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ORIGINAL ARTICLE

# Vacuum-assisted management of surgical site infections after liver transplantation: 15-year experience in a tertiary hepatobiliary center

**Paolo Magistri[1,2] · Tiziana Olivieri[1] · Valentina Serra[1] · Giuseppe Tarantino[1] · Giacomo Assirati[1] · Annarita Pecchi[3] · Roberto Ballarin[1] · Fabrizio Di Benedetto[1]**

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**Abstract**
Immune compromised as well as critically ill patients are at higher risk of surgical wound infection and dehiscence. Wound infections critically influence the outcomes after liver transplantation. In particular, it was shown that they significantly reduce the overall survival rate when compared to patients with uneventful wound healing, and their occurrence is associated with death or graft loss within 1-year post-transplantation. From January 2001 through December 2017, 763 patients underwent liver transplantation in our Institution, the Hepato-Pancreato-Biliary Surgery and Liver Transplantation Unit, "Policlinico" University Hospital, University of Modena and Reggio Emilia, Modena, Italy. We retrospectively analyzed data from our prospectively maintained database of patients treated with a negative pressure therapy device due to wound or abdominal infections. 13 patients underwent negative pressure treatments for surgical site infection after liver transplantation in our institution. Ten superficial "supra-fascial" applications (SF group) and three deeper abdominal (Ab group) were reported. Mean in-hospital stay for the SF group was 42.6 days, ranging from 8 to 80, while for the Ab group was 62 days (range 23–133), with an overall survival of 34 and 4.6 months, respectively. A multifactorial multidisciplinary approach is needed in the prevention of surgical site infections instead of mere antimicrobial prophylaxis The application of negative pressure wound therapy may help in controlling the diffusion of the infection and preventing sepsis.

**Keywords** Wound healing · Vacuum therapy · Vacuum-assisted therapy · Vacuum-assisted closure · SSI · VAC

## Introduction

Immune compromised as well as critically ill patients are at higher risk of surgical wound infection and dehiscence [1]. Multiple factors may increase the risk of infection, like the presence of foreign bodies (abdominal mesh, suture materials), serous collections and devitalized tissues. It is well known that bacterial infections can increase morbidity and mortality after organ transplantation, mainly due to immunosuppressive regimens [1–3]. Wound infections critically influence the outcomes after liver transplantation. In particular, they significantly reduce the overall survival rate when compared to patients with uneventful wound healing [4]. Moreover, their occurrence is associated with death or graft loss within 1-year post-transplantation [5]. Negative pressure technology is a suitable therapy for both superficial wound and abdominal infectious conditions [6]. The open abdomen treatment is a standpoint in the management and prevention of abdominal compartment syndrome and abdominal sepsis, and it represents a useful tool also in patients that underwent liver transplantation (LT) [6, 7]. Currently, common reasons to establish an open abdomen treatment are (1) the mismatch between volume of abdominal content and capacity of surrounding structures (i.e., visceral edema, decreased abdominal wall compliance, retraction of wound edges), (2) the necessity of a second-look (septic abdomen), and (3) the full-thickness resection of a portion of the abdominal wall due to necrotizing infections

✉ Fabrizio Di Benedetto
fabrizio.dibenedetto@unimore.it

[1] Hepato-Pancreato-Biliary Surgery, Surgical Oncology and Liver Transplantation Unit, University of Modena and Reggio Emilia, Via del Pozzo 71, 41124 Modena, MO, Italy

[2] Department of Medical and Surgical Sciences and Translational Medicine, Sapienza-University of Rome, Rome, Italy

[3] Department of Radiology, University of Modena and Reggio Emilia, Modena, Italy

or neoplasms [8]. In these settings, the temporary abdominal closure with negative pressure therapy provides a protection of the bowel from dehydration, external injury and further colonization, together with the control of fluid losses and toxics removal [8].

We herein report our experience with the management of complex wound and abdominal infections in patients treated with LT. In detail, we analyzed data from patients treated with negative pressure technology, including both superficial and deeper infections to provide a complete scenario of solutions to harmful complications that threatens patients' outcomes.

## Methods

### Patients

From January 2001 through December 2017, 763 patients underwent LT in our Institution, the Hepato-Pancreato-Biliary Surgery and Liver Transplantation Unit, "Policlinico" University Hospital, University of Modena and Reggio Emilia, Modena, Italy. Among them, 13 were treated with a negative pressure therapy device (VAC Therapy—KCI Inc.) due to wound or abdominal infections. We retrospectively analyzed data of those patients from our prospectively maintained database (Table 1).

