African Journal of Pharmacy and Pharmacology Vol. 6(25), pp. 1865-1869, 8 July, 2012
Available online at http://www.academicjournals.org/AJPP
DOI: 10.5897/AJPP12.357
ISSN 1996-0816 ©2012 Academic Journals

Full Length Research Paper

Risk factors analysis of severe acute pancreatitis complicated with acute cholecystitis in later stage

Lin Ouyang*, Can Hou, Zhihui He, Guobao Wu and Youdi Lv

ICU center, The Second Xiangya hospital, Central-south University, Changsha 410011, China.

Accepted 8 June, 2012

To explore the risk factors and clinical significance of severe acute pancreatitis (SAP) complicated with acute cholecystitis (AC) in later stage. With case-control study method, collected clinical data of 42 cases of SAP complicated with AC patients (the experimental group) and 210 cases of SAP patients (the control group) from March, 2002 to March, 2011. Then used single factor non-conditional logistic regression method and multiple factors logistic regression method to screen the risk factors of SAP-AC. Single factors logistic regression showed that biliary lithiasis, Balthazars computed tomographic (CT) score, APACHE II score, local and systemic complication, somatostatin time, total parenteral nutrition (TPN) lasting time, glucocorticosteroid application, operation, etc, significantly affected SAP-AC. And multiple factors logistic regression showed that biliary lithiasis, APACHE II score, somatostatin application time, TPN lasting time and glucocorticosteroid application significantly affected SAP-AC. This study found that biliary lithiasis, APACHE II score, somatostatin time, TPN lasting time and glucocorticosteroid application were significant risk factors of SAP-AC. More attention should be paid on its predictive value; thus, the mortality and morbidity could be clinically reduced.

Key words: Severe acute pancreatitis (SAP), acute cholecystitis (AC), risk factors.

INTRODUCTION

As one of the surgical severe diseases, severe acute pancreatitis (SAP)'s morbidity tends to rise year by year. SAP can be induced by eating or drinking too much, irrational use of drugs, and acute cholecystitis (AC). Biliary SAP is the most common inducing factor among the mentioned ones (Acevedo et al., 2011). In the wake of the treating and technique progress of SAP, the recovery rate has increased, but at present the fatality rate is still quite high (Di Fabio et al., 2011 and De-Madaria, 2011). If diagnosed timely, SAP can be remitted and cured by drugs, operations and percutaneous transhepatic gallbladder drainage (PTGBD). In the later stage of non-biliary SAP, symptoms such as high fever and shiver etc. appear in some patients. SAP in this stage was often complicated by various local and systemic complications, which became "second strikes" to patients and make the conditions worse, prognosis poorer and mortality rate higher. In this study, we collected clinical data of 45 cases of patients of SAP complicated with AC in the later stage during March, 2002 to March, 2011 in our hospital, then screened the risk factors of SAP-AC for the sake of helping clinicians to understand the complications.

*Corresponding author. E-mail: ouyanglin95@yahoo.cn.

MATERIALS AND METHODS

General information

We collected 225 patients from SICU of surgical department in our hospital during March, 2002 to March, 2011, including 45 SAP-AC cases (the experimental group) and 180 SAP cases (the control group). There were 125 male cases and 55 female cases in total; their average age is 49.52 ± 12.65 (37 to 71) years. The ultrasonic and computed tomography (CT) scan etc. within 48 h after admitted to the hospital showed there were 85 cases with cholecyslithiasis or choledocholithiasis, including 42 cases complicated with stones in intrahepatic bile duct, 78 cases without hepatolithiasis, 42 cases with hyperlipidaemia, 82 cases with obesity, 25 cases with emaciation, 42 cases with normal weight; when classified by cause, there were 71 overdrinking cases, 65 gluttony cases, 34 drug-oriented cases, 55 cases with other reasons or unexplained reasons, the average hospital stays is 42.56 ± 15.64 (32 to 69) days.

