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Topical application of Glauber's salt accelerates the absorption of abdominal fluid after pancreatectomy

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Abstract

Background Abdominal fluid collection (AFC) is one of the most common complications after pancreatic surgery, yet there are few recommendations on how to manage it. Most cases of AFC only require observation, while others may require more invasive techniques. Unfortunately, there are no drugs that effectively promote the absorption of AFCs. The aim of this study was to evaluate the potential efficacy of Glauber's salt solution for promoting the absorption of AFCs after pancreatectomy.

Methods This study included 196 patients who underwent pancreatomy and had AFCs on at least 2 cross-sectional follow-up CT images between 2020 and 2022. AFCs were defined as effusion with a diameter ≥ 3 cm and located around the pancreatic resection margin. We retrospectively investigated the relationship between Glauber's salt concentration and clinical variables.

Results The rate of clinically significant pancreatic fistula (grades B + C) was significantly higher in the control group (62.8% vs. 40.7%, $P = 0.014$). The median maximum diameter of the AFC was smaller, and the median time for the AFC to decrease to 30 mm in diameter was shorter in the Glauber's salt group than in the control group (41.9 mm vs. 53.5 mm, $P = 0.008$; 35.5 d vs. 100 d, $P < 0.001$). According to the multivariate analysis, percutaneous drainage and the application of Glauber's salt were found to be independent risk factors for AFCs decreasing to less than 30 mm in diameter (HR = 2.338, 95% CI = 1.524–3.585, $P < 0.001$; HR = 1.853, 95% CI = 1.327–2.589, $P < 0.001$). Additionally, patients with a maximum postoperative temperature exceeding 38.5 °C exhibited enhanced AFC absorption (hazard ratio (HR) = 1.850, 95% CI = 1.268–2.701; $P = 0.001$).

Conclusions Topical application of Glauber's salt solution after pancreatic surgery can promote the absorption of AFCs.

Keywords Pancreatectomy, Glauber's salt, Abdominal fluid collection

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Introduction

Over the last few decades, with advances in operative techniques and intensive perioperative care, postoperative mortality rates for pancreatic resections have decreased markedly, but morbidity rates have not changed significantly [1, 2]. Abdominal fluid collections (AFCs) are among the most common complications after pancreatic surgery. Previous research has revealed that the incidence of AFCs following pancreatic resection ranges from 15 to 60% [3–6]. However, there are few recommendations about how to manage AFCs after pancreatic surgery: some AFCs only require observation, whereas others require more invasive techniques [4, 7]. A significant proportion of patients experience clinical signs or require long-term abdominal drainage. The utilization of radiological drainage consistently results in a diminished quality of life, primarily attributable to the need for an external drainage system and the increased risk persistent pancreatic fistula [8, 9]. Additionally, endoscopic ultrasound-guided drainage is not considered a suitable approach for managing fluid collections that exhibit limited adherence to the stomach or duodenum, as these cases pose a significant risk of perforation and leakage [10]. Currently, there are no drugs that effectively promote the absorption of AFCs.

Glauber salt solution is mainly a mixture of water and sodium sulfate, which is commonly found in inland salt lakes that contain high concentrations of sodium and sulfate salts. It tastes salty and bitter, feels cold and acts on the stomach and intestine meridian. Glauber's salt was first mentioned in Variorum of Shennong's Classic of Materia Medica (Shennong Bencao Jing) because of its ability to remove cold and heat evil qi, expel the accumulations in the six fu, thereby relieving knotting and retaining the function [11]. In recent decades, Glauber's salt has also been used for treating acute pancreatitis, gastrointestinal disturbances, carbuncles, furuncles, swelling and breast carbuncles [12–14].

Based on the findings of previous studies and our experience with previous patients, we retrospectively evaluated the potential impact of Glauber's salt on with the absorption of AFCs after pancreatectomy.

