



The cost of endoscopic treatment for walled-off pancreatic necrosis

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ABSTRACT

Background: Use of minimally invasive techniques has reduced mortality in walled-off pancreatic necrosis (WON) but may be costly. The aim of this study was to evaluate the actual costs associated with the endoscopic management of patients with WON.

Methods: We included a retrospective cohort of WON patients treated with endoscopic, transgastric drainage and necrosectomy (ETDN) during 2013–2014. Costs were calculated for six sub-areas based on a micro-costing model. Students T-test and non-parametric analysis of variance were performed to evaluate costs in relation to disease etiology and outcome.

Results: We included 58 patients (50% men, median age 57 years). The most common etiologies were gallstones (57%) and alcohol (19%). Nine patients (16%) died during admission. The median length of stay was 50 days (IQR 31 days). Eighteen patients (31%) needed treatment in our intensive care unit with a median length of stay of 16 days (IQR 31 days). The mean costs and standard deviation of costs (SD) per patient were: diagnostic imaging \$2,431 (\$2,301), laboratory tests \$3,579 (\$2,477), blood products \$982 (\$1,734), endoscopic treatment \$3,794 (\$1,777), medicine \$5,440 (\$6,656), and ward cost \$41,260 (\$35,854). The mean total cost was \$57,486 (\$46,739). Post-ERCP pancreatitis and mortality predicted higher costs.

Conclusions: This study sheds light on the different costs associated with endoscopic treatment of WON. As nearly three quarters of the costs are related to ward care, initiatives aimed at reducing the length of hospital stay may have a great impact on making endoscopic treatment more cost effective.

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Introduction

While the majority of patients with acute pancreatitis suffer a mild and uncomplicated disease course, up to 20% develop a more severe course with development of pancreatic and/or peripancreatic necroses [1,2]. With time, these necroses become encapsulated with a well-defined inflammatory wall, so called walled-off necroses (WON). WON is often associated with prolonged hospital stay and high morbidity and mortality [3]. Typically, patients with WON may suffer from pain, infection, biliary and gastric outlet obstruction, and in severe cases multi-organ failure necessitating intervention. Minimally invasive techniques such as endoscopic, transmural drainage and necrosectomy (ETDN) and video-assisted

retroperitoneal debridement (VARD) have replaced open surgery in the management of WON and are now recommended as first line treatments [4]. In addition, the endoscopic technique has been further refined with the introduction of lumen apposing metal stents (LAMS) [5]. This shift in therapeutic approach has reduced morbidity and mortality but may increase costs.

The aim of this study was to assess the costs associated with the current management of patients with WON undergoing ETDN. Based on a micro-costing model, we calculated actual costs and evaluated predictors of costs for different clinical aspects of treatment of WON.

Methods

Study population and data sources

The study included all patients with WON treated with ETDN and insertion of plastic stents in our tertiary referral center from

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January 2013 to December 2014. Patients were followed for 2-years. All patient records (electronic and paper) were reviewed independently by two investigators (DR and SR). Any disagreement was resolved through discussion before analyses.

Endoscopic procedure

EDTN was performed using a curved linear array echoendoscope [3]. Initially, a 19 Gauge biopsy needle was inserted into the necrotic cavity and fluid aspirated for culturing. After creation of stoma, two double pigtail stents and a nasocystic catheter were placed for subsequent irrigation of the cavity and endoscopic debridement of loose necrotic material. Endoscopic necrosectomy was usually not performed during the index procedure. Additional placement of percutaneous catheters was done in cases of widely expanding peripancreatic collections that were not accessible by endoscopic route alone. Irrigation of the collections through nasocystic and/or percutaneous catheters was done three to six times a day. The standard irrigation volume ranged from 100 (collection less than 10 cm in largest diameter) to 250 ml (collection more than 10 cm in largest diameter). Antibiotics (gentamicin, vancomycin, or amphotericin B) were added to the irrigation fluid according to the microbiological findings. The endoscopic sessions with redilatation of the transmural tract and debridement were repeated at weekly intervals until the necrotic cavity was free of debris and vital granulation tissue was seen. At that time the nasocystic catheter was removed. The pigtail stents were removed one year after the index procedure.

Costs estimation

A micro-costing model was used by obtaining the costs in the smallest parts possible. Costs were subsequently aggregated costs for each patient [6]. This model allowed identification of the costs associated with different subareas of treatment. All prices were converted to US dollars from Danish Kroner (conversion rate: 1 U.S. dollar = 6.877 Danish kroner). Costs from 2013 were inflation adjusted (0.6%) to 2014 prices where appropriate [7].

