What is the main problem in conservative management for complicated appendicitis? A systematic review

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Research article

Keywords: Appendiceal abscess; Complicated appendicitis; Appendectomy; Conservative management

Posted Date: March 23rd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-17722/v1>

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Abstract

Background: As a classification of appendicitis, complicated appendicitis has no standardized treatment for adults.

Method: According to the related literature systematically searched on PubMed, Embase, Cochrane and Web of Science, we evaluated the efficacy of surgical treatment and conservative treatment for complicated appendicitis, especially focused on the outcomes about the length of stay, operation time, postoperative complications and unplanned additional intervention, in the literature.

Result: A total of 14 studies were involved in the meta-analysis, including 845 patients in the immediate operation group (IO) and 756 patients in the conservative management group (CM). Compared with conservative treatment, the total hospitalization time was reduced by 1 day (WMD=-1.29, 95%CI [-2.42, -0.16], $P=0.03<0.05$). The incidence of unplanned additional intervention in patients undergoing emergency surgery is lower than that of conservative treatment (OR=0.18, 95%CI [0.11, 0.30], $P<0.00001$). Surgical patients are more likely to have complications such as wound infection (OR=2.41, 95%CI [1.08, 5.38], $P=0.03<0.05$) and intestinal obstruction (OR=4.14, 95%CI [2.21, 7.75], $P<0.00001$) than conservative patients. The incidence of abdominal abscess was lower than that of conservative treatment, and the difference was not statistically significant (OR=0.9, 95%CI [0.54, 1.47], $P=0.66>0.05$).

Conclusion: Compared with conservative management patients, immediately operated patients have shorter hospitalization time and less unplanned intervention, which can significantly reduce the readmission opportunity of patients with complicated appendicitis and lighten the burden of follow-up and medical resource consumption.

Background

Appendicitis is the most common form of acute abdomen, affecting about 7–8% percent of adults¹. It can be divided into uncomplicated appendicitis and complicated appendicitis, between which complicated appendicitis is often related to the rapid development of acute appendicitis or the improper and untimely treatment², the incidence of which is about 3.8-5.0% of acute appendicitis¹. When the appendix appears to exudate, necrosis and perforation, the inflammatory factors spread into the surrounding tissues of the appendix, causing the retina and the nearby small intestine to form an appendiceal wrapping. After successful formation, an inflammatory mass or localized abscess containing pus, small intestine and retina is formed³.

For uncomplicated appendicitis, a number of studies have shown that conservative treatment with antibiotics and emergency surgery can achieve relatively good results in the adults^{4,5}. But so far, there is still a big controversy on the treatment of complicated appendicitis. Some studies have shown that immediate operation (IO) for complicated appendicitis has the advantages of short hospitalization time and low recurrence rate compared with the early conservative treatment of anti-infection and the interval

surgical resection^{6,7}. At the same time, recently published meta-analyses indicate that the postoperative complications of early surgery were significantly higher than that of conservative surgery^{6,8}.

However, most studies have no research on the short-term recurrence after early treatment and abdominal abscess appendicitis. With the improvement of level of antibiotics and medical technology, laparoscopic and percutaneous puncture drainage has gradually become a new operation for complicated appendicitis, and the treatment of complicated appendicitis has changed^{9,10}, the cure rate and complication of complicated appendicitis has been changed¹¹. The main purpose of this study is to include recent related studies and compare the complicated appendicitis treated by surgical treatment with conservative treatment through meta-analysis.

Methods

1. literature retrieval

By the free word and keywords retrieval, free words ('abscess' or 'phlegmon', 'laparoscopic' or 'open appendicectomy' or 'appendectomy', 'conservative' or 'on-surgical treatment' or 'management'), MESH: 'Appendicitis', the related articles were also listed as search results to broaden the research library. EMBASE, PubMed, Web of Science, Ovid, Cochrane and other databases were used to retrieve relevant studies in the past 20 years from 2000 to present. The obtained literature was summarized and the duplicate literature was removed.

2. Objective research acquisition

Two researchers (Chi Zhang, Xuemeng Ren) independently filtrate the target studies according to the Cochrane Handbook¹² and the unified literature standards. The author, year, research purpose, sample size and relevant effect indexes selected for the study were sorted out respectively. The collected data were reviewed and discussed by the study organizer (Peng Gao), and the controversial documents were selected or excluded by the study organizer.

