# *Patterns of Severe Pancreatic Injury Following Cardiopulmonary Bypass*

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**Severe pancreatic complications following cardiac surgery are rare, but 14 patients with severe pancreatitis have been encountered since 1971. Six of these developed acute fulminating pancreatitis following cardiac surgery and each of these died within 21 days following operation. Seven patients had less severe pancreatitis, resulting in pancreatic abscess formation and five in this group expired. One patient developed a pancreatic pseudocyst following mild acute pancreatitis and expired 4 months later. Although the etiologic mechanisms are unclear, possible factors include: prolonged cardiopulmonary bypass, "the low cardiac output syndrome," and inadequately treated or unrecognized postoperative pancreatitis. The diagnosis is based on physical examination, upper gastrointestinal series, and the abdominal CT scan. Despite aggressive surgical therapy, pancreatitis following cardiopulmonary bypass is an extremely serious condition.**

WHILE SEVERE PANCREATIC complications following cardiac surgery are unusual, Harjola and associates[1] described a patient who developed acute hemorrhagic pancreatitis following aortic valve replacement. Horton and co-workers[2] described a patient who developed acute hemorrhagic pancreatitis in addition to hemorrhagic small bowel necrosis also following aortic valve replacement, and Panebianco and associates[3] reported eight patients with autopsy findings of moderate to severe pancreatitis following cardiac surgical procedures. Feiner,[4] from this institution, reported 29 patients with postmortem findings of mild to severe pancreatitis following open heart surgery. More recently, Hanks and co-workers[5] at Duke University reported seven patients who had clinical pancreatitis following cardiac surgery with four deaths. Since 1971, we have encountered 14 patients with severe pancreatic complications following cardiac surgical procedures and these will be described.

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## Clinical Material

The autopsies on patients who underwent cardiac surgical procedures since 1971 were reviewed. Three patients had postmortem anatomical findings of severe, acute pancreatitis. This was defined as extensive, confluent zones of peripancreatic necrosis. (Although other patients did have evidence of mild to moderate pancreatitis, we did not include them in this study.) The hospital records of 11 other patients with severe pancreatic complications following open heart procedures were reviewed. Three of these patients were noted to have extensive, acute pancreatic necrosis during abdominal exploration. Seven other patients developed pancreatic abscesses requiring drainage, and one additional patient developed a pancreatic pseudocyst. The combined data of these 14 patients form the basis of this report.

## Results

Age, sex, and the cardiac operation performed are summarized in Table 1. Patients' ages ranged from 46 to 79 (mean 60.2 ± 2.11). There were seven male and seven female patients. Six patients underwent combined coronary artery bypass and valve replacement, and three patients had isolated valve replacement or commissurotomy. Four patients had coronary artery bypass, and one patient underwent resection of an acute myocardial infarction with closure of a ventricular septal defect.

Until 1978, the standard technique of myocardial protection consisted of intermittent aortic occlusion with induced ventricular fibrillation (employed in five patients) or continuous coronary artery perfusion (utilized in one patient). After 1978, multidose cold blood potassium cardioplegia was used during a single period of aortic occlusion. (This technique was utilized in the remaining

TABLE 1. *Age, Sex, Operation, Aortic Crossclamp Time, Cardiopulmonay Bypass Time, Length of Time Vasopressors and IABP Employed, and Peak 72-Hour Amylase*

| Patient No. | Age/Sex | Operation | Aortic Cross Clamp Time (min) | Cardiopulmonary Bypass Time (min) | Vasopressors IABP (days) | Peak 72-Hr Amylase |
|---|---|---|---|---|---|---|
| 1 | 62/M | VSD + Infarctectomy (Emergency) | 114 | 261 | 8D/IABP | nr nr |
| 2 | 66/F | MVR | 45 | 197 | 11D | 5400 |
| 3 | 63/M | AVR + CABX1 | 83 | 143 | 4D | 243 |
| 4 | 61/F | AVR, T.A. CABX2 | 120 | 275 | 10D/IABP | 2580 |
| 5 | 56/F | MVR, CABX2 | 0 | 106 | None | 3920 |
| 6 | 55/F | MVR | 75 | 165 | None | 920 |
| 7 | 54/M | CABX2 | 26 | 89 | None | 2222 |
| 8 | 79/F | AVR, CABX2 | 216 | 456 | 6D/IABP | 740 |
| 9 | 55/M | CABX2 | 43 | 153 | None | nr |
| 10 | 46/M | CABX1, LV aneurysm | 66 | 316 | IABP | nr |
| 11 | 68/M | AVR, CABX2 | 63 | 210 | 5D/IABP | |
| 12 | 60/F | Mitral Commissurotomy | 14 | 72 | 36 hr | nr |
| 13 | 55/M* | CABX4 | #1 53<br>#2 45 | #1 120<br>#2 140 | IABP × 6D<br>LHAD × 2D | nr<br>nr |
| 14 | 63/F | AVR, CABX2 | 75 | 168 | IABP × 3D | 2158 |
| Mean | 60.2 ± 2.1 | | 74.1 ± 11.1 | 190.8 ± 28.3 | | 2273 + 565 |