Materials and methods

Study design

All adult patients who underwent pancreatic resection between 2020 and 2022 at our academic tertiary surgery center were screened for inclusion eligibility. All postoperative CT images available within 90 days after surgery were evaluated. The specific inclusion criteria consisted of (i) postoperative abdominal CT scan showing AFCs. Fluid collection was defined as effusion with a diameter ≥ 3 cm and located around the pancreatic resection margin [15]; (ii) at least 2 follow-up abdominal CT scans. Patients requiring vascular reconstruction or multivisceral resection were not included. Of the 2756 patients who underwent pancreatic resection, 196 with AFCs and at least 2 cross-sectional follow-up CT images were included in this study. As per our institutional policy, the requirement for formal approval by an ethical committee was waived since the study was retrospective.

Postoperative care and follow-up

Experienced pancreatic surgeons performed all the operations. Pancreatic resection was modified and performed according to the patients' clinical characteristics and situation. Abdominal drains were routinely used and typically removed on postoperative day (POD) 4 to 5 if the daily drainage volume of unsuspected effluent was < 50 ml with a low amylase concentration. Prophylactic octreotide was used at the discretion of the surgeon at a dose of 100 μg s.c. starting on POD 1 and readministered every 8 h for 6 days. As a unit protocol, abdominal plain computed tomography (CT) was performed in all patients prior to drain removal (POD 4 to 5). All patients with laboratory abnormalities (high white blood cell count, elevated C-reactive protein, and persistent fever) or abdominal discomfort also underwent CT. Typically, patients presenting with symptoms of abdominal discomfort, such as abdominal pain and bloating, or those experiencing persistent fever, may be considered for the use of Glauber salt. Regardless of the presence of AFCs, routine follow-up CT scans were performed after discharge to monitor for late complications and tumor recurrence. Follow-up imaging was performed at 2- or 6-month intervals based on the histopathological diagnosis (2 months for malignant disease; 6 months for benign disease).

Postoperative complications

Postoperative complications were classified using the Clavien–Dindo classification [16]. Pancreatic surgery-specific complications, including postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and postpancreatectomy hemorrhage (PPH), were graded according to the classification put forward by the International Study Group on Pancreatic Surgery (ISGPS) [17–19]. Only ISGPS grade B/C complications were recorded. Abdominal abscess was defined as the collection of fluid diagnosed via US/CT and positive cultures obtained by percutaneous drainage or at reoperation [20]. Patients with asymptomatic AFCs were followed up with US/CT until spontaneous resolution. Patients with AFCs and clinical (abdominal discomfort and fever) or laboratory abnormalities (high WBC count and increased C-reactive protein or procalcitonin levels) were evaluated to assess their suitability for percutaneous puncture drainage, and aspirated fluid was sent for culture and amylase assays.

Fluid samples with a high level of amylase were classified as POPFs, while those with a low level of amylase were classified as symptomatic AFCs [1].

External application of Glauber's salt

The method was performed as follows. Two pieces of cotton gauze, each measuring approximately 45 cm by 80 cm, were sewn together on three sides to create a gauze bag. The gauze bag was designed with a single opening on one side and was evenly divided into five chambers using parallel suture lines. Each chamber had a width of 9 to 10 cm. Each of the five chambers were filled with Glauber's salt through the open side of the gauze bag, after which the bag was sealed. As none of the chambers touched, Glauber's salt could not pass from chamber to chamber. This procedure entails the bidaily application of Glauber salt, necessitating replacement upon solidification due to moisture absorption. Each application is maintained for a duration of 6 to 8 h. The treatment is sustained until there is either a clinical improvement in symptoms or a substantial reduction is observed through CT imaging. The design of the gauze bag and the method of filling it with Glauber's salt were filed for a patent (China, patent no. ZL 2021 2 0965074.4).

Statistics

Continuous variables are presented as medians (interquartile ranges (IQRs)) and were compared using the Mann–Whitney U test. Categorical variables are reported as frequencies (percentages) and were compared by the Pearson chi-square test. A stepwise multivariate logistic regression analysis with backward elimination was conducted to assess the risk factors for procedural management in patients with AFCs. Patient characteristics, perioperative variables, and CT scan features were analyzed in the model. Variables that exhibited a $p<0.10$ were retained for the final model. The results are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). A P value<0.050 was considered to indicate statistical significance. All analyses were conducted using the Statistical Package for the Social Science (SPSS, Inc., Chicago, IL), version 25.

