Conservative Management Of Acute Appendicitis: A Review
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Citation

Abstract
Background: Acute appendicitis still ranks as one of the most common acute surgical emergencies and appendicectomy is still the most common surgical procedure performed worldwide. Over the last century, there has been no significant change in the management of this condition. The aim of this study is to evaluate the available literature in order to determine if the conservative management of acute appendicitis with antibiotics is safe, feasible and cost effective.

Methods: A systematic literature search has enabled a thorough critical appraisal of retrieved studies. Seventeen studies were analyzed to determine rigor, reliability and validity. Results: Analysis of the included studies revealed a preponderance of support for the safety and feasibility of conservative management of acute appendicitis. However, there is paucity of evidence to bolster the conservative approach in terms of cost effectiveness. There was also conflicting evidence on the role of interval appendicectomy after conservative management. Presence of calcified appendicolith on CT or USS was regarded as a negative predictive factor for recurrence.

Conclusion: It can be concluded that the conservative management of acute appendicitis is a feasible and safe treatment modality. Recurrent appendicitis is a potential drawback, but good patient selection can help overcome this. The risk of missing serious pathology is minimal but further studies are needed for a reasoned judgment on cost effectiveness to be made.

INTRODUCTION
Despite the major changes and advances in surgical practice over the last century, acute appendicitis still ranks as one of the most common acute surgical emergencies and appendicectomy is still the most common surgical procedure performed worldwide. In the year 2008-2009, more than 44,000 cases were treated in the UK National Health Service (NHS), with more than 95% presenting as emergencies. The male to female ratio stands at 1.3:1 and more than 75% of cases were within the age range of 15-74. In the US, the individual lifetime risk stands at 8.6% for males and 6.7% for females and that of appendicectomy is 12% and 23.1% respectively. More than 300,000 appendicectomies are performed in the US yearly. The incidence of this condition is lowest in societies with a high dietary fiber intake, but in developing countries that are adopting a more refined western-type diet; the incidence continues to rise. There has been a dramatic reduction in the incidence of appendicitis in Western countries over the last three decades. Is there a relationship between falling incidence and increased use of antibiotics?

The pathogenesis of acute appendicitis involves a degree of intra-abdominal sepsis either with the opportunistic invasion of the appendiceal wall by normal intestinal flora during the initial stages or when it becomes perforated at the latter stages. The advent of antibiotics therefore revolutionized the management of appendicitis with a drastic reduction in the mortality and postoperative morbidity of patients. It is therefore right to revise the management of acute appendicitis in order to consider if use of antibiotics as a first-line treatment is feasible, safe and cost effective. The recent economic downturn and the continued squeeze on health budgets despite rising patients’ expectation for high treatment standard bring this issue into sharper focus.

Conservative treatment remains the first-line management of conditions such as acute diverticulitis, neonatal enterocolitis and salpingitis; it therefore becomes imperative to explore the possibility of extending this modality of management to acute appendicitis.

The purpose of this review is to systematically appraise the available literature in order to examine the evidence base for conservative management of appendicitis. It is also to
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ascertain if conservative management of acute appendicitis is feasible, safe and cost effective.

Seventeen studies were analyzed in this review focusing on the conservative management of acute appendicitis. There were three meta-analysis, five randomized controlled studies, five case control studies, three retrospective studies and one non-randomized study. The majority of the studies compared operative management against the conservative approach.

FEASIBILITY

All the studies that compared conservative management with appendicectomy commented on the feasibility of the conservative approach for management of acute appendicitis. The study conducted by Abes et al. focused on the pediatric age group and showed that fifteen out of sixteen patients who had conservative management were treated successfully with antibiotics. Although this is a retrospective case control study and considered a weak study on the hierarchy of evidence, the authors were able to confirm the diagnosis of appendicitis in all patients involved in this study by ultrasonography. This is a measurable and reproducible mode of diagnosis, which therefore gives this study a stronger weight as an evidence to support the feasibility of the conservative mode of treatment. It will be very unwise, however, to assume that all pediatric patients with acute appendicitis can be treated by non-operative means based on this study, at best it provides an avenue to question current practice.