The adopting and rejecting diagnostic criteria

All the patients fitted the diagnostic criteria (Acevedo et al., 2011) established by the pancreatic surgery group of the surgery branch, Chinese Medical Association. According to the four phases staging method (Ripollés et al., 2010), (Gangrene acute reaction phase, tissue liquefaction secondary infection phase, tissue infection-necrosis-fall off and later stage complications phase, pancreatitis recovery phase), cases fit the later two phases were brought into the study. Rejecting criteria: (1) cases who have underwent surgery of cholecystectomy; (2) cases who have been clarified a diagnosis as arterial blood pressure (ABP) or complicated with AC in the early stage/progressing stage;(3) cases complicated with cancer, chronic cholecystitis, immunologic diseases;(4) pregnant or of breast-feeding woman; (5) age ≥ 70 years; (6) cases directly recovered from the stage of inflammatory reaction or died in a short time. AC diagnostic criteria: (1) pain, tenderness and rebound tenderness in the right hypochondriac region, Murphy's levy (+); (2) fever, white blood cell count or C-reactive protein (CRP) value rose; (3) ultrasound or CT scan examination showed the cholecyst swelled, thickening in the walls, high tensioned, fluid surrounded etc. In accordance with these criteria, this retrospective study adopted 225 patients, among whom there were 45 secondary AC cases (20.00%) as secondary group, and the other 210 cases as control group.

Treatment

All the patients were given the treatment of inhibiting pancreatic secretion, maintaining homeostasis, preventing infection, nutritional support, the vital organs' care and support, and in necessity applying the Chinese herbal "Compound Qingyi Decoction" for assistance. All the patients were given enteral nutrition through jejunum nutrition when it was safe to applying and their vital signs smoothed, bowel function recovered. The tip of jejunum nutrition tube must locate 20 cm under the Treitz ligament. The patients were given PTGBD or surgical therapy when they were complicated with infection of pancreatic necrosis tissue, haemorrhage, peripancreatic abscess, gastrointestinal fistula, etc.

Treatment for AC

Patients complicated with AC were given PTGBD guided by ultrasound while given conventional anti-infection therapy. Puncture steps: laid patients in supine position, regularly disinfected skin and spread towels, chose proper puncture points, took a 0.4 cm incision after local anesthesia, guided by ultrasound, the catheter groups penetrated into the gallbladder along the oriented percutaneous transhepatic paths, the paths by hepar were approximately 1.5 to 2.0 cm long, exited the stylet as soon as bile could be drawn out, meanwhile, placed the pigtail drainage catheter on this opportunity, exhausted the bile and fixed the drainage tubes, conventionally delivered the bile for training and antibiotic sensitivity tests, flushed their gallbladders with normal saline or 0.5% metronidazole solution everyday from the next day until the bile drainage unblocked. The PTGBD drainage tube could not be removed until SAP has been stable and radiography showed the biliary tract unobstructed.

Note the index

Note patients' general condition, for example, age, gender, alcoholic causes, obesity, biliary lithiasis, hyperglycemia, hyper-lipidemia, APACHE II score, Balthazars CT score, meantime note the systemic complications; ALI/ARDS, AKI, AHI, Sepsis, fungus infection, shock, LAH, ACS, MODS etc. as well as occurrence of local complications (pancreatic tissue haemorrhage, necrosis infection, gastrointestinal fistula, peripancreatic abscess etc.) application time of somatostatin during the treatment, total parenteral nutrition (TPN) lasting time, EN lasting time, NMV, CRRT, sedative drugs, glucocorticosteroid applications, blood transfusion, puncture, surgery etc.

Statistical analysis

To analyze the data with statistical software SPSS 17.0, expressed measurement data with $\bar{x} \pm s$, express frequency material with percentage or (%), adopted the single factor and multifactor unconditional logistic regression analysis, $P < 0.05$ indicated statistical significance.

RESULTS

Single factor logistic regression analysis

Factors which can affect the secondary onset of AC were analyzed with single factor unconditional logistic regression analysis, then analyzed the significant variable quantity including biliary lithiasis, hyperlipaemia, APACHE II score, Balthazars CT score, fungus infection, IAH,ACS,MODS, pancreatic tissue necrosis infection, gastrointestinal fistula, pancreatic necrotic tissue haemorrhage, somatostatin application time, TPN lasting time, glucocorticosteroid application, surgery etc. with singer factor analysis detailed (Table 1).