3. Research selection and exclusion criteria

Only studies comparing surgical methods (laparoscopic or open) and conservative methods (anti-infection or including early drainage and selective appendectomy) could be included in the analysis.

According to NOS¹³ score, for eligible studies, the scores higher than 6 were defined as high-quality studies. For randomized controlled studies, evidence quality was evaluated using the method recommended by Cochrane Handbook¹². The selected study should include the following elements

- Considering the differences in children's development at different ages^{14,15}, only patients with complicated appendicitis over 12 could be selected as the study subjects.

- Outcome indicators should include at least one kind of hospitalization time, postoperative complications or the total number of complications.
- The intervention and control measures should be surgical (laparoscopic or open surgery) and conservative (antibiotics, drainage or no drainage).
- Describe the surgical treatment and conservative treatment of the treatment process and results in details.
- Report the comparative analysis with other studies or similar studies by the same author.
- Randomized controlled study or retrospective study should be including.

exclusion criteria

- The study that does not meet the selection criteria.
- Important outcome data is incomplete, and there is no report on the results of the two treatments.
- The study samples include patients with uncomplicated appendicitis.
- The research cannot obtain the required data for meta-analysis through public channels.
- The study cannot accurately deduce the outcome.

4. Interested ending and definition

The immediate operation group (IO) includes patients with complicated appendicitis who underwent emergency surgical treatment and/or exploration. The conservative management group (CM) included patients with complicated appendicitis who failed early conservative treatment, had emergency surgical treatment after early conservative treatment, had elective surgery after early conservative treatment, and did not undergo surgery at all. The outcomes used to contrast the differences between the immediate appendectomy group and the conservative management group were as follows

- The length of hospital stay includes the first time of hospital stay, the average length of hospital stay, the length of hospital stay after the operation and the total length of hospital stay with the readmission time.
- The length of antibiotics includes the time of intravenous antibiotics in the first hospitalization and the time of intravenous antibiotics after recurrent appendicitis and other complications.
- Overall complications refer to the number of complications caused by complicated appendicitis during the whole (including follow-up period). Wound infection occurs on the surface or deep layer of the skin after the wound is closed, eliminating the formation of an abscess. Abdominal abscess and ileus obstruction were defined during the whole treatment process diagnosis by imaging diagnosis or emergency surgery or interval appendectomy.
- Unplanned additional intervention refers to the unplanned medical intervention (repeated surgery, emergency surgery, puncture drainage, etc.) for recurrent appendicitis, abdominal abscess, etc. that occurs during the treatment and follow-up period.

5. Data analysis and processing

Statistical analysis was performed using the Revman 5.3 software provided by the Cochrane collaboration and the Stata 15.0. For continuous variables, Weighted Mean Difference (WMD) and Standardized Mean Difference (SMD) were used for analysis to calculate the 95% confidence interval. For some continuous variables that were difficult to calculate, the formulas of Cochrane Handbook¹², Hozo¹⁶, Luo¹⁷ and Wan¹⁸ were used for treatment. Using the odds ratio (OR) as the statistic, to analyze the dichotomous variables in the study. OR < 1 was beneficial to IO group. OR value was considered to be statistically significant at the level of $P < 0.05$. χ^2 test was used for the analysis of inter-study heterogeneity, fixed effect model was used for homogeneous study [$P > 0.05$, $I^2 < 50\%$], and random effect model was used for heterogeneous study [$P < 0.05$, $I^2 > 50\%$]. Stata 15.0 was used to analyze publication bias in heterogeneous studies. By the Egger method, $P < 0.1$ was set to analyze the existence of publication bias. The effect of publication bias on the robustness of meta-analysis was evaluated by the metatrim method¹⁹

Result

A total of 148 articles were retrieved and 14 studies were eventually included (see Fig. 1 for the procedure of literature selection), of which 845 patients were treated surgically (group IO) and 756 patients were treated conservatively (group CM). A total of 4 randomized controlled studies (RCT)^{20–23} were included, and 10 retrospective studies (RS)^{24–33} were included. The literature information of major concern is shown in the following table (Table 1).