Results

Patient characteristics and pre- and perioperative status

A total of 2756 standard pancreatic resections were performed at our institution between 2020 and 2022. Of these, AFCs were found in 228 patients. Of the 228 eligible patients, 32 underwent vascular reconstruction, multivisceral resection, or lacked multiple CT scans. Therefore, the final total number of enrolled patients was 196, including 137 in the control group and 59 in the Glauber's salt group.

Table 1 Demographic characteristics and pathological details

	Control group	Glauber's salt group	*P*
Sex (male)	83 (60.6%)	40 (67.8%)	0.338
Age (years, ±SD)	58.6 (13.3)	59.4 (11.6)	0.716
ASA score			0.871
I	72 (52.6%)	29 (49.2%)	
II	62 (45.3%)	29 (49.2%)	
III	3 (2.2%)	1 (1.7%)	
BMI (kg/m^2, ±SD)	24.07 (3.39)	23.32 (3.36)	0.157
Type of disease			0.758
Pancreatic adenocarcinoma	78 (56.9%)	30 (50.8%)	
Serous cystic tumor	13 (9.5%)	4 (6.8%)	
Solid-pseudopapillary tumor	4 (2.9%)	2 (3.4%)	
Neuroendocrine tumor	11 (8.0%)	6 (10.2%)	
Mucinous cystic tumor	1 (0.7%)	0 (0%)	
Intraductal papillary mucinous neoplasm	18 (13.1%)	9 (15.3%)	
Others	16 (11.6%)	9 (15.3%)	

ASA American Society of Anesthesiologists, BMI Body mass index

Table 2 Surgical details

	Control group	Glauber's salt group	*P*
Type of resection			0.064
Segmental resection or enucleation	11(8.0%)	8(13.6%)	
Distal pancreatectomy	77 (56.2%)	21 (35.6%)	
Pancreaticoduodenectomy	48 (35.0%)	29 (49.2%)	
Total pancreatectomy	1 (0.7%)	1 (1.7%)	
Operative time (minutes, IQR)	247 (183–315)	269 (180–327)	0.239
Estimated blood loss (ml, IQR)	200(100–400)	200(100–300)	0.133

Table 1 provides a comprehensive overview of the demographic characteristics, preoperative nutritional status, and pathological examination results of the patients. No significant differences were observed between the two groups. The surgical details are shown in Table 2. There were no significant differences in the type of resection, operative time, or estimated blood loss volume between the two groups. The incidence of delayed gastric emptying (DGE) was higher in the Glauber's salt group than in the control group (10.2% vs. 5.1%, $P=0.023$). The rate of clinically significant pancreatic fistula (grade B+C) was significantly higher in the control group (62.8% vs. 40.7%, $P=0.014$). No significant differences were found regarding postpancreatectomy hemorrhage (16.8% vs. 16.9%, $P=0.628$) or the type of AFC ($P=0.534$). The results are shown in Table 3.

Postoperative assessment and abdominal fluid collection

Postoperative changes, including AFC, body temperature and blood biochemistry, are summarized in Table 4.

Table 3 Postoperative complications

	Control group	Glauber's salt group	*P*
Postoperative complications			
DGE(B/C)	7 (5.1%)	6 (10.2%)	**0.023**
PPH(B/C)	23 (16.8%)	10 (16.9%)	0.628
POPF			**0.014**
B	63 (46.0%)	16 (27.1%)	
C	23 (16.8%)	8 (13.6%)	
AFCs			0.534
Asymptomatic AFCs	113 (82.5%)	52 (88.1%)	
Symptomatic AFCs	4 (2.9%)	2 (3.4%)	
Pancreatic fistula	11 (8.0%)	4 (6.8%)	
Abscess	9 (6.6%)	1 (1.7%)	

DGE, delayed gastric emptying; PPH, postpancreatectomy hemorrhage; POPF, postoperative pancreatic fistula; AFC, abdominal fluid collection