Ward related costs

From the hospital administrative database, we obtained information about ward admission time (in hours). The mean price per bed per day was calculated based on staffing plans and associated costs (salary, bedding, utensils used on wards) for each ward, i.e. emergency department, general wards, semi-intensive care unit (semi-ICU), intensive care unit (ICU). We were unable to use the micro-costing method for the costs associated with the treatment at the ICU due to differences in organization and data structure of the ICU cost data. A calculated proxy was therefore used for the ICU,

covering ward related costs (staffing and utensils) calculated by the financial department of our hospital.

We added a weight of 25% to ward-related costs for one of our non-specialized wards, due to important clinical differences between WON-patients and other patients admitted to the ward. We aggregated costs to calculate the price per patient and price per day in ward related costs.

Endoscopy

Information on endoscopic procedures was obtained by reviewing all individual endoscopy reports, thereby avoiding errors due to false use of procedural coding. Cost associated with endoscopic procedures were calculated from information on staffing (endoscopists and specialized endoscopic nurses), procedural time which was automatically registered, and accessories used per procedure (number of needles, dilation balloons, snares, plastic stents, nasocystic catheters etc.).

Medicine

Information about medications administered were obtained from the electronic patient medicine administration module (EPM), which was used in all wards. The module tracks prescription, dispensing, and administration of medicine in all wards except for the ICU. Unique drug identification numbers identifying each type of drug and brand were linked with price information obtained from the hospital pharmacist drug procurement database to calculate a price for each administration. In case that procurement prices changed during the year, the latest price of that year was used. Information on medicine administered in the ICU was obtained from manual review of the electronic medical records.

Additional costs

Costs of laboratory tests were obtained from an administrative database used to secure payment between hospitals in the administrative region of Copenhagen. Tests performed during admission and billed up to one month after admission were included. Costs associated with diagnostic imaging tests were calculated from national rates for individual examination types [8]. For each patient, central diagnostic imaging database was reviewed, and different types of scans registered (Table 2). Costs of blood transfusion products were obtained from the regional blood management and quality database. The prices of the different blood products are calculated in the regional database each year, according to the actual costs of producing each type blood product in the former year [9].

Statistical analysis

Statistical analysis was performed on all relevant variables using

Table 1
Base-line characteristics of included patients.

Age, years, median (IQR)	59 (24)
Gender, males/females, n	29/29
Charlson co-morbidity index at the time of symptom debut, median (IQR)	0 (1)
BMI, median (IQR)	26 (7)
Aetiology, n (%)	
Gallstone	11 (19%)
Alcohol	33 (57%)
Post-ERCP	6 (10%)
Other	8 (14%)
Days from debut of symptoms to index endoscopy, median (IQR)	35 (36)
Infected WON at index endoscopy, n (%)	49 (84)
In hospital mortality, n (%)	9 (16%)
Two-year mortality, n (%)	10 (17%)

Table 2

The overall and mean number of procedures performed during admission in 58 endoscopically treated patients with walled-off pancreatic necrosis.

Type of procedure	N	Mean number of procedures per patient (SD)
Endoscopy		
EUS with transmural drainage	72	1.2 (0.6)
Endoscopic dilatation of drainage tract and necrosectomy	287	5 (3.3)
ERCP, gastroscopy	49	0.8 (0.9)
Percutaneous drainage through self-expanding metal stent	6	0.1 (0.3)
Diagnostic Imaging		
Abdominal CT-scan	205	3.5 (2.5)
Diagnostic transabdominal ultrasound	86	1.5 (2.2)
Therapeutic transabdominal ultrasound	101	1.7 (2.6)
Chest X-ray	399	6.9 (9.9)
Other (MRCP, PET-CT, CT of cerebrum)	12	0.2 (0.5)
Supportive treatment		
Insertion of naso-jejunal feeding tube	15	0.3 (0.6)
Blood products	456	7.9 (14.1)
Drug administrations	69,715	1,202 (888.4)
Arterial embolization	2	0.03 (0.2)

descriptive statistics. Results are presented as medians, interquartile range (IQR), proportions or means with standard deviation (SD). Scatter plots were performed to check for outliers in data in the aggregated cost data and for each cost element. We tested the used variables for normality. A Mann-Whitney *U* test was performed to analyze for the economic impact of infection (comparing costs for patients with infected and sterile WON at the first drainage). We performed a Kruskal-Wallis test to evaluate whether the etiology of pancreatitis had any impact on the costs. In addition, we prepared Kaplan-Meier plots with log-rank tests to assess the duration of in-hospital stay in relation to infection and etiology. A statistical significance level of 0.05 was used. All analyses were performed in SAS 9.4.

