



Randomised Controlled Trial

Cost analysis of utilising wound edge protector in open appendicectomy to prevent surgical site infection

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ABSTRACT

Background: The rate of surgical site infection (SSI) differ with variable nature with appendicitis with a global incidence of up to 11%. Several randomised trials describe a significant reduction in incisional SSI using wound edge protectors (WEP), mainly in elective procedures. This study was designed to analyse WEP use in emergency open appendicectomy.

Method: This randomised controlled trial enrolled 200 patients who underwent emergency open appendicectomy. Permuted block randomisation was used to assign subjects to either mechanical retraction or double ring WEP. The primary endpoints were SSI rates and cost analysis between the methods.

Results: The incidence of SSI was similar, $n = 7$ (7.4%) in the control group and $n = 8$ (8.4%) in the WEP group, and demonstrates no statistically significant difference ($p > 0.05$). Cost analysis showed a statistically significant ($p < 0.001$) higher total cost in the WEP group, MYR 456.00 (414.75, 520.00) as compared to the control group, MYR 296.00 (296.00, 300.00). However, the median cost of managing patients complicated with SSI was significantly lower at MYR 750.50 (558.75, 946.50) in the WEP group when compared to the control group MYR 1453.00 (1119.00, 2592.00) ($p = 0.008$).

Conclusion: The use of WEP does not reduce the incisional SSI rate, and it is not cost-effective for application in all open appendicectomies. However, when faced with incisional SSI, the use of WEP had a significantly lower cost in incisional SSI management. Selective WEP use is economical in clinically suspected perforated appendicitis when laparoscopic appendicectomy approach is unsuitable.

1. Background

Appendicitis is among the most common abdominal surgical emergencies. The rate of surgical site infection (SSI) differ with variable nature with appendicitis. The global incidence of surgical site infection after open appendicectomy may be as high as 11% [1]. The higher rate of SSI is usually associated with perforated appendicitis. SSI is a severe complication with a devastating impact on patient outcomes. It is associated with high healthcare financial burden, prolonged hospital stay and psychological implications to patients. Reports have shown that SSI may extend hospital length of stay by up to 3–8 days and increase care costs by 2000 USD [2].

Several randomised trials and meta-analyses comparing WEP use

with conventional mechanical retractor have provided favourable outcomes in reducing SSI incidence. However, a majority of these studies focused mainly on elective, non-trauma related gastrointestinal and hepatobiliary surgeries [3–7].

To date, four small randomised trials challenged wound protector use in emergency open appendicectomy that has shown a favourable outcome in reducing SSI [8–11]. However, a systemic review of these studies was critical of the results. They were considered low-quality studies lacking standardisation, with small sample size and uncontrolled publication biases [12].

Our study aimed to compare the incidence of surgical site infection between using wound edge protector (WEP) with mechanical retraction in cases of emergency open appendicectomies. Cost analysis was also

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performed to compare the cost of anti-microbial therapy, length of hospital stay, wound care for managing post-operative complications and investigation cost.

2. Material and methods

2.1. Study population and location

We conducted a prospective single centre, randomised control trial to compare surgical site infection rates and cost analysis between WEP and conventional groups. All patients diagnosed with appendicitis requiring emergency open appendicectomy who fit the eligibility criteria were included in the study. Consent was sought once planned for surgery. This study was conducted at Sultanah Aminah General Hospital, Johor Bahru, Malaysia, till 200 required subjects were recruited (Fig. 1).

2.2. Eligibility criteria

Inclusion criteria were patients aged 12 and above with clinical signs of appendicitis and raised inflammatory markers scheduled for open appendicectomy via a Lanz incision. Patients with peritoneal pathology requiring additional procedures other than appendicectomy, conversion from laparoscopy surgery and conversion to midline laparotomy were excluded from the study.

2.3. Randomisation and blinding

Subjects were randomised to either the control arm (conventional wound retraction) or the study arm (wound edge protector). Randomisation is performed using permuted block randomisation. The grouping was revealed in the operation theatre upon induction. The patients and outcome assessor were blinded by the wound retraction method used.

2.4. Interventions

Subjects in both groups received intravenous 1.2 g Augmentin (1 g amoxicillin/200 mg clavulanic acid) before surgical incision, a standardised skin preparation using povidone-iodine and wound irrigation with saline before primary closure. In the control arm, conventional wound protection with gauze was carried out, and a mechanical retractor (Farabeuf or Langenbeck retractor) is used for wound retraction. In contrast, in the study arm, a double ring wound edge protector (WEP) is inserted upon breaching the peritoneum.

