

Comparative Study of Wound Complications following Laparotomy for Typhoid Intestinal Perforation: Primary versus Delayed Primary Closure? A Prospective Randomized trial.

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Abstract

Background

The optimal closure method, for dirty abdominal incisions, that will reduce wound complications remains controversial. The aim of this study is to compare wound complications after primary closure and delayed primary closure of laparotomy incisions following typhoid intestinal perforation (TIP).

Methods: One hundred and twelve patients with dirty abdominal wounds following laparotomy for TIP were included. They were randomized into one of the two methods of wound management viz: primary closure (PC) group and delayed primary closure (DPC) group. Patients in the PC group have their surgical incisions (skin and subcutaneous layers) closed immediately while in the DPC group, the incisions were left open (packed with saline soaked gauze) and were evaluated on postoperative day 4 for closure if pristine or for wound dressing if not appropriate for closure. Wounds were considered infected if serous or purulent discharge developed and this would necessitate taking a wound swab for microscopy, culture and sensitivity (MCS). All patients were followed up for one month after surgery. The main outcome measures were the rates of surgical site infection, wound dehiscence and the length of hospital stay (LOS).

Results: In the entire series, surgical site infection developed in 55.4 % of patients after closure of incisions. The primary closure group had a significantly higher incidence of SSI (73.2% vs. 37.5%, $p = 0.000$). There were also significantly more cases of wound dehiscence in the PC group (14.3% vs. 3.6%, $p = 0.020$) and significantly longer LOS (12.6 + 5.7 (SD) days vs. 10.1 + 3.7 (SD) days, $p = 0.006$). The overall short-term cosmetic results for DPC scars were also superior to those for PC ($p = 0.425$).

Conclusion: Delayed primary closure is the optimal incision management technique that should be utilized for laparotomy incisions following TIP. It significantly lowers the rate of superficial surgical site infection and wound dehiscence, as well as reducing the mean LOS. There was no significant difference in the short-term cosmetic appearance of the scars between the two groups.

Key words: Typhoid intestinal perforation; Wound closure methods, Wound complications

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I. Introduction

In many developing countries, typhoid fever; a febrile illness primarily caused by *Salmonella typhi*, is still a disease of enormous public health concern, even though it is almost eliminated in many developed countries.^{1,2} Typhoid fever is generally transmitted by faeco-oral route and may occasionally occur as an epidemic, particularly in areas with poor waste disposal system, and limited availability of clean drinking water.^{1,2} Involvement of Peyer's patches in the ileum leads to necrosis and ulceration, which in turn may lead to the two common complications, bleeding and perforation. Classically, perforation occurs in the third week of illness with escalation of morbidity and mortality rates.^{3,4} It has been estimated that 22 million cases of typhoid fever and 216 000 deaths occur annually worldwide.^{1,5} In Africa, population based incidence of typhoid fever is reported to range from 13 to 845 cases per 100000 population annually.¹

Typhoid intestinal perforation is the most serious surgical complication of typhoid enteritis and it is common in most developing countries.^{6,7} Unlike other perforations, the omentum does not migrate to wall off the

perforation site.^{8,9} The morbidity and mortality rates of TIP have remained in double digits in developing countries in the last quarter of the century and many patients succumb to complications such as sepsis and multiple organ failure.^{3,6} Conversely, developed countries have observed a decline in mortality to less than 5%, due mainly to timely surgery and appropriate pre- and post-operative intensive care.^{8,10} This disease affects mostly young adults who contribute enormously to the economy of their countries. It is most common in people in the low socio-economic strata.⁶

With high index of suspicion, the diagnosis of TIP could be made with a high level of accuracy based on clinical features and basic investigations.⁶ Management is anchored on adequate resuscitation with intravenous fluids, administration of appropriate broad spectrum antibiotics, correction of electrolyte derangement and correction of anaemia.³ At present, laparotomy is the preferred modality of treatment with simple closure of perforation or bowel resection and anastomosis in case of multiple adjacent perforations or unhealthy ileum, after which copious peritoneal lavage is done to reduce peritoneal cavity contamination.³ Postoperative wound complications such as surgical site infection (SSI), wound dehiscence, incisional hernia, chronic painful disfiguring scars are common. The wound complications with attendant long-term physical and psychological effects on patients have significant impact on scarce healthcare resources, with increased length of hospital stay thereby decreasing availability of hospital beds and imposing additional expenses.^{3,6,11}