Tables 1. Characteristics of the Included Studies									
Author;year	Study type	Case			Age (mean $\pm$ SD)		Inclusion criteria ^a	Matching criteria ^b	NOS
		IO	CM	IAA	IO	CM			
Aranda-Narváez, 2010 ²⁴	RS	15	15	15	35.8 $\pm$ 12	35.4 $\pm$ 12	1, 2, 3, 5	1, 2, 6, 10, 11	8
brown, 2003 ²⁵	RS	36	68	25	30.6 $\pm$ 12.3	34.8 $\pm$ 13.5	1, 2, 3, 6	1, 2, 8, 10, 11, 12	7
Deelder, 2014 ²⁶	RS	34	85	nm	41.2 $\pm$ 23.1	45.0 $\pm$ 22.1	1, 2, 3, 6	1, 2, 4, 6, 7, 8, 9, 10, 11, 12	7
Demetrashvili, 2019 ²⁷	RS	27	47	24	32.5 $\pm$ 11.7	35.2 $\pm$ 12.4	1, 2, 3, 5, 6	1, 2, 4, 5, 6, 7, 8, 10, 11, 12	7
khan S, 2016 ²⁰	RCT	150	150	150	26.08 $\pm$ 10.6	25.89 $\pm$ 9.43	1, 2, 5	1, 2, 10, 11	5
kumar, 2004 ²¹	RCT	20	20	20	31.6 $\pm$ 14.6	26.0 $\pm$ 12.4	1, 2, 3, 6	1, 2, 5, 10, 11	6
liu, 2007 ²⁸	RS	104	17	17	37 $\pm$ 10.3	41 $\pm$ 11.2	1, 2, 3, 4, 5	1, 2, 5, 3, 8, 10, 11, 12	7
Mentula, 2015 ²²	RCT	30	30	nm	46.1 $\pm$ 27.1	46.5 $\pm$ 27.2	1, 2, 6	1, 2, 3, 4, 8, 9, 10, 11	7
Motie, 2016 ²⁹	RS	24	49	25	36.0 $\pm$ 15.5	43.2 $\pm$ 19.3	1, 2, 3, 6	1, 2, 8, 10, 11, 12	6
Oliak, 2001 ³⁰	RS	67	88	52	31 $\pm$ 10	35 $\pm$ 15	1, 2, 5, 6	1, 2, 4, 8, 9, 7, 10, 11, 12	8
Pathan, 2018 ²³	RCT	50	50	50	21.5 $\pm$ 11.5		1, 2, 3, 5	1, 2, 3, 8, 10, 11, 12	5
Shekarriz, 2019 ³¹	RS	195	53	41	53.55 $\pm$ 21.8	56.02 $\pm$ 19.65	1, 2, 6	1, 2, 3, 6, 8, 9, 10, 11	8
Watanabe, 2019 ³²	RS	33	49	49	43.8 $\pm$ 19.25	39 $\pm$ 14.75	1, 2, 5, 6	1, 2, 8, 9, 10, 11	7
Young, 2018 ³³	RS	60	35	14	51 $\pm$ 19.6	50.9 $\pm$ 19.4	1, 2, 4, 5, 6	1, 2, 3, 4, 5, 10, 11	8

Tables 1. Characteristics of the Included Studies

a: Inclusion criteria: 1. male& female; 2. adult patients; 3. clinical symptoms; 4. perforated appendix; 5. appendiceal mass; 6. appendiceal abscess;

b: Matching criteria:1. gender; 2. age; 3. BMI; 4. duration of symptoms; 5. operate time; 6. ASA; 7. heart rate; 8.white cell count; 9. CRP; 10. complication; 11. hospital stay; 12.temperature.