There was no significant difference in the median duration of the postoperative body temperature being higher than 38.5 °C ($P=0.247$) or being between 38 °C and 38.5 °C ($P=0.516$). There was no significant difference in the median duration of the peripheral white blood cell count being higher than 15,000/μL, whereas in the Glauber's salt group, the median duration of the percentage of neutrophils being greater than 85% was significantly longer (4.26 days vs. 3.02 days, $P=0.016$). The median maximum diameter of the AFC in the Glauber's salt group was smaller than that in the control group, and the median time for the diameter of the AFC to decrease to 30 mm was shorter (41.9 mm vs. 53.5 mm, $P=0.008$; 35.5 d vs. 100 d, $P<0.001$). No significant difference was found in the proportion of patients who underwent drainage (15.3% vs. 11.9%, $P=0.525$). The median length of postoperative hospital stay was 14.0 days in the control group and 18.5 days in the Glauber's salt group ($P=0.001$). However, the rate of readmission was significantly higher in the control group (6.6% vs. 0%, $P=0.044$).

Stratification and abdominal fluid collection

Patients were stratified according to the type of resection. A total of 175 patients (98 patients who underwent distal pancreatectomy and 77 patients who underwent pancreaticoduodenectomy) were stratified by the type of surgery for analysis. The other predefined stratified analyses (19 patients underwent segmental resection or enucleation, and 2 patients underwent total pancreatectomy) were not conducted due to the insufficient number of studies. For patients who underwent distal pancreatectomy, no significant differences were found in the demographic characteristics, pathologic details, surgical details, or postoperative complications (Supplementary Tables 1 and Supplementary Table 2). Similar results were obtained for patients who underwent pancreaticoduodenectomy, except for the median estimated blood loss volume (Supplementary Tables 3 and Supplementary Table 4).

Among patients who underwent distal pancreatectomy, the median maximum diameter of the AFC did not significantly differ (52.5 mm vs. 53.4 mm, $P=0.527$), whereas the median time for the diameter of the AFC to decrease to 30 mm was shorter in the Glauber's salt group (39.0 d vs. 140.0 d, $P<0.001$). There was no significant difference in the duration of the postoperative body temperature exceeding 38.5 °C ($P=0.426$) or being between 38 °C and 38.5 °C ($P=0.102$); the duration of the peripheral white blood cell (WBC) count being greater than 15,000/μL ($P=0.720$); the duration of the percentage of neutrophils being greater than 85% ($P=0.530$); the rate of percutaneous drainage ($P=0.668$); or the rate of readmission ($P=0.286$). The median length of postoperative hospital stay was 12.0 days in the control group and 17.0 days in the Glauber's salt group ($P=0.010$). The results are shown in Table 5.

According to our stratified analysis of patients who underwent pancreaticoduodenectomy, the median maximum diameter of the AFC in the Glauber's salt group was smaller than that in the control group, and the median time for the diameter of the AFC to decrease to 30 mm was shorter (40.0 vs. 55.6, $P=0.002$; 27.5 days vs. 45.0 days, $P=0.035$). The median duration of the percentage of neutrophils being greater than 85% was 5.43 days in the Glauber's salt group and 3.56 days in the control group

Table 4 Postoperative assessment and abdominal fluid collection

	Control group	Glauber's salt group	*P*
The maximum diameter of the AFC (mm, IQR)	53.5 (40.9–69.1)	41.9 (37.1–62.7)	**0.008**
The time for the diameter of the AFC to decrease to 30 mm (day, IQR)	100.0 (40.5-177.5)	35.5 (17.5–60.0)	**< 0.001**
The duration of the body temperature exceeding 38.5 °C (day, ±SD)	0.24(0.594)	0.33(0.685)	0.247
The duration of the body temperature ranging between 38.0° and 38.5 °C (day, ±SD)	1.03(1.387)	0.97(1.510)	0.516
The duration for the peripheral white blood cell count exceeding 15 000/μL (day, ±SD)	2.06(2.421)	2.41(3.671)	0.560
The duration of the percentage of neutrophils exceeding 85% (day, ±SD)	3.02(2.239)	4.26(3.317)	**0.016**
Percutaneous drainage	21 (15.3%)	7 (11.9%)	0.525
Readmission	9 (6.6%)	0 (0%)	**0.044**
Length of postoperative hospital stay (day, IQR)	14.0 (10.0–21.0)	18.5 (13.8–25.3)	**0.001**

