Prognostic Factors for Outcome and Survival after Laparotomy in Patients with Pancreatic Trauma: One Single-center Experience.

Chao Yang
Jinling hospital
Baochen Liu
Jinling hospital
Cuili Wu
Jinling hospital
Yongle Wang
jinling hospital
Kai Wang
jinling hospital
Weiqin Li
Jinling hospital
weiwei ding (dingwei_nju@hotmail.com)
Jinling hospital https://orcid.org/0000-0002-5026-689X

Research

Keywords: pancreatic trauma, prognosis, risk factor, logistic regression analysis

Posted Date: April 9th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-21555/v1

Abstract

Background: Pancreatic trauma results in significant morbidity and mortality. Few studies have investigated the postoperative prognostic factors in patients with pancreatic trauma after surgery.

Methods: A retrospective study was conducted on 152 consecutive patients with pancreatic trauma who underwent surgery in Jinling Hospital, a national referral trauma center in China, from January 2012 to December 2019. Univariate and binary logistic regression analyses were performed to identify the perioperative clinical parameters that may affect the morbidity of the patients.

Results: A total of 184 patients with pancreatic trauma were admitted during the study period, and 32 patients with nonoperative management were excluded. The remaining 152 patients underwent laparotomy due to pancreatic trauma. Sixty-four patients were referred from other centers due to postoperative complications. Abdominal bleeding caused by pancreatic leakage (10 of all deaths) and severe intra-abdominal infection (12 of all deaths) were the major causes of mortality. Twenty-eight (77.8%) of the 36 patients who had damage control laparotomy survived. Univariate analysis showed that age, hemodynamic status, and injury severe score (ISS) as well as postoperative serum levels of C-reactive protein (CRP), procalcitonin, albumin and creatinine and the volume of intraoperative blood transfusion had significant effects on the mortality ($P < 0.05$). Binary logistic regression analysis showed that the independent risk factors for prognosis after pancreatic trauma surgery were age ($P = 0.012$), preoperative hemodynamic instability ($P = 0.018$), postoperative CPR ≥154 mg/L ($P = 0.016$), and postoperative serum creatinine ≥177 μmol/L ($P = 0.017$). The 30-day mortality rate was 15.8%.

Conclusions: In this single-center retrospective study, we first demonstrated that severe intra-abdominal infection and bleeding were the major factors affecting the prognosis of patients with pancreatic trauma after surgery. Preoperative hemodynamic instability, severe postoperative inflammation (CRP ≥154 mg/L) and acute renal failure (creatinine ≥177 μmol/L) were associated with a significant risk of mortality.

Introduction

Pancreatic trauma is an uncommon but important concern with a mortality rate of 3–70% in adult patients[1, 2]. It accounts for 1–2% of blunt abdominal trauma and 5–7% of penetrating abdominal trauma. The incidence of isolated pancreatic trauma is less than 1% among abdominal trauma cases[3]. Despite medical advances, the outcome remains unsatisfactory. The grade of pancreatic trauma, the location of the injury, the magnitude of associated organ injuries and the duration of the injury are considered responsible for poor outcomes[4].

The management and treatment of pancreatic trauma presents unique challenges for clinicians[5]. In 2017, the Eastern Association for the Surgery of Trauma (EAST) released practice management guidelines for adult pancreatic injuries[6]. It was recommended that pancreatic trauma injuries (grades I and II) based on the American Association for the Surgery of Trauma (AAST) grading system be managed without surgery or resection; for injuries involving pancreatic ductal injuries (grades III and IV), resectional management is conditionally recommended, but there is no recommendation for injuries with the more severe grade V. However, to date, there has been a lack of high-grade evidence from RCTs.

Deaths occur preoperatively or intraoperatively and are due to associated injuries and the consequences of uncontrolled blood loss and shock. Most deaths are usually due to severe intra-abdominal infection and multiple organ dysfunction postoperatively[7]. However, the current study addressed a major unresolved issue to evaluate the predictive factors for morbidity and mortality in a large cohort of consecutive patients. In our study, we sought to investigate the risk factors for mortality in pancreatic trauma after surgery. The results of this study can help identify the independent risk factors for prognosis in patients with pancreatic trauma and establish effective management procedures.