All subjects with complicated appendicitis received additional doses of intravenous Augmentin until they remained afebrile for 24 h. Similarly, perforated appendicitis subjects received oral Augmentin 625 mg twice a day for a total of seven days.

2.5. Follow-up

A follow-up assessment was performed via phone call on post-op day 14 and outpatient surgical clinic visit on post-op day 30. A medical officer and a wound care nurse who is blinded to the study intervention

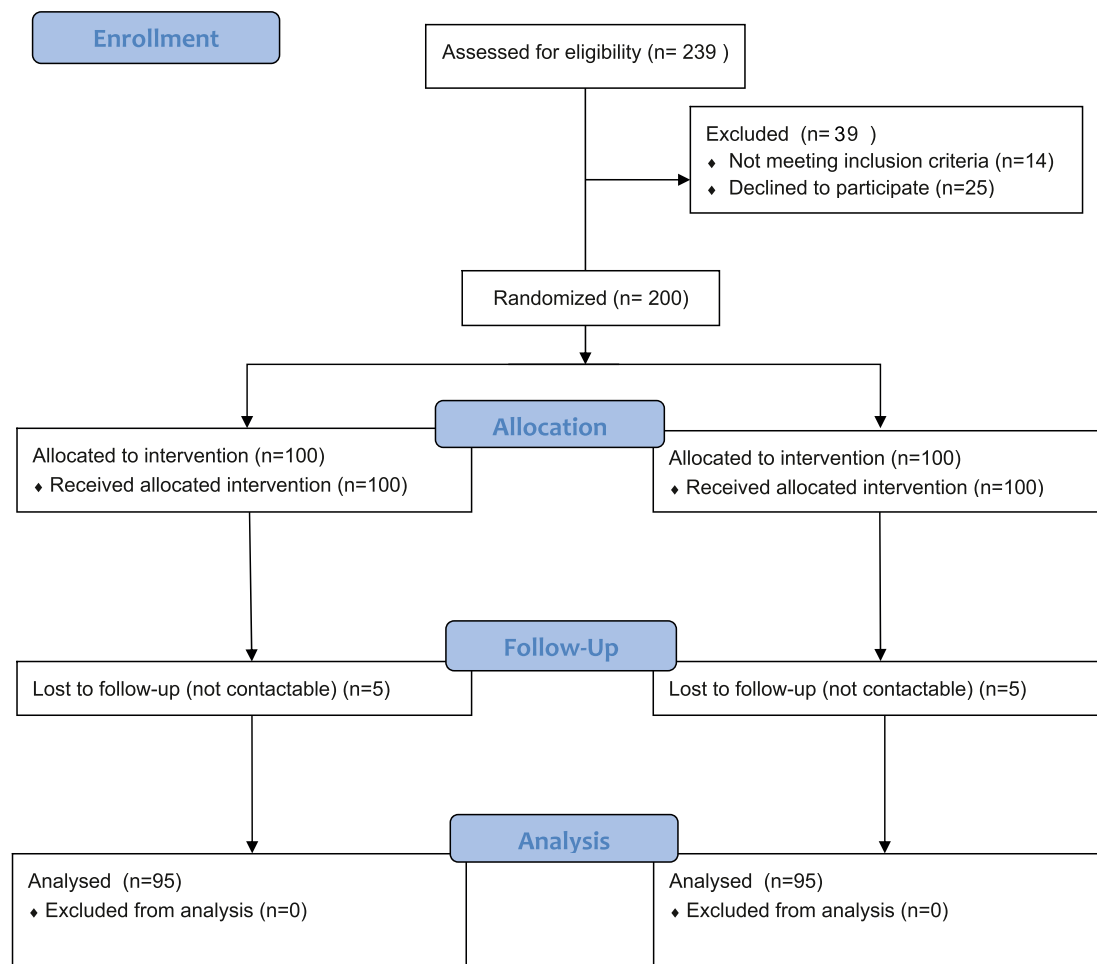


Fig. 1. CONSORT 2010 flow diagram.

performed a wound assessment. If present, the surgical site infection classification was based on the Centres for Disease Control and Prevention (CDC) guidelines. Subjects were also discharged with information and follow up sheet, which was to be produced if they sought additional treatment at any local healthcare facility to ensure complete record keeping.

2.6. Sample size

A study of independent cases and controls with one control(s) per case was planned. Sample size calculation was performed using Data Power & sample size calculation Version 3.0.43 Dupont WD 1990. This was based on a randomised control trial by Pamela Lee et al., in 2009, where SSI incidence following an open appendicectomy using conventional mechanical retraction was 14.6%, whereas wound edge protector was 1.6%.