Abbreviations: MVR = mitral valve replacement; AVR = aortic valve replacement; TA = tricuspid annuloplasty; CAB = coronary artery bypass; and LHAD = left heart assist device.

* Patient had acute graft closure requiring reinstitution of cardiopulmonary bypass and anastomotic revision.

eight patients.) All patients received nonpulsatile cardiopulmonary bypass with flow rates of 1.8–2.5 l/min/m$^2$ with mean perfusion pressures of 55–65 mmHg.

The mean period of aortic occlusion was 74.1 ± 11.1 minutes (range: 0–216 min). Mean period of total cardiopulmonary bypass was 190.8 min ± 28.3 (70 to 456 min). Three patients required inotropic agents alone after surgery for depressed cardiac function. Six patients required intra-aortic balloon counterpulsation in addition to inotropic agents for adequate cardiac support. In one patient, it was necessary to insert a left heart assist device to provide adequate cardiac support. Four patients required no pharmacological or mechanical cardiac support after surgery (Table 2).

Peak 72-hour amylase, pancreatic involvement, and the clinical course are summarized in Tables 1 and 3. In six patients, the early postoperative amylase was not recorded. In the other eight patients, peak amylase ranged from 248 to 5400 Somogyi units (normal 0–200).

### *Severe, Acute Pancreatitis*

All patients with severe, acute pancreatic necrosis had associated cardiac failure. All but one patient (no. 12) had acute renal failure and acute pulmonary failure (Table 4). Patients nos. 2, 12, and 14 were noted at postmortem examination to have extensive pancreatic necrosis. The postoperative course of both patients nos. 2 and 14 was characterized by persistent, aggressive "low cardiac output syndrome" which was refractory to all therapy. Patient no. 12 was stable for the first 6 postoperative days, then developed pneumonia on the sixth and expired on the eighth postoperative day.

Patients nos. 1, 2, and 10 had evidence of an acute abdomen 2–21 days following open heart surgery. At surgical exploration, patient no. 1 had extensive hepatic necrosis in addition to pancreatic necrosis, and patient no. 10 had extensive large and small bowel necrosis along with extensive pancreatic necrosis. Patient no. 2 was explored 36 hours following cardiac surgery and had near total pancreatic necrosis. This patient was re-explored 10 days later for an extensive pancreatic abscess. All six of these patients (nos. 1, 2, 3, 10, 12, and 14) expired.

### *Pancreatic Abscess and Pseudocyst*

Three patients (nos. 8, 11, and 13) who developed a pancreatic abscess had associated cardiac and pulmonary failure, while only one of these patients (no. 13) also had associated acute renal failure.

Patients nos. 5, 6, 7, and 9 were all initially stable following open heart surgery and had no apparent gastrointestinal symptomatology. All of these patients except

TABLE 2. *Requirements for Postoperative Mechanical or Pharmacologic Cardiac Support*

| | |
|---|---|
| 4 pts: | No inotropic agents |
| 3 pts: | Inotropic agents alone |
| 6 pts: | Inotropic agents + IABP |
| 1 pt: | Inotropic agents + IABP + LHAD |