AFC abdominal fluid collection

Table 5 Postoperative assessment and abdominal fluid collection in the distal pancreatectomy group

	Control group	Glauber's salt group	*P*
The maximum diameter of the AFCs (mm, IQR)	53.4 (40.4–66.7)	52.5 (38.6–66.1)	0.527
The time for the diameter of the AFC to decrease to 30 mm (day, IQR)	140.0 (90.0-245.0)	39.0 (31.5–79.0)	**< 0.001**
The duration of the body temperature exceeding 38.5 °C (day, ±SD)	0.25 (0.596)	0.14 (0.478)	0.426
The duration of the body temperature ranging between 38.0° and 38.5 °C (day, ±SD)	0.88 (1.190)	0.48 (0.928)	0.102
The duration of the peripheral white blood cell count exceeding 15,000/μL (day, ±SD)	2.22 (2.256)	2.81 (3.790)	0.720
The duration of the percentage of neutrophils exceeding 85% (day, ±SD)	2.53 (1.659)	3.19 (2.874)	0.530
Percutaneous drainage	10 (13.0%)	2 (9.5)	0.668
Readmission	4 (5.2%)	0 (0%)	0.286
Length of postoperative hospital stay (day, IQR)	12 (10.0–17.0)	17 (12.5–23.5)	**0.010**

AFCs Abdominal fluid collections

Table 6 Postoperative assessment and abdominal fluid collection of the pancreaticoduodenectomy group

	Control group	Glauber's salt group	*P*
The maximum diameter of the AFCs (mm, IQR)	55.6 (44.4–70.7)	40.0 (36.7–55.7)	**0.002**
The time for the diameter of the AFC to decrease to 30 mm (day, IQR)	45.0 (25.5–97.5)	27.5 (15.3–57.8)	**0.035**
The duration of the body temperature exceeding 38.5 °C (day, ±SD)	0.27 (0.644)	0.50 (0.839)	0.118
The duration of the body temperature ranging between 38.0° and 38.5 °C (day, ±SD)	1.27 (1.673)	1.39 (1.729)	0.613
The duration of the peripheral white blood cell count exceeding 15,000/μL (day, ±SD)	1.83 (2.529)	2.82 (3.982)	0.330
The duration of the percentage of neutrophils exceeding 85% (day, ±SD)	3.56 (2.858)	5.43 (3.469)	**0.007**
Percutaneous drainage	10 (20.8%)	5 (17.2%)	0.700
Readmission	2 (4.2%)	0 (0%)	0.265
Length of postoperative hospital stay (day, IQR)	19.0 (13.25–24.75)	21.0 (16.25–28.75)	0.094

AFCs Abdominal fluid collections

(P=0.007). The other clinical indices were not significantly different (Table 6).

Risk factors for the absorption of abdominal fluid

A univariate logistic regression model was constructed using potential clinical risk factors for the time required for the diameter of the AFC to decrease to 30 mm or less. All predictive factors were used in a stepwise selection process to construct the final multivariate model (Table 7). With percutaneous drainage and the application of Glauber's salt, the diameters of the AFCs were more likely to rapidly decrease to less than 30 mm (HR=2.338, 95% CI=1.524–3.585, P<0.001; HR=1.853, 95% CI=1.327–2.589, P<0.001). Patients with a maximum postoperative temperature exceeding 38.5 °C exhibited enhanced AFC absorption (hazard ratio (HR)=1.850, 95% CI=1.268–2.701; P=0.001). AFCs with a maximum diameter greater than 50 mm were absorbed more slowly (HR=0.573, 95% CI=0.421–0.778; P<0.001). The absorption rate of AFCs generated after surgery also varies across different surgical procedures. Compared with distal pancreatectomy, AFP absorption was faster following pancreaticoduodenectomy and segmental resection or enucleation (HR=2.396, 95% CI=1.704–3.371, P<0.001; HR=2.163, 95% CI=1.283–3.646, P=0.004). The same result was observed when a logistic regression analysis was conducted for patients who underwent distal pancreatectomy (Supplementary Table 5). However, the use of Glauber's salt was not an independent factor impacting the absorption of AFCs when a multivariate logistic regression analysis was conducted for patients who underwent pancreaticoduodenectomy (Supplementary Table 6).