Multifactor logistic regression analysis

Set the dependent variable ($y_{cases} = 1$, $y_{comtrol} = 0$) on the basis of AC whether to occur or not, adopted 15 significant variable in the single factor logistic regressive analysis method and multifactor logistic regressive analytical method. Screened model variable with stepwise analysis, model test ($\chi^2 = 134.689$, $P < 0.05$, $R^2 = 0.468$) showed there was statistical significance. Receiver operating characteristic (ROC) curve analysis also proved the multifactors logistic regressive analytical mode was reliable. At last, the adopted variables with statistical significance included biliary lithiasis, APACHE II score, somatostatin application time, TPN lasting time, glucocorticosteroid application, transfusion, hyperlipidemia etc. which were all significant risk factors (Table 2).

DISCUSSION

Causes which induced AC were various, commonly including biliary lithiasis, drugs, alcohol, gluttony, hyperlipemia etc. and biliary lithiasis is the most common

Table 1. single factor unconditional logistic regression analysis result for the factors which affected the secondary onset of AC.

Index	B	S.E.	Wald	P	OR	95%CI.OR	
						Lower	Upper
Age	0.021	0.016	2.985	0.075	1.013	0.975	1.095
Gender (male)	-0.081	0.336	0.055	0.817	0.916	0.468	1.799
Alcoholic causes (yes)	-0.582	0.387	2.342	0.133	0.549	0.199	1.181
Obesity (yes)	0.102	0.334	0.087	0.766	1.098	0.566	2.122
Biliary lithiasis (yes)	0.488	0.119	12.788	0.001	1.579	1.223	2.012
Hyperglycemia (yes)	1.316	0.712	5.195	0.061	4.002	1.101	9.288
Hyperlipaemia (yes)	1.309	0.544	15.112	0.001	5.999	2.274	12.266
APACHE II score	0.478	0.936	12.114	0.002	1.588	1.074	1.867
Balthazars CT score	0.356	0.538	36.472	0.001	1.365	1.187	1.532
Systemic complications							
ALI/ARDS (yes)	0.263	0.365	0.626	0.388	1.299	0.561	2.433
AKI (yes)	0.401	0.475	0.788	0.432	1.521	0.614	3.701
AHI (yes)	0887	1.198	0.533	0.4452	2.435	0.206	26.773
Sepsis (yes)	0.121	0.602	0.033	0.827	1.073	0.344	3.473
Fungus infection (yes)	1.854	0.754	6.268	0.009	7.188	1.496	31.473
Sepsis (yes)	0.191	0.597	0.048	0.867	1.288	0.486	3.824
Shock (yes)	0.906	0.547	2.702	0.115	2.423	0.888	6.506
IAH (yes)	1.711	0.387	22.000	0.001	5.412	2.677	10.721
ACS (yes)	1.387	0.712	4.534	0.043	4.423	1.212	16.971
MODS (yes)	0.887	0.367	5.124	0.018	2.466	1.139	5.336
local applications							
Pancreatic tissue necrosis infection(yes)	2.212	0.418	31.185	0.000	9.130	4.221	20.001
Peripancreatic abscess (yes)	-0.168	0.996	0.025	0.821	0.801	0.083	6.982
Gastrointestinal fistula (yes)	1.534	0.336	17.879	0.001	5.145	2.369	10,897
Pancreatic necrotic tissue haemorrhage (yes)	2.221	0.701	11.112	0.000	8.619	2.322	32.022
Somatostatin application time	0.308	0.114	9.672	0.003	1.377	1.167	1.612
EN lasting time	0.040	0.008	29.998	0.000	1.102	1.122	1.082
TPN lasting time	0.6751	0.344	2.943	0.188	1.983	0.978	4.016
CRRT (yes)	0.588	0.346	2.675	0.096	1.812	0.813	3.561
NMV (yes)	0.599	0.312	3.199	0.067	1.673	0.833	3.568
Sedative (yes)	2.488	0.412	33.556	0.076	10.776	5.002	20.129
Glucocorticosteroid application (yes)	2.781	0.465	41.546	0.000	13.785	6.217	30.129
Transfusion (yes)	1.993	0.355	28.883	0.001	7.331	3.536	14.552
Puncture (yes)	0.466	0.574	0.673	0.494	1.525	0.427	4.729
Surgery (yes)	0.666	0.376	3.356	0.087	1.925	1.012	3.810

one of the mentioned ones, It takes 50% of all the cases (Kimura et al., 2010; Lowenfels et al., 2009). So, in the early stage of SAP, namely the acute response stage, It was often complicated with AC, which makes the diagnosis easier. Parts of the patients' conditions can be controlled by pharmacotherapy.