IO: immediate operation; CM: conservative management; IAA: interval appendectomy; RS: retrospective study; RCT: randomized controlled trial; NOS: Newcastle-Ottawa scale;Nm: not mentioned

Tables 2. Outcomes of Interest					
Outcomes of Interest (study number)	Number of Studies	Number of patients		Statistical method, 95%C, P value	I ² (%)
		IO	CM		
overall hospital-stay [20–26, 28–33]	13	817	709	WMD=-1.29, 95%CI [-2.42, -0.16], P = 0.03 < 0.05	93
Post operate stay [26, 28, 32, 33]	4	224	125	SMD = 0.66, 95%CI [0.42, 0.91], P < 0.00001	55
Operate time [27, 28, 32, 33]	4	224	104	SMD = 0.26, 95%CI [-0.13, 0.64], P < 0.00001	54
Overall complication [28, 30]	2	171	105	OR = 1.65, 95%CI [0.94, 3.84], P = 0.1 > 0.05	0
Whole complication of post operates [21, 27, 29, 31, 32]	5	298	195	OR = 15.83, 95%CI [8.31, 30.14], P = 0.1 > 0.05	34
Wound infections					
wound infections [20, 21, 23, 24–32]	12	754	625	OR = 2.733, 95%CI [1.243, 6.012], P = 0.01 < 0.05	57
wound infections with percutaneous drainage [25–27, 30]	4	164	222	OR = 2.41, 95%CI [1.08, 5.38], P = 0.03 < 0.05	0
Abdominal abscess [20, 22, 23, 26–32]	10	713	618	OR = 0.9, 95%CI [0.54, 1.47], P = 0.66 > 0.05	38
Bowel obstruction [25, 26, 29–32]	6	388	392	OR = 4.14, 95%CI [2.21, 7.75], P < 0.00001	0
Unplanned additional intervention [21, 22, 24–27, 29, 30, 32, 33]	10	344	501	OR = 0.18, 95%CI [0.11, 0.30], P < 0.00001	22
Other complications					
Intestinal fistula [21, 25, 26, 28, 29]	4	217	239	OR = 2.80, 95%CI [0.75, 10.56], P = 0.13 > 0.05	0
Sepsis [23, 25, 26, 31]	4	315	256	OR = 0.95, 95%CI [0.41, 2.19], P = 0.9 > 0.05	21
Necrosis [23, 25]	2	86	117	OR = 0.15, 95%CI [0.05, 0.51], P = 0.002 < 0.05	0
Thromboembolic [30, 31]	2	262	141	OR = 1.88, 95%CI [0.26, 13.57], P = 0.53 > 0.05	0
Pulmonary [30, 31]	2	262	141	OR = 9.26, 95%CI [1.68, 51.19], P = 0.01 < 0.05	0

1. Overall hospital-stay

A total of 13 studies^{20-26,28-33} reported the overall hospital-stay (Fig. 2. A), Heterogeneity existed in these studies ($P < 0.05$; $I^2 > 50\%$), Egger test $P = 0.951 > 0.1$, with no obvious publication bias. The effective amount of SMD in the random effect model did not change significantly before and after the metatrim method ($SMD_1 = -0.580$, 95%CI [-0.696, -0.465]), ($SMD_2 = -0.735$, 95%CI [-1.338, -0.132]), the results were robust. The aggregate analysis showed that the length of stay of patients treated with surgery was about 1 day less than that of conservative treatment, and the difference was statistically significant ($WMD = -1.29$, 95%CI [-2.42, -0.16], $P = 0.03 < 0.05$).

2. Abdominal Abscess

There were 11 studies^{20,22,23,26-32} reported the occurrence of abdominal abscess (Fig. 2. B), of which Brown²⁵ classified the patients with diffuse peritonitis as abdominal abscess in the study, which did not meet the requirements of this study and was not included in the meta-analysis. The remaining 10 studies showed homogeneity ($P > 0.05$; $I^2 < 50\%$), Combined with the statistical amount OR, the results showed that the incidence of abdominal abscess was lower in surgical treatment than in conservative treatment, but the difference was not statistically significant ($OR = 0.9$, 95%CI [0.54, 1.47], $P = 0.66 > 0.05$).

3. Unplanned Additional Intervention

A total of 10 studies^{21,22,24-27,29,30,32,33} reported the occurrence of unplanned interventions during treatment in each group (Fig. 2. C), including conservative treatment failure, recurrent appendicitis, postoperative intestinal fistula, etc. With no significant heterogeneity among the studies ($P > 0.05$; $I^2 < 50\%$). The results showed that the incidence of unplanned additional interventions in IO was significantly lower than CM, and the difference was statistically significant ($OR = 0.18$, 95%CI [0.11, 0.30], $P < 0.00001$).