Materials And Methods

Study Population

The study retrospectively analyzed the clinical information of pancreatic trauma patients who underwent surgery in Jinling Hospital from January 2012 to October 2019. We excluded patients who were undergoing chemotherapy or radiotherapy, patients with immune system diseases or end-stage chronic organ failure, moribund patients with multiple severe injuries or patients who died within 6 h of injury. All study procedures were approved by the Institutional Review Board.

Data Collection

A retrospective study was conducted on the medical record data of 152 patients with pancreatic trauma who underwent laparotomy. The data analyzed included 21 parameters from the clinical information, injury conditions, lab results, and surgical information (Table 1).

Table 1
Clinical information of pancreatic trauma patients

Variable	I	II	III	IV	V	Total
Mechanism of injury						
Traffic accident	26	23	17	10	4	67(88.2)
Fall down	2	4	4	0	0	10(6.5)
Stab	6	2	0	0	0	8(5.3)
Shock	12	12	8	4	4	34(22.4)
ISS, median	17	27.5	30	31	28.5	27
Delayed diagnosis(n)	8	12	20	14	2	56(36.8)
Referral(n)	4	24	22	8	6	64
• Surgical procedures						
simple drainage	32	38	16	4	0	90(59.2)
pancreatectomy	0	0	12	0	0	12(7.9)
Whipple	0	0	0	4	2	6(3.9)
DCL	2	8	8	12	6	36(23.7)
Re-laparotomy	4	14	24	16	6	64(42.1)
Complications						
Pancreatic fistula	2	4	16	10	2	34(22.4)
Pancreatic abscess	6	20	18	10	4	58(38.2)
Abdominal bleeding	2	14	20	10	6	52(34.2)
MODS	4	8	6	2	2	22(14.5)
Death (n)	8	2	4	2	4	24(15.8)

Definitions

The severity of the pancreatic injuries was graded according to the AAST. Delayed diagnosis was defined as a diagnosis of pancreatic trauma made more than 24 h after trauma[8]. Shock was defined as a systolic blood pressure < 90 mmHg pre- or intraoperatively. Pancreatic leakage, hemorrhage and other pancreatic-specific complications were defined according to the standard ISGPF criteria[9]. ROC curve analysis showed the optimal cutoff value to be 28 for the ISS score, 154 mg/L for the CRP level, 4.26 μg/L for the procalcitonin level, and 15 mL/kg for the volume of intraoperative blood transfusion.

Statistical Analysis

The Chi-square test or Fisher's exact probability test was used for univariate analysis. Univariate analysis was conducted to analyze 21 parameters potentially associated with prognosis and to determine the variables displaying statistical significance ($P < 0.1$). The selected variables were included in multivariate analysis using a logistic regression model, and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using PASW Statistics 18 software.

Results

During the study period, 184 patients had pancreatic injuries. For the purposes of this study, only patients who had a surgical intervention were considered; therefore, 32 patients who had conservative treatment due to isolated pancreatic trauma were excluded from the analysis. The remaining 152 patients (128 men, average age 39 years) who met the criteria sustained 144 blunt injuries, and there were 8 cases of stab wounds (Table 1).

One hundred and thirty-six (89.5%) of the 152 patients had other associated intra-abdominal injuries. The spleen was the most frequently injured organ (n = 54, 35.5%), followed by the liver (n = 46, 30.3%), duodenum (n = 32, 21.1%), colon (n = 22, 14.5%), intestine (n = 20, 13.2%), stomach and bile duct (each n = 16, (10.5%). Fifty-two (34.2%) patients had associated vascular injuries, which was an important factor affecting mortality.

