

Cardiovascular Alterations Associated with Acute Pancreatitis

Raffaele Pezzilli^{1*}, Alessandra Barassi² and Gianvico Melzi d'Eril²

¹Pancreas Unit, Department of Digestive Disease and Internal Medicine, Sant'Orsola-Malpighi Hospital, Bologna, Italy

²Clinical Biochemistry Laboratory, Department of Medicine, Surgery and Dentistry, San Paolo Hospital, University of Milan, Milan, Italy

Keywords: Acute pancreatitis; Cardiac markers; Severity assessment; Acute myocardial infarction

The Question

Acute pancreatitis is clinically characterized by abdominal pain accompanied by elevated serum levels of pancreatic enzymes (amylase and lipase). Pain is the hallmark of acute pancreatitis and, as a presenting symptom, it is localized in the epigastrium in more than 60% of patients having mild or severe disease [1]. Thus, the differential diagnosis is sometime difficult because acute pancreatitis may mimic other diseases and, in particular, acute coronary syndrome [2]. In addition, the acute illness of the pancreas is associated with a number of metabolic abnormalities, such as hypocalcemia and hypophosphatemia which may cause hemodynamic changes. Variations in the concentration of ionized calcium have been directly correlated to clinically significant changes in myocardial contractility.

The Clinical Evidence

In 1934, Drummond first reported electrocardiographic changes in acute pancreatitis [3] and paroxysmic atrial fibrillation has been anecdotically reported [4]. Clinical studies have identified electrocardiographic changes and the pericardium alterations due to hemodynamic status [5]. Experimental studies have reported that in acute pancreatitis there are myocardial ultrastructural disturbances, including interstitial edema and cardiomyocyte hypoxia [6], myofiber overcontractility, intercellular edema between the cardiomyocytes, and cardiomyocyte hypertrophy with collagenization of myocardial stroma [7].

The electrocardiographic alterations in acute pancreatitis are diverse, such as tachyarrhythmia or bradyarrhythmias, atrial flutter and atrial fibrillation, supraventricular premature contractions, short PR interval, QRS prolongation, various bundle-branch blocks (such as left bundle-branch block, right bundle-branch block, and left anterior hemiblock), non-specific changes in depolarization, decreased T-wave voltage, T-wave changes, and ST-segment abnormalities; these alterations are often seen in approximately 50% of patients [8,9]. Evaluation of left ventricular function early in the natural history of acute pancreatitis has also been investigated and has been reported to be frequent in severe acute pancreatitis patients [10]. Echocardiographic assessments based on clinical parameters of severity are likely to be of help in selecting those patients who merit highly intensive treatment.

The Experimental Evidence

Easy and largely available serum markers are required to rapidly identify those patients having a cardiac involvement during the course of acute pancreatitis. In clinical practice, the presence of elevated troponin levels has been anecdotically found in patients with acute pancreatitis without myocardial acute damage. In a recent study, we evaluated the presence of elevated levels of High-Sensitivity Cardiac Troponin (hs-TnT) in patients with acute pancreatitis [11], and we found that more than 35% of them had high serum levels of this cardiac marker. However, the absence of any clinical and electrocardiographic

features of acute coronary syndrome in our patients suggests that abnormally high results should be interpreted not as acute cardiac injury but as the possible presence of rhabdomyolysis. In fact, in a study on the determination of myoglobin in acute pancreatitis patients [12], we found that 20% of acute pancreatitis patients had serum myoglobin concentrations above the upper normal limit and that patients with mild pancreatitis had serum concentrations of myoglobin similar to those with severe pancreatitis. In addition, in a prospective study assessing the clinical performance and temporal evolution of serial CPK-MB isoform, troponin I, troponin T and myoglobin, Kost et al. [13] found that troponin T had a sensitivity of 90% in detecting cardiac injury with a specificity of 91%; similar results have been reported by others [14,15]. In the Kost et al. study [13], only troponin I was able to correctly classify patients with rhabdomyolysis whereas troponin T failed to do so. In conclusion, we believe that troponin I should be used in assessing cardiac damage in acute pancreatitis patients, but additional studies exploring this possibility are needed.

The Future Direction

Other markers of cardiac damage would be useful for a more in-depth evaluation of cardiac involvement in acute pancreatitis of varying severity.