Surgical wound care is aimed at wound healing without complications, but dirty laparotomy wounds, resulting from TIP, are associated with high risk of wound complications.^{11,12} The method of wound closure has been known to influence the occurrence of SSI and other wound complications.^{11,12} Two options exist for closure of dirty abdominal wounds; Primary wound closure (PC) and Delayed-primary wound closure (DPC).¹³⁻¹⁸ However, opinions on the optimal method of closure of dirty wounds differ.¹³⁻¹⁸

We thus conducted a prospective randomized study with the aim of comparing the incidence of wound complications between PC and DPC of laparotomy incisions, in patients with TIP.

II. Methodology

This study was a prospective randomized study involving patients with clinical and operative diagnoses of generalized peritonitis secondary to typhoid intestinal perforation, who presented between June, 2009 and June, 2016. The study was conducted at the Ladoko Akintola University of Technology Teaching Hospital (LTH), Osogbo, and Wesley Guild Hospital, Ilesha, both are tertiary health institutions in South-Western Nigeria. This study was ethically approved by Ethics and Research Committee of the institutions and written informed consent was obtained from each patient before being enrolled into the study. In addition to the patients' biodata, we recorded patient-related factors that could have contributed to wound complications: Perforation - operation interval (the estimated period from the time of perforation, heralded by the onset of sudden abdominal pain, to surgery), packed cell volume (PCV), body mass index (BMI), serum protein and albumin, serum electrolyte urea and creatinine, the presence of jaundice and comorbid conditions (diabetes mellitus, malignancy, chronic steroid therapy, chemotherapy and HIV-AIDS). The operation related factors recorded were type of anaesthesia, type and length of incision, intraoperative findings, method of closure of the incision (skin and subcutaneous layer) and duration of surgery. Postoperative complications and length of hospital stay were also recorded. The inclusion criteria were male and female patients who are 16 years or older, with TIP. Exclusion criteria were patients younger than 16years, human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS) patients, diabetes mellitus, obesity, subcutaneous layer thickness of more than 2cm, malignancy, patients on steroids and chemotherapy, failure to give consent as well as death of patient before postoperative day 30. All patients received perioperative intravenous ceftriaxone and metronidazole coverage until resolution of pyrexia. Further antibiotic therapy was based on the response of the patients and results of wound swab microscopy, culture and sensitivity (M/C/S). They all had laparotomy, under general anaesthesia with endotracheal intubation, though a midline infraumbilical incision with or without supraumbilical extension. Simple closure was performed for single or isolated perforations by two suture layers. Sometimes wedge resection with primary closure was performed for large perforations or multiple adjacent perforations and segmental resection and anastomosis was performed in the presence of multiple perforations or unhealthy perforated ileal segment. Peritoneal lavage was done with warm 0.9% saline until clear effluent was obtained. Soft latex silicon coated 20FR 2-way Foley catheter was used as drain placed in the pelvis through a separate incision on the anterior abdominal wall. Mass closure of the peritoneum and linea alba was done with a non-absorbable, monofilament number one nylon sutures. Finally, the wound (skin and subcutaneous tissue) was either closed primarily or left open for delayed primary closure, according to randomization. Wounds were closed in either technique with a non-absorbable monofilament number 2/0 nylon suture material.