After LT, all patients received an immunosuppressive therapy with 20 mg of metilprednisone in combination with tacrolimus at variable doses; everolimus or mycophenolate may be added. The indications for negative pressure therapy in our center, either for superficial or abdominal complications, are as follows: (1) contamination or infection without purulent secretions, (2) delayed wound healing, (3) to avoid the retraction of wound edges, (4) presence of abdominal compartment syndrome, (5) abdominal sepsis. Curative strategies for post-operative septic complications are planned during multidisciplinary meeting involving surgeons, radiologists and anesthesiologists. Contraindications are evaluated according to the manufacturer's protocol. The treatment should never be protracted for more than 3 weeks, and the wound must show a positive healing trend by day 10. Moreover, the treatment should be stopped in case of bleeding, pain, fistula and allergy.

All patients were followed at our outpatient clinic weekly for the first month after being discharged from the hospital, and then at 3- or 6-month intervals. Follow-up examinations included clinical examination, liver function tests, abdominal ultrasound (US), CT scans and Magnetic Resonance (MR), as for every patient undergone LT.

We analyzed general features such as age, gender, body mass index (BMI), ascites pre- and post-transplant, presence of diabetes, cause of cirrhosis and reason to transplantation, presence of hepatocellular carcinoma (HCC), date of transplant and length of follow-up. Post-operative variables such as need for re-transplant, date of re-transplant, overall survival and graft survival were also reported. Wound healing-specific variables evaluated were (1) microorganisms detected, (2) immunosuppressive regimen, (3) length of negative pressure treatment, (4) number of dressing changes, (5) mean output and (6) its quality, (7) post-treatment residual incisional hernia, and (8) complications.

**Table 1** Patients' features

| | Supra-fascial treatment group ($n=10$) | Abdominal treatment group ($n=3$) |
|---|---|---|
| Male (%) | 7 (70%) | 2 (66.7%) |
| Female (%) | 3 (30%) | 1 (33.3%) |
| BMI (mean) | 22.72 | 29.81 |
| Diabetes | 2 | 1 |
| Fulminant hepatitis | 1 | 1 |
| HCV infection | 4 | 1 |
| HBV infection | 3 | 0 |
| HDV infection | 1 | 0 |
| HIV infection | 0 | 0 |
| Alcoholic hepatitis | 1 | 1 |
| NASH | 1 | 0 |
| HCC | 5 | 1 |
| In-hospital stay (mean, days) | 42.6 (range 8–80) | 62 (range 23–133) |
| Overall survival (mean, months) | 34 | 4.62 |
| Re-transplant | 1 | 1 |

## Results

13 patients underwent negative pressure treatments for surgical site infection (SSI) after LT at our Institution, 10 superficial "supra-fascial" applications (SF group) and 3 deeper abdominal (Ab group). Reasons for liver transplant were acute liver failure in 2 cases and chronic hepatitis in 11 patients, namely, 5 hepatitis C virus (HCV) related cirrhosis, 3 hepatitis B virus (HBV) related, 2 alcohol related, 1 non-alcoholic steatohepatitis (NASH). Six patients underwent LT with a diagnosis of HCC. Two re-transplants were needed, one for liver primary non-function and one for compartment syndrome (the latter was in the Ab group, while the first was in the SF group). Microorganisms isolated from the 13 patients are reported in Table 2. The mean BMI in the Ab group was 29.81, while in the SF group was 22.72. Mean in-hospital stay for the SF group was 42.6 days, ranging from 8 to 80, while for the Ab group was 62 days (range 23–133), with an overall

**Table 2** Microorganisms isolated

| Microorganisms isolated from wound infections | Microorganisms isolated from abdominal infections |
|---|---|
| *S. aureus* | *E. Coli* |
| *E. faecium/A. baumanii* | *E. Faecium* |
| *Enterococco faecium* | |
| *Klebsiella pneumoniae* | |
| *E. coli* ESBL | |
| *E. faecium* | |
| Acinetobacter | |
| *S. Epidermidis* | |
| *C. Albicans* | |