Arginine Vasopressin (AVP), also called Antidiuretic Hormone (ADH), is one of the key hormones for cardiovascular homeostasis. Despite its pivotal role in cardiovascular disease, the measurement and diagnostic use of AVP have never reached clinical practicability, due to the considerable technical challenges related to the short plasma half-life of AVP, interaction with platelets in the serum, and small quantity. Copeptin, which was described for the first time by Holwerda [16], is a glycosylated 39-amino acid long peptide with a leucine-rich core segment. Copeptin and AVP share the same precursor peptide, the 164-amino acid long preprovasopressin, which consists of a signal peptide, AVP, neurophysin II and copeptin. Thus, copeptin is the C-terminal part of pro-AVP (CT-pro-AVP) and is released together with AVP during precursor processing. In contrast to AVP, copeptin is very stable in serum or plasma at room temperature, and is easy and robust to measure. In contrast to many other biomarkers, the copeptin plasma concentration was similar in different age groups and showed no correlation with age. A particularly interesting observation was the response of circulating

***Corresponding author:** Raffaele Pezzilli, Pancreas Unit, Department of Digestive Disease and Internal Medicine, Ospedale Sant'Orsola-Malpighi Via G. Massarenti, 940138 Bologna, Italy, Tel: 39-051-636-4148; Fax 39-051-636-4148; E-mail: raffaele.pezzilli@aosp.bo.it

Received September 22, 2012; **Accepted** September 23, 2012; **Published** September 26, 2012

Citation: Pezzilli R, Barassi A, Melzi d'Eril G (2012) Cardiovascular Alterations Associated with Acute Pancreatitis. *Pancreat Disorders Ther* 2:e118. doi:10.4172/2165-7092.1000e118

Copyright: © 2012 Pezzilli R, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

copeptin levels as a result of an acute myocardial infarction [17]. Copeptin levels were higher in patients who died or were readmitted with heart failure as compared to event-free survivors. The combined measurement of plasma copeptin together with B-natriuretic peptide [18] concentrations could further improve outcome prediction in these patients and should be investigated in acute pancreatitis patients in order to select those patients who require more intensive support.

Adrenomedullin (ADM) also merits our attention; ADM is a 52-amino-acid peptide which is elevated in heart failure and post-acute coronary syndrome. Isolated in human pheochromocytoma, it is also present in the heart, brain, lung, kidney and gastrointestinal organs, and elicits its potent vasodilatory activity through an increase in cyclic adenosine monophosphate levels. Plasma concentrations of ADM are increased in patients with myocardial infarction [19] and correlate with the severity of congestive heart failure. The reliable quantification of ADM is hindered by a short half-life and technical difficulties. The identification of Mid-regional Pro-adrenomedullin (MR-proADM) [20,21] which has overcome these problems, since it is a stable peptide, possibly reflecting the concentration of ADM, is theoretically secreted in amounts equimolar to those of ADM, and most likely does not have any physiological effects which might explain its apparent stability. Plasma MR-proADM concentrations predict an adverse outcome in patients in the recovery phase of myocardial infarction and appear to add information beyond the strong predictor N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP). No studies exist using ADM and NT-proBNP in acute pancreatitis patients and this topic should be explored in order to obtain more accurate information regarding cardiac involvement in acute pancreatitis. We have also recently reported that MR-proADM is a good predictor of mortality in patients with septic shock [20] and we believe that this molecule may have a practical role in patients with infected pancreatic necrosis.

Conclusion

The precise mechanism of myocardial injury during the course of acute pancreatitis still remains unclear. In clinical practice, laboratory examinations are needed to distinguish Emergency Room patients with epigastric pain having acute pancreatitis from those with acute myocardial infarction because the treatment strategy of the two diseases differs markedly. In addition, every effort should be made to identify acute pancreatitis patients at high risk of cardiovascular disease; the new above-mentioned markers, such as ADM and NT-proBNP, can be used for this purpose.