Patients in the primary closure (PC) group had their surgical incisions (skin and subcutaneous tissue) closed immediately while in the delayed primary closure (DPC) group, the incisions were left open (packed with 0.9% saline soaked gauze) and were not manipulated until postoperative day (POD) 4 for inspection and closure if pristine or for dressing if not appropriate for closure. However, if SSI was suspected based on local features

like pain accompanied by swelling, redness, serous or purulent discharge from the wound, foul odour of the wound or systemic signs (fever, tachycardia) before POD4, the dressing was removed for wound inspection using sterile technique, wound swab was taken for M/C/S and wound dressing commenced. All patients were followed up till POD 30 for short term scar evaluation using the Stony Brook scar evaluation scale (SBSES)¹⁹. The sample size was estimated to be 48 for each group in comparison using modified Kirkwood

Formula²⁰ and sampling procedure was simple randomization, by alternating technique. Data were recorded on a pre-designed proforma. Data analysis was done using Statistical Package for Social Sciences (SPSS) version-20.

III. Results.

A total of 112 patients with TIP received the allocated intervention, (56 in the PC group and 56 in the DPC group). There were 68 males and 44 females (M: F = 1.5: 1). Their ages ranged from 16 years to 58 years (median = 28years). Both groups of patients were similar in terms of age and gender distributions, mean perforation – operation interval (POI), aetiology of dirty wound and other risk factors for wound complications. There was no significant difference in the duration of symptoms before presentation [PC 3.63 + 1.5 (SD) vs DPC 3.57 + 2.1 (SD), p = 0.856]. (Table 1)

Table 1: Patient demographics and clinical detail.

	PC (n = 56)	DPC (n = 56)	p value
Male / female	33/23	35/21	0.423
Mean Age (Years)	27.68 + 8.6	29.70 + 7.3	0.179
Length of Hospital stay (Days)	12.61+ 5.7	10.07 + 3.7	0.006
Risk factors			
ASA class (II/ III/ IVE)	6/49/1	12 /42/ 2	0.238
BMI (<18/ 18-30)	2/ 54	10/ 46	0.050
Clinically Jaundiced [Yes/ No]	8/48	4/ 52	0.180
Serum Alb (g/dl) [<3/3-5]	16/40	19/ 37	0.342
Mean DOS (Days)	3.63 + 1.5	3.57 + 2.1	0.856
Length of Incision (CM)	17.86 + 3.1	17.93 + 3.2	0.905
Number of Perforations	3.84 + 3.2	2.89 + 1.3	0.045
Duration of Op (Hours) [< 2/ >2]	51/5	56/0	0.028

Data are presented as mean + standard deviation or n (%).

Abbreviations: DPC = delayed primary closure, PC = primary closure, ASA class = American Society of Anaesthesiologists classification, BMI = body mass index, Alb = albumin, DOS – duration of symptoms, Op = operation, CM = centimeters.

Laparotomy was performed in all the patients between < 24 – 48 hours of admission and in all, 111 (99.1%) patients had ileal perforations alone, while 1 (0.9%) patients had perforations in both the ileum and the caecum. Patients with single perforation had the highest frequency and the highest number of perforations in a single patient was twenty-two. About 92% of all perforations were limited to the terminal 55cm of the ileum, majority of them were 0.5cm -1cm in diameter, ovoid or round in shape and typically located on the antimesenteric border of the ileum. The mean volume of peritoneal exudates (seropurulent and faecopurulent) drained was 1324.6mls (range 150 – 3750mls). Of all the perforations 75.9% were treated by simple closure in two layers with Vicryl 2/0 after excising the edges, 14.3% with multiple perforations or unhealthy ileum had ileal resection with ileo-ileal anastomosis, 7.1% of patients had wedge resection with primary closure and 2.7% had limited right hemicolectomy (ileocaecotomy) with ileo-colic anastomosis, because of the proximity of perforations to ileo-caecal junction and caecal perforation. A summary of the operative techniques employed is shown in Table 2.