Discussion

With advances in surgical techniques, perioperative supportive care, and nonsurgical treatment, the incidence of complications following pancreatic surgeries is gradually decreasing [21–24]. The most common complication after pancreatectomy is pancreatic fistula, which represents the main source of morbidity. Most previous studies focused on the prediction, treatment, and prevention of pancreatic fistula (POPF) [25–28]. Little is known about AFCs after pancreatectomy, which is a common occurrence [15, 29, 30]. POPFs and AFCs do not always occur together. POPFs can occur without AFCs, and vice versa. The amylase levels in drainage fluid cannot be accurately measured if there is no drain at the pancreatectomy site [31]. In contrast, AFCs measured using routine postoperative CT are more accurate. Our study focused on AFC findings, regardless of the presence or absence of POPF. We found that most AFCs resolve spontaneously, while a small number of AFCs are clinically significant and require drainage or surgical exploration.

The location and nature of AFCs usually determine the type of drainage procedure needed. Surgical drains

Table 7 Univariate and multivariate analyses of the risk factors influencing absorption of abdominal fluid

	Univariate			Multivariate		
	HR	95% CI	*P*	HR	95% CI	*P*
Application of Glauber's Salt	2.181	1.583–3.005	**< 0.001**	1.853	1.327–2.589	**< 0.001**
Readmission	1.014	0.496–2.072	0.969			
POPF			**0.020**			
0/A	-	-	-			
B	1.025	0.179–1.404	0.876			
C	1.762	1.162–2.670	**0.008**			
ASA score			0.602			
I	-	-				
II	0.899	0.673-1.200	0.470			
III	1.358	0.497–3.711	0.551			
Percutaneous drainage	2.009	1.334–3.027	**0.001**	2.338	1.524–3.585	**< 0.001**
Type of resection			**< 0.001**			**< 0.001**
Distal pancreatectomy	-	-	-			
Pancreaticoduodenectomy	2.681	1.940–3.706	**< 0.001**	2.396	1.704–3.371	**< 0.001**
Segmental resection or enucleation	2.095	1.255–3.496	**0.005**	2.163	1.283–3.646	**0.004**
Total pancreatectomy	1.345	0.330–5.492	0.679	1.083	0.257–4.559	0.913
Age ≥ 60y	1.132	0.847–1.513	0.402			
Sex, male	0.960	0.771-1.400	0.801			
BMI			0.976			
<18.5						
18.5–24.0	1.073	0.571–2.015	0.827			
>24.0	1.067	0.570–1.998	0.839			
Duration of the Postoperative body temperature exceeding 38.5 ℃	1.734	1.201–2.505	**0.003**	1.850	1.268–2.701	**0.001**
Duration of the Peripheral white blood cell count exceeding 15,000/μL	0.795	0.589–1.072	0.133			
Duration of the percentage of neutrophils greater than 85%	1.247	0.677–2.295	0.479			
The maximum diameter of the AFC exceeding 50 mm	0.635	0.473–0.853	**0.003**	0.573	0.421–0.778	**< 0.001**

POPF, postoperative pancreatic fistula; ASA, American Society of Anesthesiologists; BMI, body mass index; AFC, abdominal fluid collection; HR, hazard ratio; CI, confidence interval

are associated with a mortality rate of 20–40%. Percutaneous drainage is widely performed, fairly effective, relatively safe, and undertaken in real time under imaging guidance. It is the most common treatment and has a good success rate (80–100%) and relatively low mortality rate (1.4–15%) [8, 32]. However, percutaneous drainage is always challenging in medical procedures. There is often no safe window for insertion, which increases the risks of puncturing the organs or vessels, thus causing complications such as peritonitis, bleeding, or infection. Regular flushing of the catheter is necessary to maintain patency, and this may require catheter changes at specific intervals. Additionally, access through the flanks or buttocks causes discomfort and pain, significantly impacting the patient's quality of life. Endoscopic ultrasound-guided drainage has been shown to be a safe and effective method for AFP management. This method also has several limitations: first, the collection must be closely adhered to the stomach or duodenum; second, the collection must be considerable. Otherwise, transmural drainage could result in extravasation of gastrointestinal contents into the retroperitoneum or peritoneum [33, 34].