The 152 patients underwent a total of 284 operations (range of 1 to 6 operations). Eighty-six patients had low-grade pancreatic injuries (AAST grades I and II). One hundred and sixteen patients had definitive treatment (debridement, distal pancreatectomy, pancreaticojejunostomy or pancreatoduodenectomy) for the pancreatic injuries during the initial operation, and 36 patients with multiple complex injuries had a DCL, followed by planned reoperation and definitive management when stable. Fourteen patients underwent definite surgery six months later, 2 died, and 4 were lost to follow-up. For severe pancreatic trauma, DCL could significantly reduce mortality, although there was no significant difference. In 64 patients requiring multiple laparotomies, irrational surgical strategies and inadequate drainage were the important factors leading to relaparotomy. Overall, 24 (15.8%) patients died as a result of the injuries at a median of 12 days after the injury (range of 3 to 71 days). Two patients died due to severe traumatic brain injury on the 4th day after the operation, 10 died of recurrent intra-abdominal active hemorrhage due to pancreatic erosions, and 12 died of multiple organ failure caused by severe pancreatic necrosis, pancreatic fistula and severe intra-abdominal infection.

As a national trauma referral center, 64 patients were transferred from other hospitals due to complications after surgery, of whom 56.2% (36/64) needed a second-look relaparotomy (Fig. 1). The mortality rate in referral patients was as high as 21.9%, significantly higher than 11.4% in nonreferral patients. Among the 64 patients referred, the mortality rate in the relaparotomy group was 33.3%, which was significantly higher than 7.1% in the single-operation group. In the relaparotomy group, the number of inappropriate assessments of pancreatic injury during the initial operation was significantly higher than that in the single-operation group (72.2% vs 28.6%, $P = 0.014$).

Risk Factors for Prognosis in Patients with Pancreatic Trauma as Determined by Univariate Analysis

As shown in Table 2, there was no significant difference between the survivor and non-survivor groups with respect to sex, BMI, history of upper abdominal surgery, injury, or surgery conditions ($P > 0.1$). Age, ISS score, preoperative hemodynamic status, and the volume of intraoperative blood transfusion, as well as the postoperative CRP, procalcitonin, albumin, and serum creatinine levels, were closely related to prognosis ($P < 0.1$).

Table 2
Univariate analysis of potential risk factors of surgical prognosis in pancreatic trauma

Clinical parameters	Survivor	Non-Survivor	Chi	*P*
Age (year)	37.6 ± 14.1	47.1 ± 11.9	-2.18	0.03
Gender (M/F)	106/22	22/2	0.12	0.73
BMI (kg/m^2)	24.0 ± 2.7	25.7 ± 1.8	-1.257	0.22
ISS (< or ≥ 28)	72/56	6/18	3.95	0.04
Hemodynamic (stable/unstable)	108/20	10/14	8.298	0.00
Types of injury (MVC/falls/SW)	110/10/8	24/0/0	-1.372	0.17
AAST (I/II/III/IV/V)	26/46/34/18/4	8/6/4/2/4	-0.177	0.85
Delayed diagnosis (≤ or > 24 h)	78/50	18/6	0.361	0.58
Management of pancreatic injuries (proper/improper)	102/26	16/8	0.379	0.53
Associated abdominal injuries (0 / 1/ ≥2)	14/48/66	2/4/18	-1.362	0.17
Pre-op CRP (< or ≥ 154 mg/L)	92/36	16/8	0.001	0.98
Pre-op PCT (< or ≥ 4.26 µg/L)	40/88	4/20	0.456	0.49
Pre-op albumin (< or ≥ 30 g/L)	36/92	12/12	1.34	0.24
Pre-op creatinine (< or ≥ 177 µmol/L)	126/2	18/6	-*	0.01
Post-op CRP (< or ≥ 154 mg/L)	104/24	10/14	6.465	0.01
Post-op PCT (< or ≥ 4.26 µg/L)	120/8	18/6	4.248	0.03
Post-op albumin (< or ≥ 30 g/L)	8/120	8/16	5.257	0.02
Post-op creatinine (< or ≥ 177 µmol/L)	126/2	18/6	-*	0.01
Intra-op transfusion (< or ≥ 15 ml/kg)	84/44	4/20	9.936	0.00

Note: * Fisher exact test (when expected value T < 1); BMI: Body Mass Index; AAST: American Association for the Surgery of Trauma; ISS: Injury Severity Score.