Table 2: Surgical treatment of perforations

		Site of perforations		Total
		Ileum	Ileum + Caecum	
Surgical procedure	Simple closure	85	0	85
	Wedge resection and anastomosis	8	0	8
	Ileal segment resection and ileo-ileal anastomosis	16	0	16
	Limited right hemicolectomy	2	1	3
Total		110	2	112

In the entire series, surgical site infection occurred in 55.4 % of patients. The primary closure group had a significantly higher incidence of SSI (73.2% vs 37.5%, $p = 0.000$). Of the infected wounds, pathogenic organisms were cultured in about 71% (44/62) and the most common organism cultured was *Streptococcal species* (35.5%). (A summary of bacteria culture results are shown in Table 3)
 There also were significantly more cases of abdominal dehiscence in the PC group (14.3% vs 3.6%, $p = 0.020$) and significantly longer LOS (12.6 + 5.7 (SD) days vs 10.1 + 3.7 (SD) days, $p = 0.006$).

Table 3. Bacteria culture from wound swab (n = 62)

Culture yield	DPC	PC	Frequency	Percentage
No growth	4	14	18	29.0
Escherichia coli	2	1	3	4.8
Streptococcal species	6	16	22	35.5
Pseudomonas aeruginosa	2	3	5	8.1
Staphylococcus aureus	6	0	6	9.7
Polymicrobial	1	7	8	12.9
Total	21	41	62	100.0

Abbreviations: DPC – delayed primary closure, PC – primary closure.

Majority of the infected wounds healed by primary intention after some sutures were removed around the discharging points to allow egress of the wound discharge followed by daily wound dressing. Secondary wound closure was employed only in 9.68% (6/62) patients and all were in the PC group. Three patients (one in PC group and two in DPC group) had fascial dehiscence which later developed into incisional hernia. One patient with SSI in PC group had burst abdomen on POD11 for which he was re-operated.

Other postoperative complications (Table 4) included four cases of residual intra-abdominal abscess (2 in PC and 2 in DPC group) out of which three were re-operated and one resolved spontaneously with antibiotics. There were five cases of postoperative enterocutaneous fistula (2 in PC and 3 in DPC group) out of which one was re-operated and the remaining four cases resolved on non-operative management.

Table 4: Distribution of other postoperative complications

	Wound closure method		Total	Percent
	Primary closure	Delayed primary closure		
Residual Intraabdominal abscess	2	2	4	21.0
Partial wound dehiscence	7	2	9	47.4
Complete wound dehiscence (Burst abdomen)	1	0	1	5.3
Enterocutaneous fistula	2	3	5	26.3
Total	12	7	19	100.0

The mean length of hospital stay was 12.6 + 5.7 (SD) days for patients in PC group and 10.1 + 3.7 (SD) days for DPC group ($p = 0.006$). Overall short term cosmetic appearance of the laparotomy scar at POD30 was optimal in 29 patients in the PC group and 31 patients in the DPC group ($p = 0.425$).

IV. Discussion

Delayed primary closure of dirty incisions, in which approximation of wound margins is done three to five days after operation, has been the accepted practice for centuries.¹⁵ The rationale is that the open wound allows free egress of wound exudates resulting in a decreased risk of bacterial colonization. However, an open surgical incision that is awaiting delayed primary closure is frightening and causes anxiety to patients. This is the reason many surgeons continue to perform primary closure of such wounds.^{11,15}

To our knowledge, in this environment, there is paucity of prospective comparative studies of wound complications following primary closure and delayed primary closure of surgical incisions after laparotomy for typhoid intestinal perforations (TIP). This is also supported by Sandro Contini et al,⁸ where it was reported that Prospective studies about surgical treatment of TIP in LMICs are lacking and should be encouraged in order to provide clear-cut surgical standard and guidelines.

Furthermore, when wound complications are assessed prospectively and accurately following laparotomy for TIP, it is observed to affect more patients than previously thought.^{11,21} Moreover, many components of the bacterial contribution to SSI are now clearly understood and measures to control bacteria are being implemented.^{1,11} The host factors have now become apparent, hence the increasing focus on the patient (the host) for measures that will continue to provide improved results.^{1,11}

Majority of previous studies that have reported incidences of wound complications following laparotomy for TIP were retrospective studies, with only few studies such as study conducted by adesunkanmi et al⁵ and Phillippo et al,²² being of prospective designs. Table 5 summarizes the results of wound complications following laparotomy for TIP in the previous studies. No recent study compared wound complication rates in incisions closed primarily with that of those closed by the delayed primary method. Two previous studies included paediatric patients. Surgical site infection rate was reported in all studies, seven studies reported the rate of wound dehiscence and four studies reported the incidence of burst abdomen.