In contrast, the randomized controlled study conducted by Malik and Bari focused on the adult population. The result of this study showed that all the forty patients in the non-operative group were treated successfully with antibiotics prior to discharge. This study has some methodological flaws such as absence of a randomization technique or stratification and the absence of blinding making the acceptability of the authors’ conclusion suspect regarding the feasibility of the conservative approach. Although ultrasonography was used as a diagnostic tool in 64 (80%) patients, there was no mention of the percentage of this in each group. Although the conclusion of this study is in line with the findings of other research on this topic, its conclusion is lightweight when the methodological failing is put into context.

Another study conducted on adult patients was the randomized controlled trial by Hansson et al. This also focused on the feasibility of the conservative approach in the management of acute appendicitis. This study has a very good methodology and the result showed that 48% (97 of 202) of patients in the non-operative group had successful treatment with antibiotics, although this rose to 90% when the result was analyzed as per protocol. The reason for this was the high crossover rate from the non-operative group to the surgical group which was due to both surgeon and patient’s preference.

Crossover of patients is a running theme through all the studies analyzed in this review, which makes it difficult to accurately determine the efficacy of the conservative approach. The diagnosis of appendicitis in this study was done by use of the traditional means of history, clinical examination and laboratory tests. There was no standardized means of confirming the diagnosis in both groups. This will bring up the argument that some of the patients in the conservative group would have recovered even without antibiotics. This brings to the fore the need for an accurate and widely accepted diagnostic tool for acute appendicitis when conducting a study of this nature.

Ultrasonography and CT scan have been shown to have a high sensitivity and specificity for diagnosing acute appendicitis, and until all studies focusing on the conservative management of acute appendicitis accept this as a veritable tool to confirm diagnosis, there will always be question about the validity of the conclusions.

The meta-analysis conducted by Anderson and Petzold also touched on the feasibility of conservative treatment in the management of acute appendicitis in all age groups. The authors’ conclusion was that conservative treatment was successful in 93% of patients involved in the study. However, the low quality of the studies used in the meta-analysis calls the conclusion into question. There were only three prospective studies out of the sixty-one studies analyzed. Moreover, there was marked heterogeneity in the studies analyzed which makes the combination of the result quite inappropriate. The conclusion of the study is in tandem with other studies analyzed in this review, but the methodological flaw makes it difficult to accept based on the facts from the study.

The meta-analysis conducted by Similis et al. and Varadhan et al. all came to the same conclusion that conservative management of acute appendicitis is a feasible management option. Both of these studies have robust and comprehensive methodology. As with all the studies in this dissertation, a major drawback is the high level of crossover of patients.
Other studies that support the feasibility of the conservative management option include those conducted by Eriksson et al. which showed that all the patients in the conservative group were treated successfully.

It is clear that most of the studies analyzed support the fact that conservative management of acute appendicitis is feasible; however, it will be wrong to assume that all patients with acute appendicitis can be managed by this means. The high level of crossover noted in all the studies is an indicator that there is a significant incidence of failure in this management approach. There is also the fact that most surgeons are still not convinced of the advantage of this treatment approach. Overall, it can be stated that in selected patients, conservative management of acute appendicitis produces similar if not better result than operative treatment.

**SAFETY**

In order to make a recommendation about a new modality of treatment, it is important to assess its safety compared to what was previously obtained. All the studies that compared conservative management with appendicectomy also focused on its safety. The safety of this treatment option was assessed in the studies by comparing its complication rate with that obtained in patients who had appendicectomy. Hansson et al.\(^9\) reported a threefold reduction in the complication rate of patients who were managed conservatively. All the other studies also reported a similar outcome. It is easy to understand the rationale for this, as with the absence of an operative intervention, the common postoperative complications are eliminated.

The main safety issue in the conservative management of acute appendicitis is the delay that occurs in the definitive treatment of those patients who will fail conservative treatment and will subsequently require surgical intervention. The question that needs asking is if the benefits derived from conservative management are worth the risk of a potential generalized peritonitis with its attendant postoperative morbidity and mortality. It can be argued that management of acute diverticulitis follows the same pattern of initial conservative treatment with surgical intervention indicated if the symptoms become refractory to treatment or progress. Most of the studies reviewed in this study showed that the majority of patients could be managed conservatively without subsequent adverse event for the initial 24 hours post presentation.