TABLE 3. *Pancreatic Pathology and Clinical Summary*

| Patient No. | Pancreatic Pathology | Clinical Summary |
|---|---|---|
| 1 | Severe, acute pancreatitis | Pt had persistent cardiac, pulmonary, and renal failure PO. Explored 21D PO for acute abdomen had extensive pancreatic and hepatic necrosis. Expired 22D PO. |
| 2 | Severe, acute pancreatitis | Pt had persistent cardiac, pulmonary, and renal failure. Expired 11D PO. Autopsy demonstrated extensive pancreatic necrosis. |
| 3 | Severe, acute pancreatitis and pancreatic abscess | Pt explored 36D PO for acute abdomen, extensive pancreatic necrosis found; pt developed pulmonary and renal failure; re-explored 12D PO for pancreatic abscess. Expired 15D PO. |
| 4 | Pancreatic pseudocyst | Pt had mild cardiac, pulmonary, and renal failure PO which improved. Explored 14D PO for acute abdomen; pt found to have acute pancreatitis and gastrostomy and jejunostomy performed. Pancreatic pseudocyst eroded into splenic artery and pt expired 120D PO. |
| 5 | Pancreatic abscess | Pt had elevated serum amylase PO; received oral alimentation and then developed abdominal pain. Pt placed on NG suction. Pancreatic abscess drained 30D PO. Expired 60D PO from pulmonary sepsis. |
| 6 | Pancreatic abscess | Pt had persistent abdominal pain and elevated amylase PO. Explored 9D PO for sepsis; abscess drained. Pt discharged 60D PO. |
| 7 | Pancreatic abscess | Pt received oral alimentation 3D PO; developed abdominal pain 5D PO; explored 9D PO for sepsis. Expired 25D PO with refractory sepsis. |
| 8 | Pancreatic abscess | Pt had moderate cardiac and pulmonary failure PO; enteral tube feedings initiated; explored 21D PO for abdominal sepsis and extensive abscess drained; expired 29D PO from sepsis. |
| 9 | Pancreatic abscess | Pt received oral alimentation PO; developed abdominal pain 6D PO; NG suction initiated. Pancreatic abscess drained 21D PO; discharged 105D PO. |
| 10 | Severe, acute pancreatitis | Pt had severe cardiac, pulmonary and renal failure PO. Explored 6D PO for acute abdomen and found to have extensive small and large bowel necrosis in addition to extensive pancreatic necrosis. |
| 11 | Pancreatic abscess | Pt had moderate cardiac and pulmonary failure PO. Enteral tube feedings initiated; patient developed severe abdominal pain 10D PO with elevated amylase; NG suction initiated. Pancreatic abscess drained 42D PO; pt expired 70D PO. |
| 12 | Severe, acute pancreatitis | Pt had mild cardiac failure PO; developed pneumonia 6D PO; expired 8D PO from respiratory failure. Autopsy demonstrated acute pancreatic necrosis. |
| 13 | Pancreatic abscess | Pt had severe cardiac, pulmonary, and renal failure PO. Enteral tube feedings initiated; pt developed intermittent abdominal distention and received NG suction. Pancreatic abscess drained 63D PO; pt expired 65D PO from sepsis. |
| 14 | Severe, acute pancreatitis | Pt had severe cardiac, pulmonary, and renal failure PO; expired 72D PO from severe multisystem failure. Autopsy demonstrated extensive pancreatic necrosis. |

no. 6 were started on oral alimentation, despite an elevated postoperative amylase. All of these patients gradually developed abdominal pain and distention with symptoms and signs of acute pancreatitis. They were then treated with nasogastric suction, but subsequently developed clinical and radiographic signs of pancreatic abscess.

Patients nos. 8, 11, and 13 had all received enteral tube feeding in the early postoperative period. These patients similarly developed clinical symptoms and signs of acute pancreatitis. Despite nasogastric suction, all of these patients developed pancreatic abscesses.

All patients required wide surgical debridement and drainage 9 to 63 days following open heart surgery. Only two patients (nos. 6 and 9) survived. All other patients ultimately developed multisystem failure and sepsis and expired.

TABLE 4. *Presence of Cardiac, Renal, and Pulmonary Failure in Patients with Severe, Acute Pancreatitis*

| Patient No. | Cardiac Failure | Renal Failure | Pulmonary Failure |
|---|---|---|---|
| 1 | + | + | + |
| 2 | + | + | + |
| 3 | + | + | + |
| 10 | + | + | + |
| 12 | + | − | − |
| 14 | + | + | + |

TABLE 5. *Presence of Cardiac, Renal, and Pulmonary Failure in Patients with Pancreatic Abscesses and Pseudocyst*

| Patient No. | Cardiac Failure | Renal Failure | Pulmonary Failure |
|---|---|---|---|
| 4 | + | + | + |
| 5 | − | − | − |
| 6 | − | − | − |
| 7 | − | − | − |
| 8 | + | − | + |
| 9 | − | − | − |
| 11 | + | − | + |
| 13 | + | + | + |

Patient no. 4 developed mild, acute pancreatitis after surgery in addition to mild renal, pulmonary, and cardiac failure. She was treated with nasogastric suction but subsequently developed a pancreatic pseudocyst. The cyst eventually eroded into the duodenum and the patient expired following surgical drainage.