4. Wound infection

A total of 12 studies were included in the incision infection (Fig. 3. D), among which there were 3 RCTs^{20,21,23}, and 9 retrospective studies²⁴⁻³². The summarized results showed that patients in the CM group had a lower incidence of incision infection than those in the IO group ($OR = 2.733$, 95%CI [1.243, 6.012], $P = 0.01 < 0.05$). The studies were heterogeneous. ($P < 0.05$, $I^2 > 50\%$). With wound infection as indicators, Egger method was used to indicate the existence of publication bias ($P = 0.001 < 0.1$), and $P = 0.464 > 0.05$ after the use of metatrim method, suggesting the possibility of publication bias and the meta-analysis results of wound infection were not robust. Further analysis showed that in the four studies, percutaneous drainage was performed as required in the CM group (386 participants in the four studies^{25-27,30}). Compared with the IO group, the difference was statistically significant ($OR = 2.41$, 95%CI [1.08, 5.38], $P = 0.03 < 0.05$). No heterogeneity was found among the studies ($P > 0.05$; $I^2 = 0\%$) (Fig. 3.E).

5. Post-operate Stay

Four studies^{26,28,32,33} reported the length of postoperative stay (Fig. 4. F), with inter-study heterogeneity($P < 0.05$; $I^2 > 50\%$), and the Egger method was used to analyze the postoperative hospitalization time, and no significant publication bias was found ($P = 0.859 > 0.1$). Meta-analysis results showed that the postoperative hospitalization time of patients undergoing surgical treatment was longer than that after interval operate, and the difference was statistically significant ($SMD = 0.66$, 95%CI [0.42, 0.91], $P < 0.00001$).

6. Intestinal Obstruction

Six studies^{25,26,29-32} reported the presence of intestinal obstruction in the surgery group and the conservative group (Fig. 4. G), and each study showed homogeneity ($P > 0.05$; $I^2 = 0\%$). The results showed that the incidence of intestinal obstruction was higher in surgical treatment than in conservative treatment ($OR = 4.14$, 95%CI [2.21, 7.75], $P < 0.00001$).

7. Post-operate complication

In the analysis of postoperative complications (Fig. 4. H), there were 5 studies^{21,27,29,31,32} included. No significant heterogeneity was found among the studies ($P > 0.05$, $I^2 < 50\%$). The result showed that compared with conservative treatment, postoperative complications were more common in immediate appendectomy ($OR = 15.83$, 95%ci [8.31, 30.14], $P = 0.1 > 0.05$).

8. Other Outcomes

The analysis results of operate time^{27,28,32,33}, overall complications^{28,30}, intestinal fistula^{21,25,26,28,29}, sepsis^{23,25,26,31}, necrosis^{23,25}, DVT^{30,31}, pulmonary infection^{30,31} are shown in Table 2.

Discussion

We've found that the total time of admission decrease by about 1 day compared with conservative treatment. Despite the high heterogeneity, the outcome of the event was not reversed after the estimation by the metatrim method, indicating the robustness of this meta-analysis. At the same time, the incidence of unplanned additional intervention in patients undergoing emergency surgery is lower than that of conservative treatment, which means that patients undergoing conservative treatment were more likely to have emergency surgery or repeated admission due to failure of conservative treatment, recurrent appendicitis, abdominal abscess, and potential malignancy. This was the same as Mentula's²² conclusion.

However, patients undergoing IO are more prone to complications such as wound infections and intestinal obstructions than conservative management patients. This may be related to the dirtier abdominal environment in the emergency surgery, and the conservative treatment group has a selective drain of the abdominal abscess to improve the environment.

Notably, the meta-analysis of abdominal abscess shows that the incidence of abdominal abscess is lower with surgery than with conservative treatment. Although there is no statistically significant difference between the two, the results indicated that surgical treatment is more effective than conservative treatment in emptying the pus. Unfortunately, due to the lack of rigorous RCT researches, and the variety of patients, it is difficult to accurately determine the merits of surgical versus percutaneous drainage for abdominal abscess.

To date, there is no standard treatment for complicated appendicitis with localized perforation, abscess, or mass formation. In some areas, IO for complicated appendicitis remains the preferred treatment for many surgeons. In recent years, the evidence that conservative treatment is a superior way of the complicated appendicitis has been questioned²⁶. Some patients with conservative treatment finally have worse symptoms and lead to more surgical treatment. Not only that, the patient has to show a response for this anti-infective treatment to continue. These patients with the conservative management failure are eventually excluded from the analysis, this situation may cause data analysis more inclined to non-surgical treatment.