Risk Factors for Surgical Prognosis in Patients with Pancreatic Trauma Determined by Binary Logistic Regression Analysis

Sequential logistic regression analysis was conducted using the 8 parameters selected from the above analysis as independent variables and death as the dependent variable (Table 3). The results showed that the independent risk factors for surgery prognosis included age ($P = 0.012$), hemodynamic instability ($P = 0.018$), postoperative CRP ≥ 154 mg/L ($P = 0.016$), and creatinine ≥ 177 μmol/L ($P = 0.017$).

Table 3
Risk Factors of Surgical Prognosis in Pancreatic Trauma Determined by Binary Logistic Regression Analysis

	B	**S.E**	**Wals**	**Sig.**	**Exp (B)**	**95% C.I. of Exp (B)**	
						Lower limit	**Upper limit**
Age	0.197	0.079	6.322	0.012	1.21	1.04	1.421
Hemodynamic status	-4.215	1.785	5.579	0.018	0.15	0.00	0.488
ISS	0.576	1.360	0.179	0.672	1.77	0.12	25.584
Post-op CRP	-3.906	1.625	5.775	0.016	0.02	0.00	0.487
Post-op PCT	1.706	1.480	1.329	0.249	5.50	0.30	100.217
Post-op albumin	1.006	1.334	0.569	0.451	2.73	0.20	37.354
Post-op Cr	-5.887	2.464	5.709	0.017	0.00	0.00	0.347
Volume of transfusion	-1.547	1.299	1.417	0.234	0.21	0.01	2.718

Discussion

Although pancreatic injury is rare, it has an overall mortality of 3–70%[10]. In this study, we included a large retrospective documented cohort of patients with pancreatic trauma treated in a referral trauma center. The mortality rate was 15.8% in this severe pancreatic injury group (ISS median was 27), lower than previous reports[11, 12]. Determining the risk factors that affect the prognosis of patients undergoing surgery for pancreatic trauma is very important for preventing complications and reducing the mortality rate. Here, we conducted univariate and binary logistic regression analyses on several mortality-related parameters collected during the perioperative period. Our study first indicated preoperative hemodynamic instability, postoperative severe inflammation, renal function failure and age to be important determinants of postoperative mortality in pancreatic trauma.

This study indicated that postoperative severe infection (CRP ≥ 154 mg/L) may be an important prognostic factor for survival after surgery in pancreatic trauma. It is currently considered the most valuable acute-phase response indicator[13]. The levels of trypsin released during pancreatic trauma can cause the pancreas and its surrounding tissues to self-digest and cause the influx of a large number of inflammatory factors, such as cytokines, into the blood, which in turn triggers a series of inflammatory responses and results in a drastic increase in CRP. CRP is also a reliable predictor of in-hospital mortality in acute pancreatitis. In this study, the incidence of complications, including postoperative pancreatic fistula, intestinal fistula, and sepsis, was higher in the nonsurvival group. The CRP concentration was significantly higher in patients with postoperative infections.

Multivariate analysis indicated that preoperative hemodynamic instability was also an independent risk factor for surgery prognosis in pancreatic trauma. Traumatic bleeding is the most common cause of hemodynamic instability[14]. Approximately 80% of patients with hemorrhagic shock die in the operating room, and nearly 50% of patients with hemorrhagic shock die within the first 24 hours after injury. Accompanying large vessel injury, hemorrhagic shock associated with pancreatic trauma can cause erosion of the surrounding blood vessels due to pancreatic juice leakage. Repeated intraperitoneal hemorrhage is an important mortality risk in patients with pancreatic trauma[15]. In this study, the mortality rate was as high as 41.2% in unstable patients but only 8.5% in patients with stable hemodynamic status. Logistic regression analysis showed the risk of death in patients with hemorrhagic shock to be 0.150 times that of patients with stable hemodynamic status. For patients with traumatic hemorrhagic shock, the keys to successful damage control resuscitation (DCR) include active control of bleeding, rapid blood and fluid resuscitation, and accurate determination of the endpoint of resuscitation[16]. Despite the use of aggressive resuscitation in patients with hemorrhagic shock, patients are often stressed by repeated hemorrhagic shock, and the mortality rates remained high.