Our study demonstrates that DPC is the optimal wound closure method after laparotomy for typhoid intestinal perforation because it lowers the incidence of wound complications and shortens the length of hospital stay when compared to PC.

TABLE 5. Results of previous studies of wound complications following laparotomy for TIP.

Authors	Location	Study type	Sample Size(n)	Age (Years)	ICM	Wound Complications (%)
Adesunkanmi et a(1997) ¹³	Ile-Ife/ Nigeria	Pros	24/20	NR	PC/DPC	SSI (70.8/ 70), WD (37.5/35), BA(NR)
Ugwu et al(2005) ⁶	Jos/Nigeria	Retros	101	19 (Mean)	PC	SSI (30.7), WD (18.8), BA (3.9)
Hafiz et al (2006) ²⁵	Multan	Retros	31	15-30 (Range)	PC	SSI (37.5), WD (NR), BA (25)
Usang et al (2009) ¹⁵	Ile-Ife/Nigeria	Retros	32	12 (Median)	PC	SSI (59.4), WD (15), BA (NR)
Aziz et al (2010) ²⁷	Turkey	Retros	22	37 (Mean)	PC	SSI (18.2), WD (NR), BA (NR)
Phillipo et al (2012) ²²	Tanzania	Pros &Retros	104	18.5 (Median)	PC	SSI (55.5), WD/ BA (3.2)
Ugochukwu et al (2013) ²⁴	Enugu/Nigeria	Retros	86	25 (Mean)	PC	SSI (63.6), WD (15), BA (NR)
Deepak et al (2014) ²⁶	Sagar/ India	Retros	155	28.7 (Median)	PC	SSI (76.8), WD (NR), BA (11.6)
Kenneth et al (2014) ³	Enugu/ Nigeria	Retros	50	24.5 (Mean)	PC	SSI (44), WD (NR), BA (NR)
Poras et al (2015) ²⁸	India	Retros	646	29 (Mean)	PC	SSI (80.9), WD (13.3), BA (NR)
Manikanta et al (2016) ²⁹	Bangalore/ India	Pros	50	32.6 (Mean)	PC	SSI (38), WD (24), BA (NR)
Aliyu et al (2017) ²³	Maiduguni/ Nigeria	Retros	268	14.8 (Mean)	PC	SSI (21.6), WD (6.7), BA (NR)

Abbreviations: TIP = Typhoid intestinal perforation, ICM = Incision closure method, Retros = Retrospective, Pros = Prospective, PC = Primary closure, DPC = Delayed primary closure, SSI = Surgical site infection, WD = Wound dehiscence, BA = Burst abdomen, NR = Not reported.

However, more accurate risk classification scores, by including all possible risk factors in the NNIS criteria as well as host defense mechanisms (immunosuppression / immunosuppressive agents, co-morbidities like diabetes mellitus, subcutaneous fat thickness etc.), as well as perforation to operation interval can help the physician to more accurately estimate the probability of postoperative wound complications, as this will influence the physician's judgment on whether to utilize PC or DPC, thus lead to better wound management decisions. A long delay before surgery, either due to late presentation to the hospital, delayed diagnosis or to protracted referral time, may worsen the surgical outcome.⁸

V. Conclusions

It is an international research priority to find a reliable wound closure method to reduce wound complications following laparotomy for typhoid intestinal perforation (TIP), because of its attendant significant morbidity, mortality and financial cost. This is particularly important in the developing countries where TIP is common. Our study showed that delayed primary wound closure is a sound incision management technique that should be utilized after laparotomy for TIP. It significantly lowers the rate of SSI as well as fascial dehiscence and significantly reduces the LOS following laparotomy for TIP. Moreover, there was no statistically significant

difference in the overall short-term cosmetic appearance of the scars between PC and DPC groups. However, a well designed, large-numbered multicenter RCT is warranted.

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