The study required 91 subjects in each arm to reject the null hypothesis (90% power). The Type I error probability associated with this test is 0.05. We used an uncorrected chi-squared statistic to evaluate the null hypothesis. With an estimated 10% dropout, the sample size for each arm was 100, with 200 subjects required.

2.7. Ethical approval

This study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice Guideline. This study protocol and consent were approved by the Malaysian Research Ethics Committee, National Medical Research Register (NMRR-15-1152-24206) and institutional ethics committee (The National University of Malaysia's Ethics Committee) (FF 2015-168). This study is registered with the Chinese Clinical Trial Registry (ChiCTR2100046575).

The work has been reported in line with the CONSORT criteria.

2.8. Statistical analysis

Subjects' names were kept on a password-protected database and linked only with a study identification number for this research. The study identification number instead of patient identifiers were used on subject datasheets. Descriptive and statistical analysis was then performed on the data retrieved from the proforma using SPSS version 25. Kolmogorov-Smirnov test was used to assess the normality distribution of the continuous variables. If the test is significant (p-value less than 0.05), the distribution is non-normal and vice-versa. Normally distributed continuous variables were presented as mean + (standard deviation) and compared using an independent t-test with a significant p-value at less than 0.05. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test with a significant p-value at less than 0.05. No regression analysis, confounding adjustment or appendicitis severity stratification analysis performed for this study.

3. Results

3.1. Characteristic of study cohort

Overall, 200 patients were enrolled in this study with equal distribution to each group. The mean ages were 26 and 27-years-old respectively, for the control and WEP groups. There were no significant differences concerning socio-demographic and co-morbidities characteristics. (Table 1). A 5% dropout was observed as these subjects were uncontactable during follow up.

3.2. Surgical characteristic

Of the 200 open appendicectomies performed, 114 (57%) were acute

Table 1
Socio-demographic and Co-morbidities characteristic.

Characteristics	Control n (%)	WEP n (%)	p-value
^a Age (years), mean ± s.d.	26.35 ± 10.38	27.25 ± 10.19	0.545
^b Gender			0.110
Male	54 (56.8)	43 (45.3)	
Female	41 (43.2)	52 (54.7)	
^b Ethnicity			0.777
Malay	55 (57.9)	55 (57.9)	
Chinese	12 (12.6)	8 (8.4)	
Indian	9 (9.5)	11 (11.6)	
Others	19 (20.0)	21 (22.1)	
^a Height (m), mean ± s.d.	1.63 ± 0.09	1.63 ± 0.08	0.544
^a Weight (kg), mean ± s.d.	61.75 ± 15.05	60.90 ± 11.69	0.660
aBody Mass Index (kg/m ²), mean ± s.d.	23.21 + 5.02	22.92 + 3.90	0.487
^b Diabetes Mellitus			0.613
Yes	1 (1.1)	3 (3.2)	
No	94 (98.9)	92 (96.8)	
^b Smoking			0.180
Yes	20 (21.1)	13 (13.7)	
No	75 (78.9)	82 (86.3)	
^b Immunosuppressive			0.477
Yes	2 (2.1)	0 (0.0)	
No	93 (97.9)	95 (100.0)	

* Significant if p-value <0.05.

^a Independent t-test.

^b Chi-square test.

appendicitis, and 77 (38.5%) were found to have a perforated appendix. There were a total of 9 (4.5%) cases of a normal appendix on histopathology. There was no significant difference in the severity of appendicitis between the study arms (Table 2). Duration of surgery was significantly faster with the use of a wound edge protector group. The dropouts in each group consisted of one normal appendix, three acute appendicitis and one perforated appendix each.

3.3. Outcome characteristics

The overall outcome was similar in the two groups with a similar length of stay and days of medical leave, as indicated in Table 3.

There was no significant difference in the rate of SSI among the groups. There was only one readmission from each group due to SSI. One subject in the WEP group developed a case of severe organ space SSI. This resulted in an additional 13 days of hospital stay, laparoscopic pelvic drainage, and a prolonged course of anti-microbial therapy which significantly added to the overall cost incurred by the WEP group that developed a complication.

3.4. Cost analysis

Cost analysis was considered based on the duration of anti-microbial

Table 2
Surgical characteristics.