Correlation analysis of the risk factors associated with prognosis also revealed that the occurrence of acute kidney injury (creatinine ≥ 177 μmol/L) was significantly higher in the nonsurvivor group. Posttraumatic AKI is a clinical syndrome that includes sequential events such as trauma-induced renal dysfunction, oliguria or anuria, failure to excrete metabolites, rapid azotemia, fluid and electrolyte imbalance, acid-base imbalance, and a variety of functional changes[17]. Direct renal injury, ischemia-reperfusion injury, rhabdomyolysis, hypovolemic shock, celiac compartment syndrome, and sepsis may contribute to AKI in pancreatic trauma patients. Posttraumatic AKI is an independent risk factor for death after trauma, and it can be used for the early evaluation of kidney injury[18]. After AKI, renal function may recover if the primary cause has been removed, inflammation is controlled, tissue perfusion is preserved, and electrolyte and acid-base balances are well maintained. Few patients develop chronic renal deficiency after trauma.

Although this study represents the largest series of patients with pancreatic trauma, there are several limitations when interpreting these conclusions. First, some on-duty surgeons, especially during the night shift, have limited experience with pancreatic trauma in China. In fact, few surgeons ever see a severe pancreas injury during a lifetime, let alone achieve vast operative experience with these dreaded injuries. A large number of “second-hand” patients have been referred due to the lack of definitive guidelines and appropriate management strategies, which is determined by the current medical running systems. Second, these data were generated from a highly selective cohort of patients treated in a large-volume well-resourced tertiary referral academic level I trauma center. Although these results might be similar to those of other major trauma centers, they may not be applicable to lower-level hospital systems. Finally, and the most obvious, is the limitation that comes with a retrospective, observational study spanning a long time (8 years). One would think that the evolution in knowledge and practice of fluid resuscitation, acute traumatic coagulopathy, transfusion protocols and concepts of damage control surgery and, more recently, damage control resuscitation to have changed over the period. The improvement of health care facilities, clinical strategies and surgeries' preferences may have contributed to the differences; thus, these findings might not provide an authoritative or comprehensive analysis of the current situation.

Conclusions

In conclusion, this study included a large retrospective documented cohort of patients with pancreatic trauma and found that preoperative hemodynamic instability, postoperative severe inflammation, renal function failure, and age were associated with a high mortality rate. Dedicated multidisciplinary involvement with excellent nutritional support, critical surgical care, continuous blood purification and interventional radiological procedures are essential components of care in severe pancreatic trauma patients.

Declarations

Ethical Approval and Consent to participate: All study procedures were approved by the Jinling hospital of Institutional Review Board.

Consent for publication: None declared.

Availability of supporting data: None declared.

Competing interests: None declared.

Funding：Supported by the National Natural Science Foundation of China (Grant No. 81770532 to Dr. Weiwei Ding) and Military Logistics Research Project (Grant No. CLB18J031, to Dr. Weiwei Ding).

Authors' contributions：Chao Yang and Baochen Liu analyzed data and submitted the study. Kai Wang conducted a clinical work. Cuili Wu and Yongle Wang collected the data. Weiwei Ding and Weiqin Li planned the study.

Acknowledgements: None declared.

Authors' information Division of Trauma and Surgical Intensive Care Unit, Research Institute of General Surgery, Jinling Hospital, Nanjing University School of Medicine, Nanjing 210002, Jiangsu Province, P.R.China.

References

1. Shibahashi K, Sugiyama K, Kuwahara Y, Ishida T, Okura Y, Hamabe Y. Epidemiological state, predictive model for mortality, and optimal management strategy for pancreatic injury: A multicentre nationwide cohort study. Injury. 2020;51:59–65.