**Table 3** Negative pressure therapy

| | Supra-fascial treatment group ($n=10$) | Abdominal treatment group ($n=3$) |
|---|---|---|
| Length of therapy (mean, days) | 13.9 (range 3–21) | 9.3 (8–10) |
| No. of dressings changed (mean) | 2.9 (range 0–6) | n.r. |
| Output (mean) | 135 (range 50–400) | n.r. |
| Incisional hernia | 3 | 1 |
| Low pre-operative ascites | 2 | 1 |
| Mild pre-operative ascites | 3 | 0 |
| Severe pre-operative ascites | 1 | 1 |
| Low post-operative ascites | 3 | 0 |
| Mild post-operative ascites | 6 | 1 |
| Severe post-operative ascites | 1 | 0 |

*n.r.* not reported

survival of 34 and 4.6 months, respectively (Table 1). Data on negative pressure treatment are reported in Table 3. The mean length of therapy was 13.9 days (range 3–21) in the SF group and 9.3 days in the Ab group (range 8–10). Two patients in the Ab group ultimately died due to multi-organ failure (MOF). In detail, the first one underwent re-laparotomy on post-operative day 13 due to clinical and radiological suspect of caval anastomosis stricture, followed by abdominal fascia dehiscence. Death from MOF occurred on post-operative day 23. The second patient developed a biliary fistula on post-operative day 20, with abdominal drains positive for *E. Coli*. The patient underwent re-laparotomy, with construction of a bilio-digestive anastomosis and started abdominal negative pressure therapy. The patient underwent a second re-laparotomy for recurrent biliary fistula and ultimately died on post-operative day 30 due to MOF.

The treatment was successful for 60% of the patients in the SF group, while the others had their wound defect healed for second intention (Fig. 1). The prevalence of incisional hernia in the SF group was 30%, while in the Ab group was 100%.

## Discussion

In this study, we reported our experience with the use of vacuum-assisted therapy for the management of SSI after LT. Currently, there is no evidence on benefits and harms of antibiotics for prophylaxis of SSI among liver transplant recipients [9, 10]. A recent review by the Cochrane Collaboration analyzed methods of preventing bacterial sepsis and wound complications in liver transplantation, reporting 31.6% infection rate (193/611 participants) and a positive association between infective complications and selective bowel decontamination [11]. Hospital stay longer than 21 days, ICU stay longer than 6 days, reoperation, high glucose levels (> 180 mg/dL), presence of a vascular graft, pre-operative length of hospital stay (> 7 days), and duration of anesthesia have been reported as major risk factors for surgical site infection [12]. Asensio and colleagues reported their experience with 107 patients with SSI after liver transplantation in a population of 1222 patients [13]. They noted that 76% of the infections occurred during the first 4 weeks after surgery, while the incidence declined progressively after the second post-operative week. Moreover, they noted a specific site-related incidence for certain pathogens, namely, *S. Aureus* in incisional surgical site infections and Enterococcus spp in deepest infections. A previous liver or kidney transplant and a biliary reconstruction by choledocho-jejunostomy were also related to a higher risk of SSI in the first month after LT. Notably, the use of mycophenolate mofetil in triple-association was associated to a higher risk of SSI compared to the steroids plus calcineurin inhibitors regimen [13]. In addition, Hellinger et al. reported a statistically significant association at the multivariate analysis between SSI, donor liver mass-to-recipient body mass ratio of less than 0.01, and increased operative time [5]. Of note, the same group in 2011 published an interesting work demonstrating that differences in the surgical practices of individual surgeons are associated with risk for surgical site infections after liver transplantation [14].

Zanus and colleagues reported in 2010 their experience with a 53-year-old patient who developed a necrotizing pancreatitis after positioning a percutaneous trans-hepatic biliary drain (PTBD) for an anastomotic biliary stricture [15]. The patient previously received sequential transplantation of the liver in 1995, for HCV-related cirrhosis, and