References

- Uomo G (2001) Presentazione clinica. La pancreatite acuta in Italia. Studio osservazionale su 1005 casi. *Press Service (Firenze)* 17-22.
- Pezzilli R, Bellacosa L, Barakat B (2010) Abdominal pain and ECG alteration: a simple diagnosis? *Adv Med Sci* 55: 333-336.
- Drummond J (1934) Cardiac abnormalities of abdominal origin. *S Afr Med* 8: 520-526.
- Gullo L, Labriola E, Di Benedetto S, Priori P, Iannacci P, et al. (1988) Acute pancreatitis associated with paroxysmal atrial fibrillation. A case report. *Panminerva Med* 30: 111-113.
- Di Carlo V, Nespoli A, Chiesa R, Staudacher C, Cristallo M, et al. (1981) Hemodynamic and metabolic impairment in acute pancreatitis. *World J Surg* 5: 329-339.
- Banks PA (2002) Epidemiology, natural history, and predictors of disease outcome in acute and chronic pancreatitis. *Gastrointest Endosc* 56: S226-S230.
- Saulea A, Costin S, Rotari V (1997) Heart ultrastructure in experimental acute pancreatitis. *Rom J Physiol* 34: 35-44.
- Pezzilli R, Barakat B, Billi P, Bertaccini B (1999) Electrocardiographic abnormalities in acute pancreatitis. *Eur J Emerg Med* 6: 27-29.
- Rubio-Tapia A, García-Leiva J, Asensio-Lafuente E, Robles-Díaz G, Vargas-Voráčková F (2005) Electrocardiographic abnormalities in patients with acute pancreatitis. *J Clin Gastroenterol* 39: 815-818.
- Pezzilli R, Billi P, Bertaccini B, Gullo L (1996) Pericardial effusion and left ventricular function in acute pancreatitis. *Am J Gastroenterol* 91: 997-1000.
- Barassi A, Iammarino MT, Casadei R, Melzi d'Eril GV, Pezzilli R (2012) Is Troponin T a Useful Marker of Myocardial Damage in Acute Pancreatitis? *JOP J Pancreas* 13: 550.
- Pezzilli R, Billi P, Cappelletti O, Barakat B, Miglio F (1999) Rhabdomyolysis and acute pancreatitis. *J Gastroenterol Hepatol* 14: 168-171.
- Kost GJ, Kirk JD, Omand K (1998) A strategy for the use of cardiac injury markers (troponin I and T, creatine kinase-MB mass and isoforms, and myoglobin) in the diagnosis of acute myocardial infarction. *Arch Pathol Lab Med* 122: 245-251.
- Francis GS, Tang WH (2004) Cardiac troponins in renal insufficiency and other non-ischemic cardiac conditions. *Prog Cardiovasc Dis* 47: 196-206.
- Tanindi A, Cemri M (2011) Troponin elevation in conditions other than acute coronary syndromes. *Vasc Health Risk Manag* 7: 597-603.
- Holwerda DA (1972) A glycopeptide from the posterior lobe of pig pituitaries. I. Isolation and characterization. *Eur J Biochem* 28: 334-339.
- Khan SQ, Dhillon OS, O'Brien RJ, Struck J, Quinn PA, et al. (2007) C-terminal proasopressin (copeptin) as a novel and prognostic marker in acute myocardial infarction: Leicester Acute Myocardial Infarction Peptide (LAMP) study. *Circulation* 115: 2103-2110.
- Klersy C, d'Eril GV, Barassi A, Palladini G, Comelli M, et al. (2012) Advantages of the lognormal approach to determining reference change values for N-terminal propeptide B-type natriuretic peptide. *Clin Chim Acta* 413: 544-547.
- Asakawa H, Nishikimi T, Suzuki T, Hara S, Tsubokou Y, et al. (2001) Elevation of two molecular forms of adrenomedullin in plasma and urine in patients with acute myocardial infarction treated with early coronary angioplasty. *Clin Sci (Lond)* 100: 117-126.
- Pezzilli R, Barassi A, Pigna A, Morselli-Labate AM, Imbrogno A, et al. (2012) Time course of proadrenomedullin in the early phase of septic shock. A comparative study with other proinflammatory proteins. *Panminerva Med* 54: 211-217.
- Palladini G, Barassi A, Perlini S, Milani P, Foli A, et al. (2011) Midregional proadrenomedullin (MR-proADM) is a powerful predictor of early death in AL amyloidosis. *Amyloid* 18: 216-221.