2. Jurkovich GJ. Pancreatic trauma. J Trauma Acute Care Surg. 2020;88:19–24.
3. Addison P, Iurcotta T, Amodu LI, et al. Outcomes following operative vs. non-operative management of blunt traumatic pancreatic injuries: a retrospective multi-institutional study. **Burns** & **trauma** 2016;4:39.
4. Rozich NS, Morris KT, Garwe T, et al. Blame it on the injury: Trauma is a risk factor for pancreatic fistula following distal pancreatectomy compared with elective resection. J Trauma Acute Care Surg. 2019;87:1289–300.
5. Soreide K. Pancreas injury: the good, the bad and the ugly. Injury. 2015;46:827–9.
6. Ho VP, Patel NJ, Bokhari F, et al. Management of adult pancreatic injuries: A practice management guideline from the Eastern Association for the Surgery of Trauma. **The journal of trauma and acute care surgery** 2017;82:185–199.
7. De Simone B, Sartelli M, Coccolini F, et al. Intraoperative surgical site infection control and prevention: a position paper and future addendum to WSES intra-abdominal infections guidelines. World J Emerg Surg. 2020;15:10.
8. Kao LS, Bulger EM, Parks DL, Byrd GF, Jurkovich GJ. Predictors of morbidity after traumatic pancreatic injury. The Journal of trauma. 2003;55:898–905.
9. Liang TB, Bai XL, Zheng SS. Pancreatic fistula after pancreaticoduodenectomy: diagnosed according to International Study Group Pancreatic Fistula (ISGPF) definition. **Pancreatology** 2007;7:325 – 31.
10. Wiik Larsen J, Soreide K. The worldwide variation in epidemiology of pancreatic injuries. Injury. 2019;50:1787–9.
11. Krige JE, Kotze UK, Setshedi M, Nicol AJ, Navsaria PH. Surgical Management and Outcomes of Combined Pancreaticoduodenal Injuries: Analysis of 75 Consecutive Cases. **Journal of the American College of Surgeons** 2016;222:737 – 49.
12. Antonacci N, Di Saverio S, Ciaroni V, et al. Prognosis and treatment of pancreaticoduodenal traumatic injuries: which factors are predictors of outcome? **Journal of hepato-biliary-pancreatic sciences** 2011;18:195–201.
13. Apple CG, Miller ES, Loftus TJ, et al. Effect of Beta-Blockade on the Expression of Regulatory MicroRNA after Severe Trauma and Chronic Stress. J Am Coll Surg. 2020;230:121–9.
14. Jensen SD, Cotton BA. Damage control laparotomy in trauma. Br J Surg. 2017;104:959–61.
15. Cole E, Weaver A, Gall L, et al. A Decade of Damage Control Resuscitation: New Transfusion Practice, New Survivors, New Directions. **Ann Surg** 2019.
16. Chico-Fernandez M, Barea-Mendoza JA, Perez-Barcena J, Llompart-Pou JA. Plasma-first resuscitation to treat haemorrhagic shock in urban areas. Lancet. 2020;395:562.
17. Hatton GE, Du RE, Pedroza C, et al. Choice of Reference Creatinine for Post-Traumatic Acute Kidney Injury Diagnosis. J Am Coll Surg 2019;229:580–8 e4.
18. Hatton GE, Du RE, Wei S, et al. Positive Fluid Balance and Association with Post-Traumatic Acute Kidney Injury. **J Am Coll Surg** 2019.