As the follow-up of patients after discharge became more detailed, opponents of the strategy raised some issues caused by conservative treatment, such as recurrent appendicitis, missed potential malignancies, and unconsolidated appendicitis progressing to appendiceal mass. This study clearly explained that conservative treatment caused more additional operations to patients through the summary of studies in recent 20 years. At the same time, through statistical reasoning, this meta-analysis proves that surgical patients have shorter hospital stay.

Longer hospital stays, more antibiotic treatment and more unplanned treatments often result in higher costs for some patients. Recurrent appendicitis and potential tumors often mean multiple imaging and laboratory tests. It not only increases the burden of patients, but also causes a large occupation of medical resources. Repeated admissions also tend to increase the cost of inpatient management. While the complications of emergency surgical treatment of complicated appendicitis often occur at the first admission, and even some minor complications such as wound infection can be treated by lower-level medical institutions. In this respect, surgical treatment of complicated appendicitis is obviously better than conservative treatment.

The results of this study should be interpreted in light of the limitations of the study. Most studies did not report a clear intravenous antibiotic use time, so it cannot to summary the results evaluation. There are differences of low age of children's organ development, therefore biggish differences with anti-infection ability. This study only focuses on people over the age of 12, does not apply to children. Although the heterogeneity of analysis results in some studies is low, it should be noted that the overall clinical status of patients in each group varies considerably. Even if there is statistical equivalence of some key results between the two groups, the utilization of medical resources and perioperative care are inconsistent. Unfortunately, although several studies have demonstrated the effectiveness of laparoscopic surgery in emergency surgical treatment of complicated appendicitis^{34,35}, there is a lack of rigorous RCTS for

laparoscopic versus conservative treatment. Few RCTs were included in this study, and some RCT studies for the outcome and descriptions of the process are not clear. A number of studies demonstrate the effectiveness of the complication of laparoscopy appendectomy²², but some retrospective studies put the main treatment as open appendectomy. We don't have enough RCT experiments compared laparoscopic and conservative management.

Conclusions

Immediately operation patients have shorter hospitalization time and less unplanned intervention than people who are in conservative management. It means that immediately operation can significantly reduce the readmission opportunity of patients with complicated appendicitis and lighten the burden of follow-up and medical resource consumption. In the future, randomized controlled trials involving more laparoscopic surgery versus conservative treatment will be able to better demonstrate the effectiveness of IO and contribute to the establishment of appropriate methods for the treatment of complicated appendicitis.

Abbreviations

IO
immediately operation;
CM
conservative management;
IAA
interval appendectomy;
RS
retrospective study;
RCT
randomized controlled trial
WMD
Weighted Mean Difference
SMD
Standardized Mean Difference

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data in this article are derived from published articles, and the data generated or analysed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests.

Funding

All financial support in this study came from corresponding author sponsorship

Authors' contributions

Each author is responsible for the design of the study, the analysis of the data and the drafting and revision of the article, and ensure that questions related to the accuracy or integrity of any part of the work

The Corresponding authors Peng Gao ensure that all listed authors have approved the manuscript before submission, including the names and order of authors, make it certain that no author on earlier versions have been removed or new authors added, and all data comply with the transparency and reproducibility standards of both the field and journal.

Acknowledgements

Thanks to Lelong Qu and Bailing Zhang for their help on English writing. And Zhenlu Li give the help of data-gathering approach.

Authors' information

The author Chi Zhang is a graduate student of the affiliated hospital of Qingdao university, who is engaged in emergency surgery. He has come into contact with many patients with acute appendicitis in his work, and has great interest in the treatment of acute appendicitis.

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Figures

Figure 1

Figure 1. Study flow diagram

Figure 2

Figure 2: A. Overall hospital stay. B. Abdominal abscess. C. Unplanned additional intervention

Figure 3

Figure 3: D. Wound infection. E. Wound infection in percutaneous drainage patients

Figure 4

Figure 4: F. Post-operative stay, G. Intestinal obstruction. H. Post-operative complication