ELSEVIER

European Journal of Cardio-thoracic Surgery 21 (2002) 411–416

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Risk factors for intestinal ischaemia in cardiac surgical patients ☆

S. Ghosh[a,*], N. Roberts[a], R.K. Firmin[a], J. Jameson[b], T.J. Spyt[a]

[a]*Department of Cardiothoracic Surgery, University Hospitals Leicester, Glenfield Hospital, Leicester LE3 9QP, UK*
[b]*General Surgery, University Hospitals Leicester, Glenfield Hospital, Leicester LE3 9QP, UK*

Received 2 November 2001; received in revised form 23 December 2001; accepted 23 December 2002

Abstract

Objective: Mesenteric ischaemia is an uncommon (<1%) but serious complication of cardiac surgery associated with a mortality >50%. Predictors of this complication are not well defined, and diagnosis can be difficult and prompt surgical intervention can be lifesaving. **Methods and results**: In a retrospective case-note analysis from May 1994 through to May 2000, we identified mesenteric ischaemia in 39 of 5349 consecutive patients (0.07%) undergoing cardiac surgery with cardiopulmonary bypass. By logistic multivariate analysis, we have identified six possible predictors of intestinal ischaemia: duration of cross-clamp, use of significant inotropic support, intra-aortic balloon counterpulsation for low cardiac output, need for blood transfusions, triple vessel disease and peripheral vascular disease. In all patients a combination of four predictors were present. Patients who survived this complication had surgical intervention earlier (6.4 ± 3.8 h) than those who did not (16.9 ± 10 h). **Conclusions**: The diagnosis and prompt treatment of mesenteric ischaemia post cardiac surgery requires a high degree of awareness. These predictors may be useful in alerting medical staff to the possibility of gastro-intestinal ischaemic complications after cardiac surgery particularly that early surgical intervention reduces mortality.

Keywords: Intestinal ischaemia; Cardiac surgery

1. Introduction

Gastro-intestinal (GI) complications following cardiac surgery are uncommon (0.41–3.7%) but associated with a high mortality (13.9–52%) [1–11]. One of the reasons for variation in incidence and mortality lies in the diversity of diagnoses covered in such studies and therefore the wide variety of treatments available. Arguably the most lethal GI pathology following cardiopulmonary bypass is that of intestinal ischaemia with reported mortality much higher than other diagnoses (71–100%) [2,6].

The difficulty in making the diagnosis contributes heavily to the catastrophic end result. A high index of suspicion is important for an early diagnosis. Critically ill patients following cardiac surgery are often ventilated and sedated for lengthy periods and therefore signs and symptoms of abdominal pathology are vague and non-specific making diagnosis even more difficult and delayed. Several predictors of GI complications have been described [12] but those specific to intestinal ischaemia are still poorly defined.

There is emerging evidence in the literature to suggest that early diagnosis and prompt surgical intervention can improve outcome in these patients [13]. However, the timing of surgery has not been established and with this in mind, we investigated the risk factors which may predict mesenteric ischaemia in a retrospective study of patients in our unit for a 6 year period.

2. Materials and methods

2.1. Patient selection

A retrospective case-note and database analysis took place of patients undergoing elective cardiac surgical procedures involving the use of cardiopulmonary bypass between May 1994 and 2000. GI complications were identified in 142 patients with 39 of these suffering intestinal ischaemia diagnosed at laporotomy or post-mortem from a total population of 5349 cases.

During the same period, patients who underwent cardiac procedures and did not develop ischaemic complications were selected as controls. For each case, four control patients were matched as follows: same age (±5 years),

☆ Presented at the joint 15th Annual Meeting of the European Association for Cardio-thoracic Surgery and the 9th Annual Meeting of the European Society of Thoracic Surgeons, Lisbon, Portugal, September 16–19, 2001.

* Corresponding author. Tel.: +44-116-250-2485; fax: +44-116-270-9664.

E-mail address: sudip.ghosh@uhl-tr.nhs.uk (S. Ghosh).

1010-7940/02/$ - see front matter
PII: S1010-7940(02)00015-5

same gender (male or female), same operation date (±3 days), and same left ventricular function (±5%). GI complications were defined as any abdominal symptoms or signs which led to a general surgical consultation. Patients with nausea, vomiting or transient abdominal distension which settled quickly were not included. Operative co-morbidity was defined as follows. Obesity was defined as body weight greater than 20% of normal weight estimated by the Lorentz formula. Diabetes was defined as the need for insulin or any oral antidiabetic medication. Preoperative renal insufficiency was determined by serum creatinine levels higher than 120 μmol/l). Inotropic support was defined as infusions of Dopamine over 5 mcg/kg per min and the use of adrenaline or any other intravenous (IV) inotrope, e.g. noradrenaline.