Figures

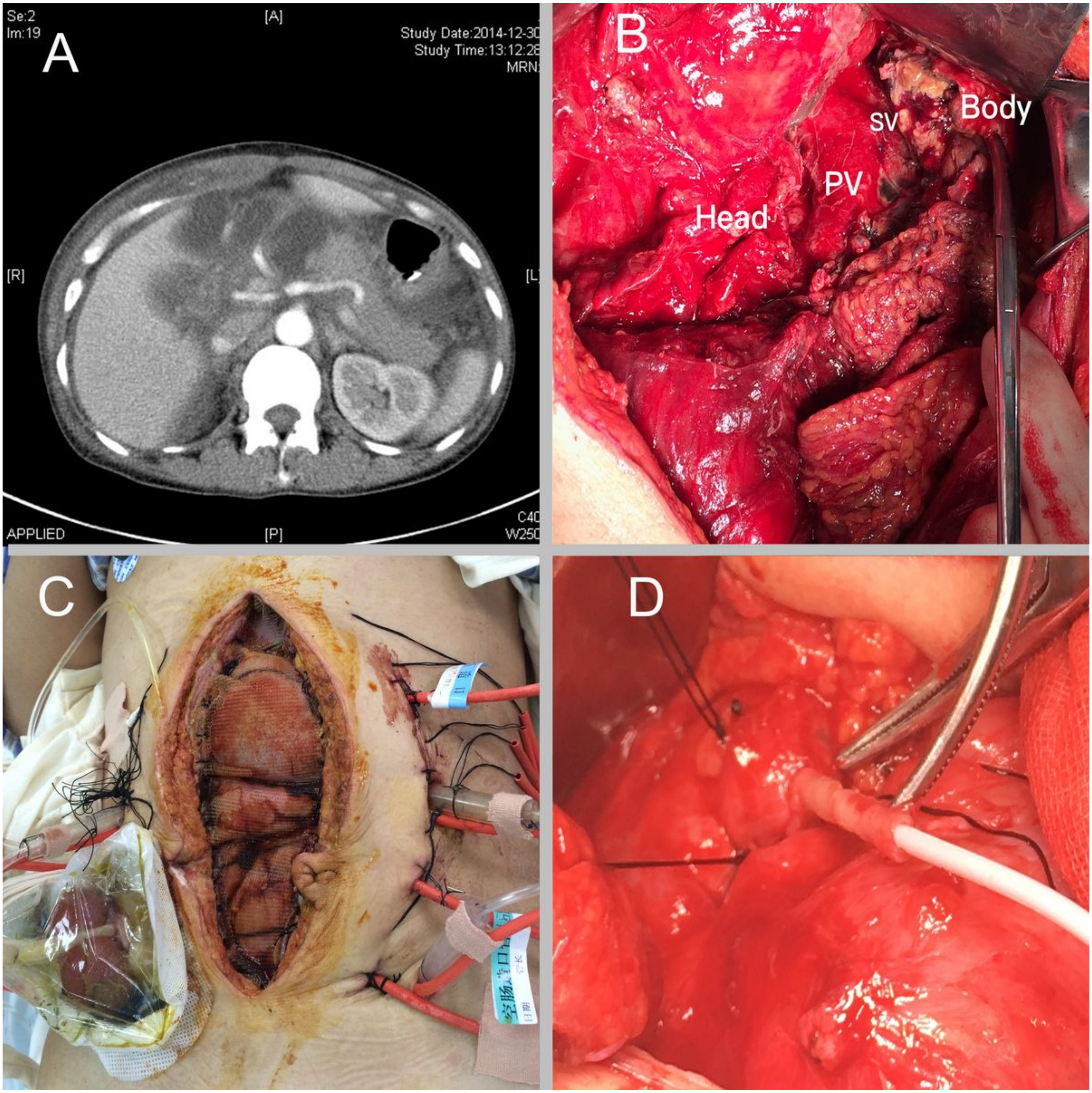

Figure 1

A 45-year-old female patient was transferred because of hemodynamic instable three days after motor vehicle crash. A. Contrast-enhanced CT scan taken 3 days after injury showed the complete transection of pancreatic neck and peripancreatic fluid collection; B. The intraoperative finding confirms completely transection at the left side border of the superior mesenteric vein and several intestinal perforations (one in duodenum, two in ileum) were also found and repaired; C. Damage control laparotomy was performed, including intestinal stoma, external drainage of pancreatic main duct, closed suction drainage of abdominal cavity and temporary abdominal closure (TAC). Primary facial closure was reached 2 weeks after the first laparotomy; D. A definitive pancreaticojejunostomy was performed six months later. Note the white indwelling tube of pancreatic main duct.