

Optimal fluid volume administration in acute pancreatitis: Some developments for an open question

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Introduction

Acute pancreatitis is an inflammatory disease of the pancreas whose treatment includes fluid resuscitation. However, aggressive fluid therapy (infusion of high fluid volumes) has been considered associated with the development of complications in the patient's evolution. The optimal volume of fluids to administer to the patient in the first hours is an open question with an obvious interest in clinical practice. This study aimed to determine if the volume of fluids administered in the first hours is associated with the development of particular complications and also to establish a critical value for the volume of fluids above which the risk of complication development becomes imminent. Local, late and systemic complications, as well as the presence of infection and need for surgery, were the complications assessed in this study.

Methods

All patients with the diagnosis of acute pancreatitis, admitted to the intermediate surgical care unit in Tondela-Viseu Hospital Centre, between 2007 and 2016, were included in the study sample. Data for these 216 patients include demographic information and clinical variables such as hematocrit, C-reactive protein (CRP), type of crystalloid used (Ringer's lactate, normal sodium chloride, normal polyelectrolytic solution), use of colloids, type of pancreatitis (edematous, necrotizing), glycemia (controlled, uncontrolled), etiology (ethanol, gallstones, others), pancreatitis classification (ATLANTA 2012), time of evolution (<12h, 12-24h, >24h), among others.

For each complication, the patients were divided into two groups: the group of patients who developed (D) and the group who did not develop (ND) the complication. In the first stage, the two groups were compared concerning several clinical and demographic variables to determine which variables or factors were associated with the development of the complication. Qui-square tests or Fisher's exact tests were used for qualitative variables and t-tests or Mann-Whitney tests were used for quantitative ones.

After observing that the amount of fluids administered in the first 24 hours, and in the first 48 hours, significantly differentiated the two groups, D and ND, ROC (Receiver Operating Characteristic) analysis was used to evaluate the discriminative ability of these variables in the separation of the two groups and also to obtain a critical value of fluids that could better discriminate them. Furthermore, considering the critical value found in the ROC analysis, the significance of the impact of an administration of fluids above the critical value was assessed through logistic regression. Logistic regression models were estimated only with two variables at each time: the dummy variable indicating a fluid administration above the critical value and each one of the variables significantly related with the complication development as indicated by the first stage of the statistical analysis (univariate comparisons of groups D and ND). This strategy was adopted as, for several complications, group D included around 20 patients, which made it unreasonable to construct regression models with many variables (Peduzzi et al., 1996).

Results

Table 1 presents the AUCs (Area Under Curve) for the ROC curves associated with each complication and the cutoff values found for both 24h and 48h fluids volume. Except for systemic complications, the AUCs for fluids at 48h are approximately equal to 0.8 suggesting an excellent discriminant ability to distinguish patients with the complication. The AUCs for the fluids at 24h are only slightly lower. The logistic regression models indicate that a fluid administration greater than the cutoff value is significantly associated with a higher risk of complication, when controlled, one at a time, the other variables that have shown to be significantly associated with the complication.

Table 1: AUC and cutoff values obtained from ROC analysis

Complication	Fluids at 24 hours		Fluids at 48 hours	
	AUC	Cutoff	AUC	Cutoff
Local complications (29 patients)	0.742 (p<0.0005)	4000 ml	0.793 (p<0.0005)	7000 ml
Late local complications (18 patients)	0.836 (p<0.0005)	4200 ml	0.858 (p<0.0005)	7700 ml
Systemic Complications (127 patients)	0.646 (p<0.0005)	3550 ml	0.675 (p<0.0005)	6400 ml
Presence of Infection (17 patients)	0.793 (p<0.0005)	4100 ml	0.846 (p<0.0005)	7200 ml
Surgery need (17 patients)	0.752 (p<0.0005)	4100 ml	0.807 (p<0.0005)	7200 ml

Discussion and conclusions

Management of acute pancreatitis is still challenging and, in particular, early fluid therapy is still a matter under discussion. Evidence has been provided on the relation of an aggressive fluid therapy with the development of complications (Stigliano et al., 2017; Gravante et al., 2009). This study supports that evidence and suggests values of fluids below 7700 ml in the first 48 hours in order to avoid complications.

References

- Gravante G, Garcea G, Ong SL, Metcalfe MS, Berry DP, Lloyd DM, Dennison AR. Prediction of mortality in acute pancreatitis: a systematic review of the published evidence. *Pancreatology*. 2009;9(5):601-14.
- Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *Journal of clinical epidemiology*. 1996 Dec 1;49(12):1373-9.
- Stigliano S, Sternby H, de Madaria E, Capurso G, Petrov MS. Early management of acute pancreatitis: a review of the best evidence. *Digestive and Liver Disease*. 2017 Jun 1;49(6):585-94.