Results

A total of 58 patients with WON underwent ETDN during the inclusion period (Table 1). In 53 patients (of which 49 proved to be

infected by culturing) ETDN was performed on strong clinical and/or biochemical suspicion of infection, in three patients ETDN was performed due to gastro-intestinal obstruction, and in two due to intractable pain.

Eighteen patients (31%) needed treatment in the ICU. Nine patients (16%) died during admission with the mortality being highest during the first 90 days after admission (Fig. 1). One additional patient died 10 months after discharge. The median length of stay was 50 days (IQR 31). The median length of stay in the ICU was 16 days (IQR 31).

There was no difference in length of hospital stay between sterile and infected WON at the time of index endoscopy or among different etiologies (log rank = 0.08 and 0.27, respectively).

The median number of drug administrations was 1,045 (IQR 1,181). Thirty-three (56%) patients received blood products. The median number of diagnostic imaging was 7 (IQR 17). The median number of endoscopies was 7 (IQR 4) (Table 2).

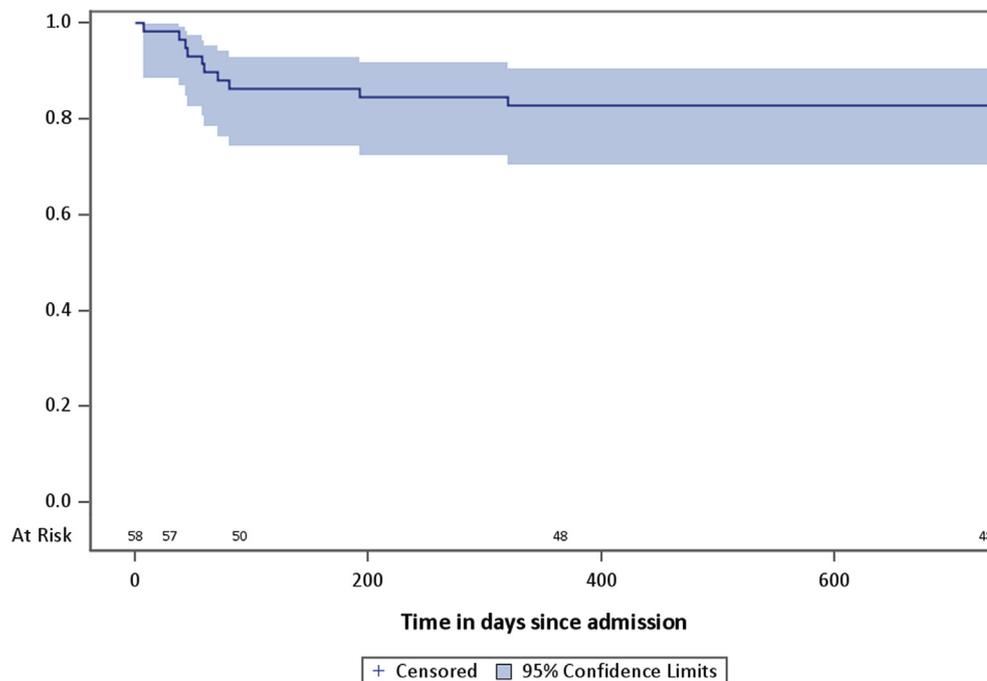


Fig. 1. Kaplan-Meier survival plot for the first two years after admission, with patients at risk at 0, 30, 90, 365 and 730 days.

Table 3

Costs per patient for different subareas and total costs in US \$.

Type	Mean	Standard deviation (S)	Sum	% of total cost
Endoscopic treatment	\$3,794	\$1,777	\$220,065	6.6%
Blood products	\$982	\$1,734	\$56,943	1.7%
Diagnostic imaging	\$2,431	\$2,301	\$141,002	4.2%
Wards	\$41,260	\$35,854	\$2,393,071	71.8%
Lab analyses	\$3,579	\$2,477	\$207,574	6.2%
Drug administration	\$5,440	\$6,656	\$315,541	9.5%
Total costs	\$57,486	\$46,739	3,334,195	100%

Costs

Ward costs accounted for 72% of the total treatment costs (Table 3). Of the ward costs, 34.4% were related to stay in the ICU.