A few patients' conditions can be remitted by PTGBD or cholecystectomy. But in clinical practice, we have found that a few patients could also suffer the secondary onset of AC with symptoms such as hyperpyrexia in the later stage of SAP, namely the infection stage/residual infectious period and recovery stage. At that time, the patients were often complicated by various local and systemic complications, additionally the secondary onset AC had no specific clinical manifestation and often cross mixed with manifestations such as systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndro (MODS), all the result in a lack of cognition toward the situation which often lead to a delayed diagnosis or misdiagnosis (Sanjay et al., 2008).

Table 2. Multifactor logistic regressive analysis result on factors which affected the secondary onset of AC (Stepwise analysis).

Index	B	S.E.	Wald	P	OR	95%CI.OR	
						Lower	Upper
Biliary lithiasis	1.198	0.721	5.135	0.013	3.012	1.820	4.749
APACHE II score	0.287	0.067	14.998	0.001	1.274	1.027	1.501
EN lasting time	0.028	0.008	14.221	0.001	1.001	9.989	1.012
Somatostatin application time	0.321	0.153	4.198	0.031	1.399	1.021	1.683
Glucocorticosteroid application	1.772	0.619	9.952	0.003	5.410	1.902	14.893
Transfusion	1.633	0.664	11.151	0.003	6.332	2.299	15.001
Hyperlipidemia	1.883	0.712	10.119	0.002	5.675	2.003	14.668
Constant	-5.171	0.990	26.215	0.000	0.002		

Second strike to the patients is “second strikes” which make the condition worse. Gangrenous cholecystitis may also occur during the course of SAP and disturb the recovery process, aggravate the physiological metabolic disturbance, make the infection uncontrollable and the treating more difficult. If gangrenous cholecystitis SAP do occur as a secondary onset of AC patients, the situation will inevitably be very critical, and the prognosis will be very poor (Scheele and Kujath, 2006; Mizaushev，1983). So the assessment of the related risk factors of SAP prognosis is beneficial to correct intervention in time, improve the prognosis, reduce the hospital expenses and hospital mortality.

So far, there are lots of classification systems to classify the advanced paramedics (AP)’s severity, including Ranson score system (Aphinives et al., 2011). Acute pancreatitis: assessment severity with Ranson score and CT evaluation [J]. J Med Assoc Thai, 2011, 94(4):437-40, APACHE II (Alhajeri and Erwin, 2008) and Balthazars CT score system etc. But the Ranson score system cannot be established without 48 h, examinations such as CT cannot be easily accomplished by bedside, APACHE II needed to be accomplished within 24 h, but there are so many indexes and it is very complicated to assess. Dispute on which standard is better and more valuable for prognosis still existed, so it is necessary to clearly know which standards can assess the occurrence of SAP-AC more accurately.

This study evaluates every index which may affect the SAP-AC comprehensively. Firstly, acquired 15 index which may affect the morbidity by screening with single factor analysis, then the 15 index were adopted as multifactor model, ultimately we got indexes as: Biliary lithiasis, APACHE II score, somatostatin application time, TPN lasting time, glucocorticosteroid application, transfusion and hyperlipidemia. The patients got higher risk to suffer a secondary AC and gangrenous cholecystitis when they were complicated with Biliary lithiasis, got higher APACHE II score, were given somatostatin and TPN for longer time, and massive transfusion and glucocorticosteroid application. They are all the intimate risk factors of SAP-AC. This conclusion was similar with the result reported by Schutte and Malfertheiner (2008) and Shinzeki and Ueda (2008). Consulting those indexes clinically can generally predict the occurrence risk of SAP-AC, if clinicians use them for reference and combined with their clinical experiences to make an early prediction. Tt has certain significance for reference to reduce the morbidity SAP-AC.