## Discussion

The precise incidence of pancreatitis following cardiac surgery is unclear. Feiner[4] noted that mild to severe pancreatitis was present in 16% of 182 cardiac surgical patients in whom an autopsy was performed. Warshaw and O'Hara[6] noted an incidence of 11% of acute pancreatitis in 101 patients in whom an autopsy was performed following cardiac surgery. They noted that the incidence increased to 35% in those patients who also had associated acute tubular necrosis. However, patients who expire nearly after cardiac surgery may be more likely to develop pancreatitis. Furthermore, the presence of pancreatitis may further adversely affect their outcome. Thus, the true incidence of postcardiac surgical pancreatitis is probably not as high as suggested by Feiner[4] and Warshaw.[6] Conversely, since there are no precise laboratory or radiographic techniques available to determine the presence of pancreatitis, the incidence of postcardiac surgical pancreatitis is most likely higher than 0.13% reported by Hanks and associates[5] or 0.12% at NYU (14 patients from a total of 12,000).

The etiologic mechanisms for postcardiac surgical pancreatitis are unclear. Feiner[4] suggested thromboemboli, venous thrombosis potentiated by venous stasis, and ischemia secondary to splanchnic vasoconstriction as possible mechanisms of injury. Warshaw and O'Hara[5] noted a correlation between ischemia, shock, and acute pancreatitis with a significantly increased incidence of pancreatitis in those patients who had associated acute tubular necrosis. Indeed, 10 of 14 of our patients had overt cardiac failure, which may have resulted in pancreatic ischemia.

Murray and co-workers[7] and others[8,9] have noted an abnormal amylase to creatinine clearance ratio in patients in whom nonpulsatile cardiopulmonary bypass is employed. Murray[7] noted an abnormal amylase to creatinine clearance ratio in 9 of 10 patients in whom nonpulsatile bypass was employed. Two of these patients had mild elevations in their serum amylase after surgery although none had clinical pancreatitis. However, in only one of ten patients in whom pulsatile bypass was employed was an elevated amylase to creatinine clearance ratio present. As these authors suggest, nonpulsatile bypass may alter or reduce pancreatic microcirculation. As they also state, the increased renal excretion of amylase following nonpulsatile bypass may be related to nonspecific low molecular weight proteinuria, rather than pancreatic dysfunction. Since pulsatile bypass is not routinely employed in most cardiac surgical centers, and since it was not employed in our patients, the true effect of nonpulsatile bypass on pancreatic dysfunction cannot be accurately assessed at present.

Other etiologic factors may also include chlorothiazide diuretics,[10,11] hypercalcemia,[12] and possible complement activation.[13,14] Previous clinical studies from our institution suggest that premature oral feedings in patients with pancreatitis may contribute to abscess formation.[12,15] Indeed, six of eight patients in whom an abscess ultimately developed did receive premature oral or enteral feedings.

The diagnosis of severe, fulminating acute pancreatitis following open-heart surgery can be quite obscure. Patients with profound "low output syndrome" seem to be more susceptible. The occurrence of pancreatitis in these patients may further contribute to their overall cardiac, renal, and pulmonary deterioration. Most of these patients will have an elevated serum amylase. They will generally demonstrate progressive, unrelenting systemic deterioration. All of these patients in our series expired 3–21 days following cardiac surgery.

Patients who ultimately develop a pancreatic abscess or pseudocyst generally have less fulminant pancreatitis. In four of our patients early clinical pancreatitis was not suspected, although these patients had marked elevations in the postoperative serum amylase. (In the other three patients, no postoperative amylase was recorded.)

The frequency and significance of hyperamylasemia in postcardiac surgical patients is not known. We now suggest that any patient with an elevated serum amylase following cardiac surgery be routinely placed on nasogastric suction. If the patient has a persistently elevated amylase or clinical signs suggestive of pancreatitis, an abdominal CT scan should be performed. Initial therapy should consist of nasogastric suction and intravenous or jejunal alimentation. Repeat CT scans can be performed every 3–4 weeks. If the patient continues to deteriorate or has definite signs of pancreatic abscess, then surgical therapy, which includes extensive debridement and drainage, should be undertaken.[15] As suggested by our studies, some of these patients may have been inadequately or incorrectly treated in the immediate postoperative period, which may have exascerbated their pancreatitis. Unfortunately, despite aggressive surgical therapy, the results have been quite poor. Only two of nine patients with postcardiac surgical pancreatic abscess or pseudocyst survived.

In conclusion, mild to severe pancreatitis following cardiac surgery is probably more common than previously thought. Severe, fulminating acute pancreatitis is an extremely lethal condition and is usually related to a low output syndrome. Patients who ultimately develop a pan-

creatic abscess or pseudocyst may have had early mild pancreatitis, or subclinical pancreatitis which was inadequately treated. Finally, despite aggressive surgical therapy, patients with postcardiac surgical pancreatic abscesses or pancreatic pseudocysts have an extremely poor prognosis.

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