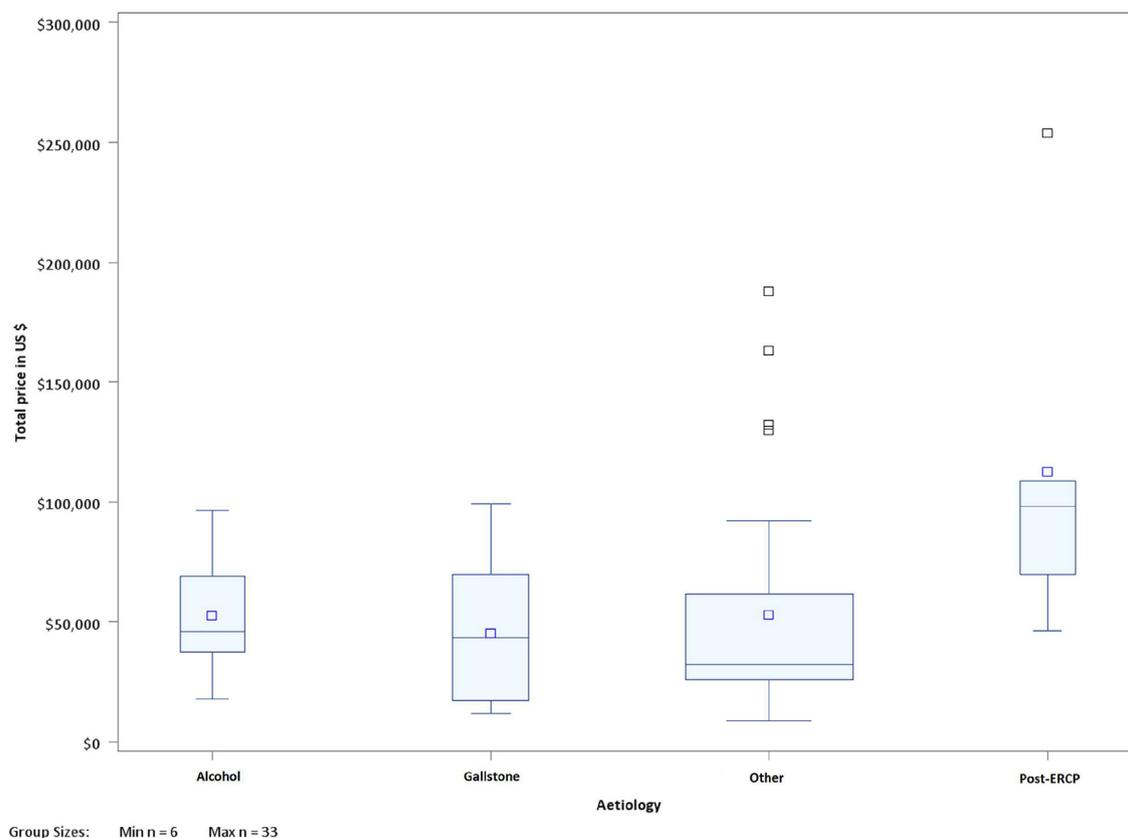
The mean cost for patients with sterile WON at the first drainage was \$41,985 (SD 34,074) compared to \$60,333 (SD \$48,449) for patients with infected WON ($P = 0.20$). The mean costs for treating patients with post-ERCP pancreatitis were significantly higher than for other etiologies ($p = 0.048$), (Fig. 2). The main cost driver for these patients were longer mean length of stay with 82 days for the post-ERCP vs. 52 days of stay for all other etiologies, ($p = 0.04$).

Discussion

This study includes 58 patients with WON; 84% with culture proven infected necrosis at the index endoscopy. The mean total cost during admission amounted to \$57,486 per patient. The mean length of stay was 55 days and 72% of the total costs were related to ward costs. The mean cost of admission in the Danish Healthcare

system was just below \$4,500 in 2014 [8] with an average length of stay of 3 days, making treatment of patients with WON being costlier than the average Danish inpatient by a factor 10. The mean costs associated with infected necrosis were \$18,000 higher than costs associated with sterile necrosis. This difference was, not statistically significant, possibly due to the small proportion without infections. The cost of management of patients with post-ERCP WON was significantly higher compared with other etiologies, the difference being driven by the longer length of stay for post-ERCP patients. However, our data do not allow us to make firm conclusions on the reasons for this difference in length of stay.

Current guidelines recommend the use of minimally invasive techniques such as ETDN and VARD for the treatment of WON [4]. These recommendations are based upon reports of reduced morbidity and mortality with the use of minimally invasive techniques [10]. A recent randomized trial compared ETDN and VARD and found no difference in mortality or major outcome, although ETDN was more successful in some of the minor outcomes [11]. Findings from that study led to the recommendation that ETDN



*Mean cost for each etiology is indicated with a prism symbol. Costs for outlier patient are shown with a round symbol.