Characteristics	Control n (%)	WEP n (%)	p-value
 ^{a <td>50.17 ± 31.55</td> <td>41.31 ± 21.50</td> <td>0.025*</td>}	50.17 ± 31.55	41.31 ± 21.50	0.025*
^b Findings			0.821
Normal	3 (3.2)	4 (4.2)	
Acute	56 (58.9)	52 (54.7)	
Perforated	36 (37.9)	39 (41.1)	

* Significant if p-value <0.05.

^a Independent t-test.

^b Chi-square test.

Table 3
Outcome characteristics.

Outcome	Control n (%)	WEP n (%)	p-value
 ^a Length of stay (days), mean ± s.d.	3.73 ± 2.14	3.89 ± 1.63	0.627
 ^a Medical Leave (days), mean ± s.d.	11.04 ± 6.16	10.10 ± 7.27	0.276
 ^b Readmission			
Yes	1 (1.1)	1 (1.1)	>0.99
No	94 (98.9)	94 (98.9)	
 ^a Duration of antibiotics (minutes), mean ± s.d.	5.18 ± 4.12	5.95 ± 6.11	0.313
 ^b Surgical Site Infection (SSI)			
Yes	7 (7.4)	8 (8.4)	0.788
No	88 (92.6)	87 (91.6)	
 ^b SSI based on findings (n = 15)			
Normal	0 (0.0)	0 (0.0)	0.832
Acute	3 (42.9)	3 (37.5)	
Perforated	4 (57.1)	5 (62.5)	

* Significant if p-value <0.05.

^a Independent t-test.

^b Chi-square test.

therapy, haematological, imaging investigations, length of hospital admission, wound care management cost and procedures performed. The average currency exchange rate of 4.04 Malaysian Ringgit (MYR) to 1 USD was used for cost calculations. Overall cost analysis showed a significantly higher total cost when WEP was used, Malaysian Ringgit MYR 456.00 (414.75, 520.00) compared to using mechanical retraction, MYR 296.00 (296.00, 300.00). This is likely due to the price of the single-use WEP device, which cost MYR 160.00 for each subject. Median total cost subgroup analysis of patients who suffered incisional SSI was statistically significant (p = 0.008) at MYR 1453.00 (1119.00, 2592.00) vs MYR 750.50 (558.75, 946.50) in the control group and WEP group, respectively. This is mainly due to additional costs with laboratory investigation and dressing costs required to manage SSI in the control group, reflective of the severity of the wound (Table 4).

4. Discussion

The incidence of surgical site infection following open appendicectomy is shown to be up to 11% [1]. Although the gold standard operative

Table 4
Cost analysis.

Items	Control MYR	WEP MYR	p-value
	Median (IQR)		
Overall			
Antibiotics	55.00 (22.00,77.00)	55.00 (33.00,77.00)	0.327
Hospital Stay	9.00 (9.00,15.00)	12.00 (9.00,15.00)	0.190
Lab investigation	160.00 (160.00,240.00)	200.00 (160.00,240.00)	0.687
Dressing	600.00 (600.00,1200.00)	120.00 (120.00,160.00)	0.001*
Total	296.00 (296.00,360.00)	456.00 (414.75,520.00)	<0.001*
SSI complicated			
Antibiotics	198.00 (104.00,252.00)	104.50 (79.75,147.00)	0.082
Hospital Stay	15.00 (6.00,24.00)	13.50 (9.75,20.25)	0.907
Lab investigation	540.00 (460.00,1120.00)	280.00 (125.00,465.00)	0.027*
Dressing	600.00 (450.00,1200.00)	120.00 (120.00,160.00)	0.001*
Total	1453.00 (1119.00,2592.00)	750.50 (558.75,946.50)	0.008*

Mann-Whitney U test. MYR Malaysian Ringgit.

* Significant if p-value <0.05.

intervention for appendicitis is laparoscopic, conversion to open appendicectomy is common in perforated appendicitis, indirectly reflecting the increased incidence of SSI. Surgical site infection is associated with a high healthcare burden and psychological impact on the patient. In elective surgery, measures are taken to reduce surgical site infection by optimising modifiable risk factors. However, some elements may not be controlled in emergency surgeries. The limitation of time to surgery from diagnosis in emergencies may also hamper the preparation of an ideal surgical patient. In cases of appendicitis, a higher rate of SSI observed in subjects with perforated appendicitis. Developing a more effective and reproducible primary prevention strategy for superficial SSI among patients undergoing a contaminated or dirty abdominal operation is arguably a logical step towards reducing SSI risk.

The wound edge protector (WEP) was developed based on the concept of combining a non-traumatic surgical wound retractor with a protective membrane covering the incisional margin in abdominal surgeries. A WEP is believed to limit intraoperative contamination of enteric bacteria while concomitantly preserving the temperature and humidity of the surgical wound [3,4].