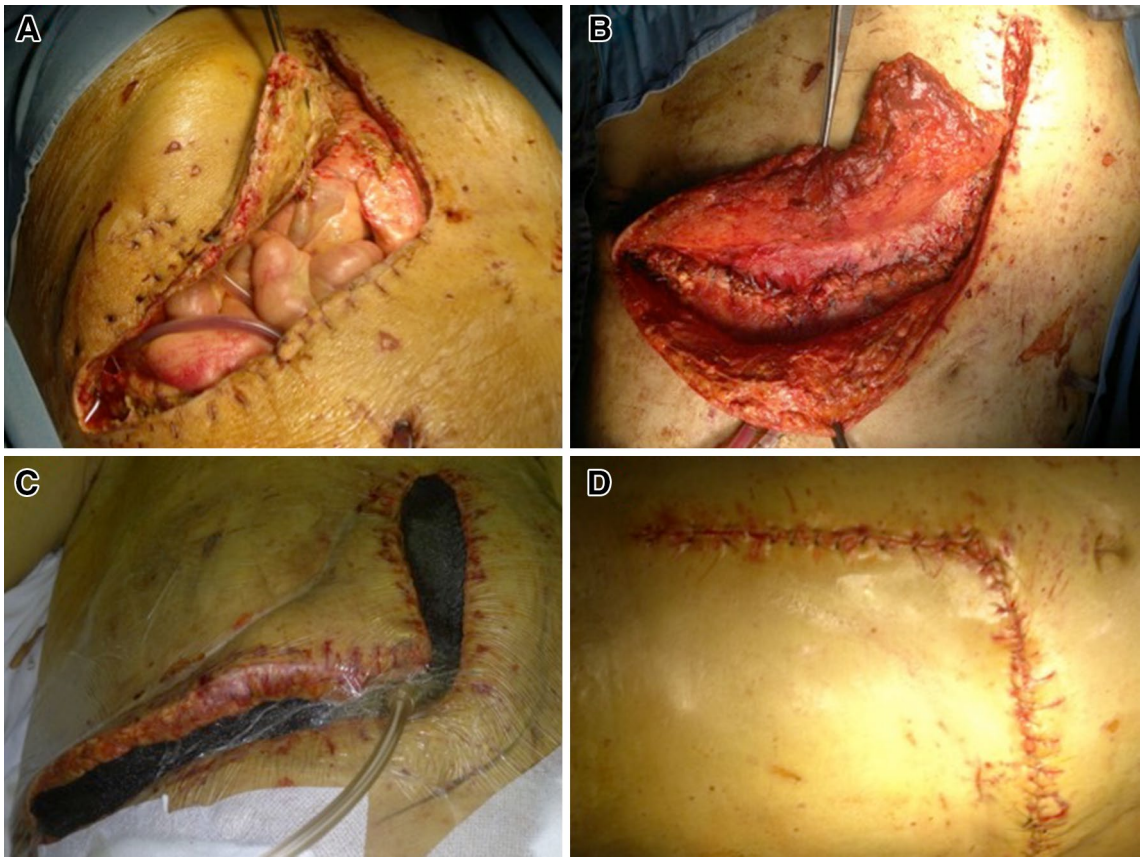


**Fig. 1** Example of vacuum-assisted management of surgical site infection: supra-fascial application. **a** Re-laparotomy and debridement. **b** Closure of the fascia. **c** Supra-fascial application of VAC system. **d** Direct closure of the skin 4 days after treatment

of a single kidney in 2005, because of chronic renal failure. He underwent a first surgical approach on September 2008 with abdominal washout and drainage, a second revision on post-operative day 19 and a surgical revision for bleeding on post-operative day 29. At this time, vacuum-assisted closure was used to perform repeated abdominal washouts. The patient underwent 14 re-laparotomies; vacuum therapy was discontinued on March 2009 and he was discharged on April 2009 with minimal antibiotic therapy, normal liver, and kidney function and a full recovery of his physical autonomy, with no evidence of any onset of diabetes.

In 2015 Dondossola et al. reported two cases of patients underwent LT and successfully treated with negative pressure therapy for wound infections caused by extensively drug-resistant Gram-negative bacteria [16]. The two patients were a 63-year-old man underwent LT for decompensated portal hypertension and HCC progression and a 50-year-old man, who had received a LT 3 years before for HCV-related cirrhosis, underwent liver re-transplantation due to liver abscess secondary to late hepatic artery thrombosis. They both developed wound infection from Klebsiella Pneumoniae-XDR. Sequential negative pressure wound therapy with antibiotic instillation (NPWTi) and standard negative pressure wound therapy (NPWT) were adopted in both cases. The first patient was discharged on POD 83 after 24 days of systemic antibiotics therapy, and wound healing was achieved after 102 days. The second patient was discharged on post-operative day 108, he received wound treatment twice a week in the outpatient clinic, and NPWT was discontinued 2 months later. 3 months later he underwent skin closure with programmed incisional hernia later repaired.