Given the increased risk of procedural morbidity associated with repeat surgery and drainage, further research is needed to explore less invasive and more conservative options for the management of AFCs. Glauber's salt is mineral-based and used in traditional Chinese medicine. These crystals are primarily composed of hydrated sodium sulfate with traces of magnesium sulfate, sodium chloride, and calcium sulfate. Glauber's salt is salty and cold in nature and is known for its ability to resolve blood stasis, stagnation, constipation, dryness, hardness, inflammation and swelling [11]. It is used internally for treating constipation due to excess heat, abdominal pain due to fluid accumulation, and intestinal abscesses and is used externally for treating breast abscesses and painful hemorrhoids. Pharmacological research has shown that Glauber's salt strongly stimulates the reticuloendothelial system, enhancing its phagocytic ability and anti-inflammatory effects [12, 13]. By stimulating nerve reflexes, it increases local blood flow, improves local blood circulation, restores vascular function, quickly reduces temperature and pain, and alleviates swelling [14]. Furthermore, the ability to limit the absorption or encapsulation of intra-abdominal or pancreatic stump effusions

may reduce the risk of biochemical fistulas progressing to Grade B or C fistulas. Additionally, the topical administration of Glauber salt has been shown to expedite the resolution of mucosal edema in the postoperative digestive tract, particularly at sites of gastrointestinal anastomosis, and to facilitate the recovery of gastrointestinal motility.

Based on traditional Chinese medicine theory and clinical practice, we explored the application of Glauber's salt for promoting AFC absorption. We found that the median maximum diameter of the AFCs was significantly smaller in the Glauber salt group than in the control group (41.9 mm vs. 53.5 mm, $P=0.008$). The median maximum diameter of the AFCs in the control group was close to that reported in previous studies [15, 29, 35]. Additionally, the median time for the diameter of the AFC to decrease to 30 mm was shorter in the Glauber salt group than in the control group (35.5 days vs. 100 days, $P<0.001$). A similar result was observed in the subgroup analysis of the pancreaticoduodenectomy group (39.9 mm vs. 55.6 mm, $P=0.002$; 27.5 d vs. 45.0 d, $P=0.035$). According to univariate and multivariate Cox regression analyses, Glauber's salt concentration was an independent factor positively influencing the absorption of AFCs with diameters greater than 30 mm. According to the univariate analysis, in the pancreaticoduodenectomy subgroup, the application of Glauber's salt was a positive predictor of AFC resorption to less than 30 mm, although this difference was not significant according to the multivariate analysis. This could be partially due to the small sample size, varying locations of the AFCs, and the diverse nature of the AFCs.

Variation in the incidence of AFCs has been observed in different studies. In the study conducted by Bassi et al., routine US imaging was used to diagnose fluid collections < 50 mm in diameter on POD 3 after pancreaticoduodenectomy or distal pancreatectomy in 17 out of 114 patients [5]. Bruno et al. showed that 30 out of 50 patients who underwent pancreaticoduodenectomy with a soft pancreas were diagnosed with AFCs on POD 7 through routine CT scans [6]. In the study of Sierzega et al., 14% (97 out of 709) of patients, routinely monitored via postoperative ultrasound, developed asymptomatic abdominal fluid collections (AFCs) that spontaneously resolved after an average of 22 days. Additionally, 8% (52 patients) required percutaneous drainage of accumulated fluid [1]. Tjaden et al. reported that AFCs occurred in 43% of patients who underwent distal pancreatectomy [31]. In Song et al.'s study, 755 patients (68.5%) had AFCs detected on multiple CT scans. In the present study, we defined AFCs as a minimal of 30 mm of accumulated fluid on postoperative CT scans [1]. 8% of patients in this study had a diagnosis of AFCs. 1% of patients required percutaneous drainage of collected fluid. This discrepancy in the incidence rate of AFCs seems to be due to the different definitions of AFCs and different follow-up imaging modalities. Furthermore, the data from retrospective studies are inherently biased because imaging tests are typically performed only on patients showing symptoms indicative of intra-abdominal complications. Therefore, numerous facets of the natural progression of AFCs still need clarification, which is essential for making informed clinical decisions in the initial postoperative stage. At our institution, we routinely perform postoperative plain CT scans on all patients who underwent pancreatectomy. In this respect, the availability of real-life data such as those in the present study provides useful information for clarifying the nature of the progression of AFCs and guiding therapeutic decisions.