The use of wound edge protectors to reduce SSI have shown mixed results in the available published data. Although several randomised trials and meta-analyses conclude favourable outcomes in reducing SSI incidence using WEP, others have shown no improvement, especially in dirty abdominal surgeries. Moreover, many of these trials are performed among elective non-trauma related gastrointestinal and hepatobiliary surgery [3–7]. Multicentre United Kingdom ROSSINI trial involving a range of elective and emergency laparotomy reported wound edge protector use does not reduce the rate of SSI [13]. We found several studies that reported the benefit of WEP to reduce SSI during appendicectomies; however, a systemic review of these studies highlights a moderate to high risk of overall publication bias [12]. In short, it can be summarised that the benefit of using WEP to reduce SSI is based on low-quality evidence at best.

This study was performed at a public healthcare facility in Malaysia with no similar regional data. We used a prospective study design with non-biased randomisation, complied strictly with CDC’s SSI criteria, had a uniform distribution of cases and ensured that the personnel performing the follow-up assessment was blinded to add strength to our study.

We found that our study population’s ideal range of key modifiable risk factors doesn’t affect the SSI risk. Although our data demonstrated no significant differences in incisional SSI even with WEP, there was a considerable reduction in operative time in the WEP group. This is likely due to the uniform distribution of tissue provided by the device and improved exposure being the common feedback among surgeons. The severity of complications among both groups was also similar.

Cost analysis demonstrates non-effectiveness when WEP used in all cases of open appendicectomies. This was expected as the WEP was single-use that resulted in the additional cost to the patient. Moreover, the cost of the other factors assessed was similar in both groups that were homogenous in terms of post-operative outcome. However, a subgroup analysis revealed that the WEP group’s overall cost of managing incisional SSI cases following open appendicectomy is less. We postulate the benefit of WEP in reducing the degree of contamination hence reducing the need for extensive dressing for SSI in the WEP group. Mechanical retraction may also contribute to tissue injury from overzealous retraction.

We observed that our present study has several limitations. Firstly, this study was a single centre with a small sample size of events involving perforated appendix. Normal appendix removed during appendicectomy is included as part of the analysis. We would have preferred to have observed the effect of WEP in more complicated cases of appendicitis involving dirty wounds. As for the cost consideration, most costs have been subsidised by the public healthcare system. Therefore, if the actual fee was applied, a broader gap in cost-effectiveness between the study group could be observed.

5. Conclusion

The use of WEP does not reduce the incisional SSI rate, and it is not cost-effective for application in all open appendectomies. However, when faced with incisional SSI, the use of WEP had a significantly lower cost in incisional SSI management. Selective WEP use is economical in clinically suspected perforated appendicitis when laparoscopic appendectomy approach is unsuitable.

Provenance and peer review

Not commissioned, externally peer reviewed.

Funding

This research is funded by The National University of Malaysia for the purchase of wound edge protectors.

Consent to participate

Patient and next of kin participation is entirely voluntary for this study, and written consent was obtained from all patients before surgery.

Ethical approval

This study protocol and consent were approved by the Malaysian Research Ethics Committee, National Medical Research Register (NMRR-15-1152-24206) and institutional ethics committee (The National University of Malaysia's Ethics Committee) (FF 2015–168).

This study is registered with the Chinese Clinical Trial Registry (ChiCTR2100046575).

Contributors

JM involved in clinical care, data collection, conceptualisation and drafting of the manuscript. VM was involved in data collection and clinical care. AA provided conceptualisation, revision of the manuscript and integral in publishing this manuscript. RIA, ZZ and RJ transform ideas to practical application, constructive feedback and correction of the manuscript. All the authors read and approved the final manuscript. SO was involved in data entry and statistical analysis.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request

Registration of Research Studies

Name of the registry: Chinese Clinical Trial Registry
 Unique Identifying number or registration ID: ChiCTR2100046575
 Hyperlink to your specific registration (must be publicly accessible and will be checked): <http://www.chictr.org.cn/listbycreator.aspx>

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Declaration of competing interest

This research is funded by The National University of Malaysia for purchase of wound edge protector. On behalf of all authors, the corresponding author states that there is no conflict of interest. This study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guideline. This study protocol and consent were approved by the Malaysian Research Ethics Committee, National Medical Research Register (NMRR-15-1152-24206) and institutional ethics committee (FF 2015–168). Patient and next of kin participation is entirely voluntary and written consent was obtained from all patient prior to surgery.

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