Ditillo et al. conducted a retrospective review of 1081 adult patients who had appendicectomy to determine if it is safe to delay appendicectomy and concluded that the risk of developing advanced pathology and postoperative complications increases with time; therefore, delayed appendicectomy is unsafe. In contrast, the study conducted by Abou-Nukta et al. to determine whether delaying appendicectomy for 12 hours to avoid disturbing the operating room schedule and to minimize the number of operations during the night negatively affects the outcome of patients with acute appendicitis concluded that in selected patients, delaying appendectomies for acute appendicitis for 12 to 24 hours after presentation does not significantly increase the rate of perforations, operative time, or length of stay.

It is apparent from these two studies that appendicitis does progress with time, but there are patients in which a 12 to 24 hours delay will not cause any increased morbidity. Anecdotal evidence from local practice shows that the majority of patients presenting with acute appendicitis can have a delay of 12 to 24 hours before having surgery without any adverse outcome. It can therefore be deduced that patients presenting with acute appendicitis without evidence of generalized peritonitis can be safely managed conservatively with antibiotics for the first 12 to 24 hours.

**COST EFFECTIVENESS**

The cost effectiveness analysis of any new intervention can help inform policy makers on better ways of allocating limited resources. The most commonly used outcome measure for cost effectiveness is the quality adjusted life years (QALY). With the recent economic downturn and government cuts in public sector spending, it has become even more imperative to determine if a new intervention is cost effective and if it can replace or complement a present treatment modality.

Acute appendicitis is a common clinical condition that cuts across all age spectrums in society. Its present treatment involves hospital admission, use of theatre space and time, expertise of surgical practitioners and care of nursing staff. In a study conducted in the United States by Merhoff et al., it was stated that the median cost for a laparoscopic appendicectomy was $2,915 while that for open appendicectomy was $1,747. The most significant cost was the operating room time. The opportunity cost in theatres is estimated to be £15 a minute per theatre per session in the NHS.

It is therefore important to determine if the conservative management of acute appendicitis is able to reduce the cost of managing this condition. Only one study analyzed in this
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review focused on the cost effectiveness of the conservative treatment option. The study conducted by Turhan et al. to assess the cost effectiveness of non-operative treatment of acute appendicitis concluded that conservative management is more cost effective. The study result showed that the average cost of non-operative treatment including all radiological investigations and recurrent admissions was $433 compared to $559 for operative treatment.

This study had methodological flaws and also there was no outcome measure used to calculate the cost effectiveness. The result of the study also did not include the cost to the patient for repeated hospital admissions and time taken off work in both groups. It is therefore difficult to ascertain the cost effectiveness of the conservative treatment option based on this study. Studies that are more robust are needed to answer this particular question.

RECURRENT AND INTERVAL APPENDICECTOMY

A major complication of conservative management of acute appendicitis is the risk of recurrence, which is a major obstacle in convincing surgeons and patients of the benefit of this management option. All the studies that compared conservative management with operative management in this review reported on this complication. The recurrence rate varied between studies from 5% in the study conducted by Liu et al. to 35% in the study done by Eriksson and Granstrom with an average follow-up period of one year. The majority of the patients who developed recurrence were managed operatively but a few were managed conservatively with good result.

Two studies focused on the predictive factors for negative outcomes in nonoperative management of acute appendicitis. The study conducted by Shindoh et al. concluded that elevated C-reactive protein (CRP) levels and presence of calcified appendicolith on ultrasonography or CT scan might predict a negative outcome. There was no cut-off level for CRP given in this study as the majority of patients who present locally with acute appendicitis do have an elevated CRP level. The study by Tsai et al. on this issue concluded that presence of calcified appendicolith and history of appendicitis is a high predictor of recurrence. Although both studies are case control trials, a common outcome for failure of conservative treatment seems to be presence of a calcified appendicolith on imaging.

In a retrospective study conducted by Dixon et al. on the assessment of the severity of recurrent appendicitis, it was argued that patients managed nonoperatively for perforated appendicitis who later developed recurrent appendicitis exhibited a milder clinical course at recurrence. This then brings up the issue of the necessity of interval appendicectomy for patients who had conservative treatment. Kaminski et al. conducted a retrospective review to assess the need for interval appendicectomy for these patients and concluded that there was no need for this intervention. This study has methodological flaws and there was no objective assessment of the diagnosis of appendicitis in the cohort of patients evaluated.

