlled trials. *Dig Surg*. 2011;28(3):210-21.
3. Andersson RE. Evaluation of the appendicitis inflammatory response score for patients with acute appendicitis. *World J Surg*. 2012;36(7):1546-7.
4. Schiff GD, Hasan O, Kim S, Abrams R, Cosby K, Lambert BL, et al. Diagnostic error in medicine: analysis of 583 physician-reported errors. *Arch Intern Med*. 2009;169(20):1881-7.
5. Schiff GD. Minimizing diagnostic error: the importance of follow-up and feedback. *Am J Med*. 2008;121(5 Suppl):S38-42.
6. Croskerry P, Nimmo GR. Better clinical decision making and reducing diagnostic error. *J R Coll Physicians Edinb*. 2011;41(2):155-62.
7. Diener MK, Wolff RF, von Elm E, Rahbari NN, Mavergames C, Knaebel HP, et al. Can decision making in general surgery be based on evidence? An empirical study of Cochrane Reviews. *Surgery*. 2009;146(3):444-61.
8. Sandell E, Berg M, Sandblom G, Sundman J, Fränneby U, Boström L, Andrén-Sandberg Å. Surgical decision-making in acute appendicitis. *BMC Surg*. 2015 Jun 2;15:69.
9. Andersson RE. The natural history and traditional management of appendicitis revisited: spontaneous resolution and predominance of prehospital perforations imply that a correct diagnosis is more important than an early diagnosis. *World J Surg*. 2007;31(1):86-92.
10. Ellis H. Acute appendicitis. *Br J Hosp Med (Lond)*. 2012;73(3):C46-8.
11. Paulson EK, Kalady MF, Pappas TN. Suspected Appendicitis. *New England Journal of Medicine*. 2003;348(3):236-42.
12. Arora S, Sevdalis N, Nestel D, Woloshynowych M, Darzi A, Kneebone R. The impact of stress on surgical performance: a systematic review of the literature. *Surgery*. 2010;147(3):318-30, 30 e1-6.
13. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg*. 2013;100(3):322-9.
14. Panagiotopoulou IG, Parashar D, Lin R, Antonowicz S, Wells AD, Bajwa FM, et al. The diagnostic value of white cell count, C-reactive protein and bilirubin in acute appendicitis and its complications. *Ann R Coll Surg Engl*. 2013;95(3):215-21.
15. Doria AS. Optimizing the role of imaging in appendicitis. *Pediatr Radiol*. 2009;39 Suppl 2:S144-8.
16. Petroianu A. Diagnosis of acute appendicitis. *Int J Surg*. 2012;10(3):115-9.
17. Prystowsky JB, Pugh CM, Nagle AP. Current problems in surgery. Appendicitis. *Curr Probl Surg*. 2005;42(10):688-742.
18. Jiang X, Meng HB, Zhou DL, Ding WX, Lu LS. Comparison of clinical outcomes of open, laparoscopic and single port appendicectomies. *Ann R Coll Surg Engl*. 2013 Oct;95(7):468-72.