The treating technology and prognosis of SAP are both challenging topic inclinical research, and lots of scholars have conducted their research on this. Risk factors and prognosis of SAP has been reported a lot by domestic and overseas scholars. Kochhar et al. (2011) considered that fungus infection is closely related with the prognosis of acute pancreatitis. Balnykov and Petrenko, (2010) considered that lower Glasgo scale score, leukocytosis and hypoproteinemia etc. are intimately related risk factors of pancreatitis prognosis. Martínez et al. (2006) and Hong et al. (2011) both considered that obesity is an intimately related risk factor of morbidity and prognosis of SAP. The reports on risk factors which affect prognosis of AC are not entirely consistent. Further study is demanded to reach a consensus. SAP-AC is a complicated and polytropic pathological evolution process including both local pancreatic pathological changes and systemic reactions. Ideal indexes to evaluate the risk factors of SAP-AC should have characteristics as follows: early to predict the course of disease, early to evaluate the criticality and prognosis relevance; the assessment method is simple to operate, convenient for clinically applications, without aggression, well repeatable. So far, there is no predictive model to precisely evaluate the criticality of SAP-AC. Clinical evaluation often assessed by adopting single index with doctors’ working experiences. It is rather experimental and deflective.

More attention should be paid to the fact that the SAP-AC risk factors demonstrated in this article do not equal the risk factors of morbidity and prognosis in SAP, but they are surely closely related. Risk factors of SAP-AC are rarely reported; this study tentatively summarizes the topic, though shortages are unavoidable. The predictive

value needs to be further studied and confirmed, before it can be perfectly use in clinical practice.

REFERENCES

Acevedo TA, Targarona MJ, Málaga RG (2011). Identifying the severe acute pancreatitis. Rev. Gastroenterol. Peru., 31(3): 236-240.

Alhajeri A, Erwin S (2008). Acute pancreatitis: value and impact of CT severity index. Abdom. Imag., 33(1): 18-20.

Aphinives P, Karunasumetta C, Bhudhisawasdi V (2011). Acute pancreatitis: assessment severity with Ranson score and CT evaluation. J. Med. Assoc. Thail., 94(4): 437-440

Balnykov SI, Petrenko TF (2010). Prediction of the outcome in patients with necrotic pancreatitis. Khirurgiia (Mosk), (3): 37-40.

De-Madaria E (2011). The pancreas and the biliary tract. Acute pancreatitis. Gastroenterol. Hepatol., 34(S2): 89-92.

Di FF, Abu HM, Johnson CD (2011). Acute pancreatitis: mild, severe or potentially fatal. Pancreatology, 11(4): 373-375.

Hong S, Qiwen B, Ying J (2011). Body mass index and the risk and prognosis of acute pancreatitis: a meta-analysis. Eur. J. Gastroenterol. Hepatol., 23(12): 1136-1143.

Hong W, Dong L, Huang Q (2011). Prediction of severe acute pancreatitis using classification and regression tree analysis. Dig. Dis. Sci., 56(12): 3664-3671.

Kimura Y, Arata S, Takada T (2010). Gallstone-induced acute pancreatitis. J. Hepatobiliary Pancreat. Sci., 17(1): 60-69.

Kochhar R, Noor MT, Wig J (2011). Fungal infections in severe acute pancreatitis. J. Gastroenterol. Hepatol., 26(6): 952-959.

Lowenfels AB, Maisonneuve P, Sullivan T (2009). The changing character of acute pancreatitis: epidemiology, etiology, and prognosis. Curr. Gastroenterol. Rep., 11(2): 97-103.

Martínez J, Johnson CD, Sánchez-Payá J (2006). Obesity is a definitive risk factor of severity and mortality in acute pancreatitis: an updated meta-analysis. Pancreatology, 6(3): 206-209.

Mizaushev BA (1983). A case of gallbladder amputation in acute gangrenous cholecystitis and pancreonecrosis. Klin Khir, (9): 56.

Ripollés T, Martínez MJ, López E (2010). Contrast-enhanced ultrasound in the staging of acute pancreatitis. Eur. Radiol., 20(10): 2518-2523.

Sanjay P, Yeeting S, Whigham C (2008). Endoscopic sphincterotomy and interval cholecystectomy are reasonable alternatives to index cholecystectomy in severe acute gallstone pancreatitis (GSP). Surg. Endosci., 22(8): 1832-1837.

Scheele J, Kujath P (2006). Candida peritonitis in a patient with necrotising cholecystitis and pancreatitis. Mycoses, 49(4): 340-342.

Schutte K, Malfertheiner P (2008). Markers for predicting severity and progression of acute pancreatitis. Best Pract. Res. Clin. Gastroenterol., 22(1): 75-90.

Shinzeki M, Ueda T (2008). Prediction of early death in severe acute pancreatitis [J]. J. Gastroenterol., 43(2): 152-158.