It can be deduced that there is a high level of recurrence following conservative management of acute appendicitis, but the need for interval appendicectomy requires more detailed studies.

RISK OF SERIOUS PATHOLOGY

Managing acute appendicitis conservatively runs the risk of missing other significant pathological conditions of the appendix such as malignant or inflammatory bowel disease. All the studies in this dissertation reported on this issue although it was clear that it forms a very small percentage of appendiceal pathologies. Most of the authors recommended the routine follow-up of patients managed conservatively with colonoscopy, barium studies or virtual colonoscopy, especially in patients older than 40. Burgess and Done conducted a retrospective review of patients who had appendicectomy over a 15 years period to determine the incidence of adenocarcinoma of the appendix. Eleven cases were documented at a rate of 1 in 956 appendicectomy specimens.

It is clear that missing a potentially life-threatening condition while managing appendicitis is quite rare, but when it occurs, it is not in the best interest of the patient or the surgeon.
## Figure 1

Table 1: Summary of appraised studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Aim(s)</th>
<th>Number of patients</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strickland et al. (2017)</td>
<td>Meta-analysis compare outcomes of appendectomy and conservative management</td>
<td>12/7</td>
<td>Conservative management of complicated appendicitis is associated with a decrease in complications and recurrence compared with initial appendectomy.</td>
</tr>
<tr>
<td>Anderson and Phelan (2015)</td>
<td>Meta-analysis outcome of conservative management of complicated appendicitis</td>
<td>81 studies</td>
<td>There is support for the practice of non-surgical treatment without appendectomy in patients with appendiceal abscess or phlegmon.</td>
</tr>
<tr>
<td>Verbalis et al. (2018)</td>
<td>Meta-analysis compare antibiotics therapy versus appendectomy for acute appendicitis</td>
<td>801</td>
<td>Antibiotics are safe and feasible for managing acute appendicitis.</td>
</tr>
<tr>
<td>Eriksson and Gerdhagen (2015)</td>
<td>RCT compare the result of conservative treatment with antibiotics and surgery in patients presenting with acute appendicitis</td>
<td>41</td>
<td>Conservative treatment of appendicitis with antibiotics produced less pain with patients requiring less analgesic treatment with a high recurrence rate.</td>
</tr>
<tr>
<td>Hanson et al. (2009)</td>
<td>RCT evaluate the safety and feasibility of antibiotics for treatment of acute appendicitis</td>
<td>368</td>
<td>Antibiotics treatment is a safe first-line therapy in unresected patients with acute appendicitis.</td>
</tr>
<tr>
<td>Bland et al. (2007)</td>
<td>RCT compare antibiotic therapy with surgery in acute appendicitis</td>
<td>352</td>
<td>Antibiotics can be treated successfully with antibiotics.</td>
</tr>
<tr>
<td>Hall and Sloger (2005)</td>
<td>RCT compare the result of conservative treatment with antibiotics and surgery in patients presenting with acute appendicitis</td>
<td>80</td>
<td>Antibiotics treatment in patients with acute appendicitis is quite effective.</td>
</tr>
<tr>
<td>Liu et al. (2006)</td>
<td>Case-control study measure the experience of conservative management of acute appendicitis in a large public teaching hospital</td>
<td>19</td>
<td>Consensus on the value and efficacy of initial non-operative management for perforated appendicitis is not supported by a recent meta-analysis.</td>
</tr>
<tr>
<td>Henry et al. (2005)</td>
<td>Case-control study compare the result of conservative treatment with antibiotics and surgery in patients presenting with acute appendicitis</td>
<td>313</td>
<td>Lower complication rate and shorter length of stay in patients managed conservatively.</td>
</tr>
<tr>
<td>Cole et al. (2004)</td>
<td>Case-control study evaluate the utility and efficacy of initial non-operative management for perforated appendicitis not complicated by a palpable mass</td>
<td>206</td>
<td>Patients with perforated appendicitis with localized abdominal tenderness and absence of peritoneal signs and effectively treated in an initial non-operative fashion.</td>
</tr>
<tr>
<td>Samuels et al. (2002)</td>
<td>Case-control study compare the result of non-operative treatment of acute appendicitis</td>
<td>82</td>
<td>Early surgical intervention was beneficial cost conservative management in the management of appendiceal mass.</td>
</tr>
<tr>
<td>Abaza et al. (2000)</td>
<td>Case-control study assess the efficacy of non-operative treatment of acute appendicitis</td>
<td>136</td>
<td>Patient presentation less than forty-two hours from onset of symptoms of abdominal tenderness and hemodynamically stable could be treated conservatively.</td>
</tr>
<tr>
<td>Teitelbaum et al. (2000)</td>
<td>Case-control study evaluate operative versus non-operative management of acute appendicitis with regards to safety and cost effectiveness</td>
<td>258</td>
<td>Non-operative management of appendicitis is a good alternative to surgical management in terms of success rate and cost effectiveness.</td>
</tr>
<tr>
<td>Lin et al. (2017)</td>
<td>Cohort study determine if interval appendectomy in patients following conservative management of perforated appendicitis</td>
<td>49</td>
<td>Interval appendectomy provides diagnostic and therapeutic benefit to patients and an individualized approach to each patient following conservative treatment should be adopted.</td>
</tr>
<tr>
<td>Samuels et al. (2008)</td>
<td>Cohort study measure the impact that patients treated non-operatively for acute appendicitis do not require routine interval appendectomy</td>
<td>112</td>
<td>Interval appendectomy after failed non-operative management is not justified and should be abandoned.</td>
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<tr>
<td>Shalaby et al. (2009)</td>
<td>Case-control study identify the factors that may contribute to the negative outcome of initial non-operative management of appendiceal perforation</td>
<td>388</td>
<td>Elevated C-reactive protein level concentration and presence of cultured appendicolitis may predict negative outcomes in nonoperative management of appendicitis.</td>
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<tr>
<td>Tan et al. (2008)</td>
<td>Case-control study assess the predictive factors for recurrence of appendicitis after non-operative management of appendicitis</td>
<td>30</td>
<td>Presence of a positive appendicitis on CT imaging or a history of appendicitis is a high predictor of recurrence of appendicitis.</td>
</tr>
</tbody>
</table>
CONCLUSION