Fig. 2. Box-plot showing distribution of costs for different etiologies*.

should be considered as the primary choice in treatment of WON [12]. However, both ETDN and VARD are techniques that are often time consuming and may lead to prolonged length of hospital stay, thus potentially increasing treatment costs. Interestingly, no significant difference in mean total costs was found between these two treatment modalities. At the time we collected data for present study, VARD was not performed in our center. However, since then we have performed both VARD alone and VARD in combination with ETDN. Especially the combination of the two seems promising in reducing the length of stay and thereby the total costs.

A study from New Zealand evaluated the costs associated with the management of patients admitted with acute pancreatitis [13]. The study included 577 patients admitted from 2005 to 2008. Twenty-five patients underwent necrosectomy, in 13 by using a minimally invasive technique whereas the remaining patients underwent open necrosectomy. The authors calculated fixed costs per diagnostic, intervention, treatment, and bed day to estimate the cost of treatment. The median overall costs were US\$ 56,674, some 20% higher than the costs found in our study. The study found no difference between the type of intervention and costs but concluded that the sample size entailed a risk of type II error. Likewise, due to sample size, additional analyses evaluating predictors of costs were not possible. In the recently published TENSION trial [11], the mean total costs per patient from randomization until 6-month follow-up were €60 228 for the endoscopic step-up approach and €73 883 for the surgical step-up approach. The resulting mean difference of €13 655 per patient was not significant. The mean costs of the index interventions (i.e. all drainage and necrosectomy procedures) were €3785 in the endoscopy group and €2851 in the surgery group. Median costs related to endoscopic treatment in our study were \$3271, approximately one third less than in TENSION trial.

In a subgroup of patients, WON resolves spontaneously without need for intervention. It would be of interest to estimate their costs and compare to the costs of patients needing intervention. Due to the retrospective nature of present study and the fact that our department serves as a tertiary referral center, we were not able to perform these calculations.

Recently, lumen apposing metal stents (LAMS) have been introduced for the treatment of pancreatic fluid collections [5]. The stent is fully-covered and shaped with two bilateral anchor flanges between a saddle. A dedicated through-the-scope delivery system, where the tip serves as an electro cautery device enables extraluminal access and deployment of the stent [14]. Initial results from primarily retrospective case series were promising. However, a recent randomized controlled trial failed to demonstrate superiority in terms of number of necrosectomies needed, treatment success, clinical adverse events, readmissions, length of hospital stay, and overall treatment costs [15]. The study was launched before the introduction of a novel 20 mm diameter LAMS. Whether this large diameter stent can contribute to reduction in the overall costs remains to be investigated. None of the patients in our study were treated with LAMS.

A number of limitations must be considered when interpreting our results. A major limitation is a retrospective data collection and that all procedures were performed in a single tertiary referral center, rendering it difficult to extrapolate the costs to other settings. Also, different hospital setups have different costs. The Danish hospital system is generally viewed as an efficient hospital system with costs on par with other OECD countries [16]. As the majority of costs related to endoscopic treatment of WON are costs associated with care staff, medical centers in other countries with lower salaries might see their costs differ significantly from ours. In this setting, a more precise breakdown of the costs in different types of care and health givers (nurses, assistant nurses, resident

doctors, interns etc.) would have been of interest, but limitations in hospital data did not make this possible. We added a weight of 25% to one of our non-specialized wards who has a long expertise in treating patients with WON. This percentage is somewhat hypothetical, although it is based on more experienced nurses involved in the treatment and estimates from the economic administration of the hospital. On average, the 25% added weight increased the costs of each patient by \$3679, increasing the total cost of treatment with 6.3%. Use of nasocystic drainage and irrigation with antibiotics is not a standard treatment. However, the cost associated with this particular treatment are negligible in comparison to the overall costs. We were only able to obtain total cost for the ICU stay at a more aggregated level than other wards. We assumed that there was no waste related to the administration of intravenously administered medications whereby we may have underestimated the total medicine costs. In our analysis, we did not include administrative overhead from the hospital or the department. This was not done because administrative cost differs greatly between hospitals and countries making comparison with other studies difficult. We did not include investment or depreciation. Another important drawback is a lack of formal comparison group.

In conclusion, this study sheds light on the different costs associated with endoscopic treatment of WON. As nearly three quarters of the costs are related to ward care, initiatives aimed at reducing the length of hospital stay will probably have a great impact, making endoscopic treatment even more cost effective. Some of the potential actions could include a combination of different minimally invasive techniques (i.e. percutaneous plus endoscopic approach), more aggressive necrosectomy, as well as improved understanding and optimization of supportive treatment. Our breakdown of cost might help others to review their current setup of treating patients with WON endoscopically.

Ethics

The study was approved by the Regional data protection Agency (AHH2012-58-0004).

Funding

None.

Conflicts of interest

None to declare.

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