Interestingly, a highest postoperative body temperature exceeding 38.5 °C was an independent factor positively associated with the diameters of AFCs decreasing to less than 30 mm according to univariate and multivariate Cox regression analyses. Ralph et al. showed that body temperature was highly valuable in differentiating between infected and noninfected AFCs [36]. In clinical practice, clinicians may recommend more aggressive treatment for patients whose postoperative body temperature exceeds 38.5 °C. Additionally, an increase in body temperature can alter the systemic inflammatory response; however, this change in response has not been associated with the absorption of AFCs [37, 38]. A large, prospective study is needed for further validation.

Several limitations associated with the present study warrant mention. First, this was a single-center retrospective study that included a relatively small number of patients. In addition, there was heterogeneity in this study regarding the surgical type and transection of the pancreas, length of postoperative hospital stay and use of Glauber's salt. Second, we previously used Glauber's salt after the development of AFCs. Therefore, this analysis could be performed only for patients with AFCs and not for patients whose abdominal fluid collection was less than 30 mm in diameter. Based on these results, we are currently planning a prospective multicenter study to validate the preventive effect of Glauber's salt supplement in all patients undergoing pancreaticoduodenectomy and distal pancreatectomy (ChiCTR2300077500). Third, the present study demonstrated that a postoperative body temperature greater than 38.5 °C was an independent factor that promoted AFC absorption. However, due to the limited data, further investigations are needed to explore the relationship between inflammatory reactions and the absorption of AFCs.

Conclusions

AFCs after pancreatomy are frequently observed. Most AFCs resolve spontaneously, with no surgical or puncture interventions. The utilization of Glauber's salt after pancreatic surgery expedites the absorption of AFCs. Whether Glauber's salt can help decrease the incidence of AFCs requires further study.

Abbreviations

AFC	Abdominal fluid collection
POD	Postoperative day
CT	Computed tomography
POPF	Postoperative pancreatic fistula
DGE	Delayed gastric emptying
PPH	Postpancreatectomy hemorrhage
ISGPS	International Study Group on Pancreatic Surgery
WBC	White blood cell
HR	Hazard ratio
IQR	Interquartile range
OR	Odds ratios
CI	Confidence intervals
SPSS	Statistical Package for the Social Science

Supplementary Information

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Supplementary Material 1

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Not applicable.

Author contributions

WW designed this study; JL analyzed the data and drafted the paper. JL, JH and YH collected the data and revised the manuscript. HX, CL, JL and QM supervised the data collection and inputting. BZ, JX, SS and XY provided critical comments on various drafts of the paper. All authors read and approved the final manuscript. JL, JH and HR equally contributed to this work and should be considered as co-first authors.

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Data availability

All publicly available data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate

This study was approved by the Clinical Research Ethics Committee of Fudan University Shanghai Cancer Centre, approval number [2402291-Exp9]. All procedures involving human participants in this study were in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration. The requirement for written informed consent from each patient was waived owing to the retrospective design of the study by the Clinical Research Ethics Committee of Fudan University Shanghai Cancer Centre, approval number [2402291-Exp9].

Consent for publication

The manuscript is approved for publication by all the authors.

Clinical trial number

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Competing interests

The authors declare no competing interests.

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