Acute appendicitis is a condition that affects every age group, with no racial or social bias. The management of this condition has not changed significantly over the last century despite the remarkable strides that have been made in disease management. The era of evidence-based medicine has brought to the fore the need to subject the current surgical management of acute appendicitis to scrutiny. It is therefore on this premise that this review was based.

This review was able to critically appraise seventeen studies. All the studies that focused on the feasibility of the conservative approach reported a positive outcome when the crossover of patients was not factored in. It is therefore reasonable to conclude that in well-selected patients, conservative management of acute appendicitis is a feasible modality of management.

Ten studies focused on the safety of the conservative approach. It was discovered that the rate of complication was significantly reduced in the conservative approach when compared to appendicectomy. It can also be deduced that most patients can be managed conservatively for 12-24 hours without adverse outcome, with surgery reserved for refractory cases. The conservative treatment of acute appendicitis can therefore be considered a safe initial alternative to the present operative approach in patients without evidence of generalized peritonitis.

An important marker for the usefulness of any new intervention is its cost effectiveness. Only one of the studies analyzed evaluated this parameter. Due to the poor methodology, it is difficult to accurately assess the cost effectiveness and cost benefit of the nonoperative means of management. It is therefore reasonable to conclude that more high-quality studies are needed to ascertain the cost effectiveness of this treatment modality.

Recurrence of acute appendicitis is a clear drawback for the conservative management of acute appendicitis. It can be as high as 35% in some studies. However, there is evidence to support the fact that recurrent appendicitis tends to run a milder course, and can be managed conservatively during this episode. There is also evidence stating that presence of calcified appendicolith is a predictor of negative outcome for conservative management of acute appendicitis. There is no convincing evidence to support or refute the need for interval appendicectomy.

The conservative approach to managing acute appendicitis makes the possibility of missing a serious pathology such as malignancy and inflammatory bowel disorders quite concerning. However, studies have shown that the risk of this is minimal and the patients can be followed up with outpatient investigations to rule out these conditions.

It can be safely concluded that the conservative management of acute appendicitis is a feasible and safe treatment modality. Recurrent appendicitis is a potential drawback, but good patient selection can help overcome this. The risk of missing serious pathology is minimal but further studies are needed for a reasoned judgment on cost effectiveness to be made.

References

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