In 2017 Hobeika and colleagues reported their experience with the management of open abdomen after LT [17]. In their, series 46 patients could not undergo immediate fascial closure, and 24 were treated with negative pressure therapy (VAC group). When compared to the "Skin-Only-Closure (SOC) group, the two groups showed similar morbidity ($p = 0.55$) and comparable major complications. In particular, one patient in the VAC group needed an urgent re-laparotomy due to bleeding. However, the proportion of ventral hernia at 1 year after liver transplant was lower in the VAC group than in the SOC group (4.8% vs. 58.8%, $p = 0.0006$).

Chan and colleagues reported in 2018 their experience to identify differences in perioperative blood loss and use

**Table 4** Literature review: negative pressure therapy after liver transplantation

| First author | Year | No. of patients | Reason for negative pressure therapy | Negative pressure system | Major findings |
|---|---|---|---|---|---|
| Zanus | 2010 | 1 | Acute pancreatitis occurring in a sequential liver and kidney transplant | Abdominal VAC therapy | Successful abdominal wound closure after 6 months |
| Dondossola | 2015 | 2 | Wound infection | VAC Ulta and VAC system | Efficient association of local instillation of focused antibiotics applied to NPWTi for deep wound infection by MDR and XDR-GN bacteria |
| Hobeika | 2017 | 24 | Immediate fascial closure technically not possible | AB therapy | Lower incidence of ventral hernia compared to the skin-only closure group |
| Chan | 2018 | 34 | At the discretion of the primary transplant surgeon based on their intraoperative data | VAC therapy | Application of VAC secondary to massive intraoperative exsanguination was safely utilized |

*n.r.* not reported

of blood product comparing patients who underwent damage control laparotomy (DCL) with VAC (34 patients) and primary abdominal closure (PAC, 167 patients) during liver transplantation [18]. In this series, damage control strategies were employed at the discretion of the primary transplant surgeon based on discretional assessment of intraoperative blood loss, hemodynamic stability, reconstruction, donor liver size, massive bowel edema and perceived tissue quality of the bile ducts. VAC patients had significantly higher intraoperative blood loss (10.7 L) compared to patients who underwent PAC (4.4 L), and received on average 9 L compared to 5 L of volume in the PAC group in addition to significantly more FFP, PLT, crystalloid and colloid requirements in the first 24-h post-transplant in the ICU ($p < 0.001$). However, no statistically significant differences were found at the follow-up in terms of morbidity and mortality. Authors concluded that use of VAC is a feasible alternative to primary closure in the setting of severe bleeding. Although highly biased, this paper reports a large experience in challenging scenarios during liver transplantation and represents an interesting milestone about damage control strategies in liver transplant for massive hemorrhage.

To the best of our knowledge this is the largest report in literature on the application of supra-fascial negative pressure therapy in the setting of liver transplant (Table 4). Although biased from the retrospective nature and the little number of patients, our data support the feasibility of the application of negative pressure therapy in severely ill and immunocompromised patients. Treating more efficiently and quicker SSI means also reducing the amount of antibiotic administered, which is of particular importance in LT recipients to prevent the development of drug resistances.

In a report published in 2011, the FDA highlighted 12 cases of deaths and 174 cases of adverse events in patients using negative pressure therapy devices between 2007 and 2011. Interestingly, most of those injuries occurred in outpatients, in a home-care setting. Therefore, is advisable to pay more attention in teaching patients and caregivers the use of this technology. Moreover, the principal cause of death was acute bleeding, while the most frequent adverse event occurred was wound infection: this paradoxical condition may be related to the delay in changing the dressings or to the presence of necrotic tissue [19, 20].

## Conclusions

Given the current state of the art highlighted from the literature, a multifactorial multidisciplinary approach is needed to prevent surgical site infections instead of mere antimicrobial prophylaxis. Moreover, the use of antimicrobials should be evaluated wisely due to the incessant outbreaks of new etiological agents. In this setting, the application of negative pressure wound therapy may be of help in preventing sepsis. However, more efforts should be spent to exert an effective action to reduce known risk factors.

**Author contributions** PM and FDB: study concept and design. TO and GT: literature review. VS and GA: data analysis. PM, RB and AP: manuscript drafting. RB, AP and FDB: critical revision.

## Compliance with ethical standards

**Conflict of interest** All authors have seen and approved the manuscript and are fully conversant with its contents. None of the authors has personal, financial or political interest in the material.

**Research involving human participants and/or animals** This article does not contain any studies with human or animal subjects performed by any of the authors.

**Informed consent** For this type of study formal consent is not required.

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