2.2. Anaesthesia and cardiopulmonary bypass

Anaesthetic protocols were similar in all patients, using IV midazolam hydrocholride, propofol, atracuronium bromide and fentaynl citrate. Cardiopulmonary bypass was conducted under moderate systemic hypothermia (28–34°C), with non-pulsatile, filtered arterial flow and gravity venous drainage. A hollow-fibre oxygenator was used. Myocardial protection was achieved using either antegrade cold, crystalloid or warm blood cardioplegia.

2.3. Statistical analysis

Statistical analysis was performed using SPSS Base 9.0 statistical software (SPSS Inc, Chicago, IL) and advice sought from a qualified statistician. Continuous variables were expressed as mean ± standard deviation and were compared using unpaired two-tailed *t*-test. Categorical variables, expressed as percentages, were analyzed with a χ^2 test of a Fisher exact test. To identify risk factors for intestinal ischaemia, univariate analysis of pre, intra and post-operative variables were performed by comparing cases and controls. To evaluate independent risk factors for intestinal ischaemia, significant and marginally significant (*P* value <0.2) univariate risk factors were examined using forward stepwise logistic regression analysis. Coefficients were computed by method of maximum likelihood. A two-tailed p value less than 0.05 was used to indicate statistical significance.

3. Results

A total population of 5349 patients was identified of which 142 suffered GI complications (incidence 2.9%). A total of 39 patients developed intestinal ischaemia (incidence 0.07%). Of the thirty nine patients with intestinal ischaemia 25 (64%) had undergone isolated coronary bypass grafting, eight (20.5%) had valve and bypass graft surgery, three (7.7%) had bypass grafts plus double valve surgery and the remainder had valve surgery only.

Mortality for the total sample population was 4.1% compared to 34% in the 142 patients with GI complications. A total of 25–39 patients with intestinal ischaemia died within 30 days of cardiac surgery leading to a mortality rate of 64.1%. The variety of GI diagnoses are shown in Fig. 1.

Patient outcomes are shown in Table 1 which illustrates the significantly higher mortality and length of hospital stay in those patients with GI complications, with the highest in patients undergoing surgical intervention.

3.1. Pre-operative factors

Pre-operative patient variables for the 39 patients developing intestinal ischaemia and the 156 controls are shown in Table 2. As expected, age, sex and mean left ventricular ejection fraction were identical for the 39 cases and 156 controls. Prevalence of smoking, obesity, renal failure, dyslipidaemia, stroke, chronic pulmonary disease were not significantly different between the two groups. However, there was a trend toward an increased prevalence of hyper-

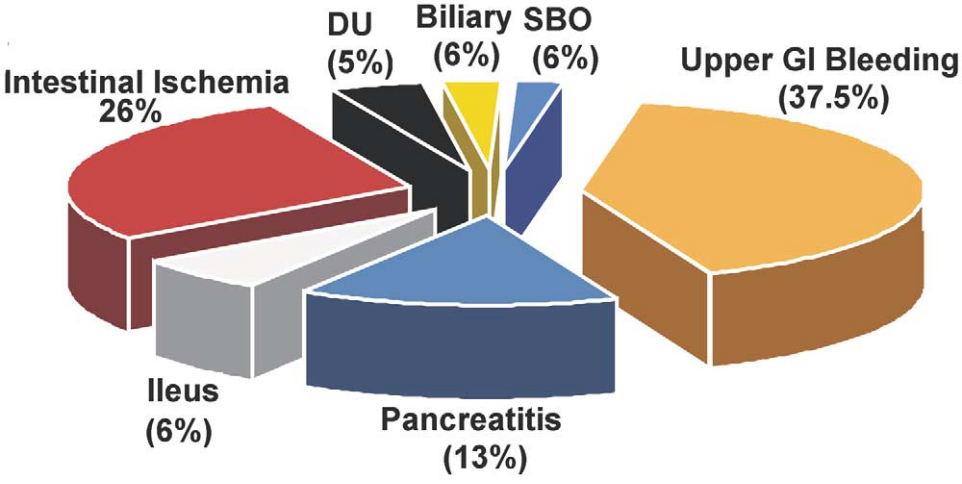

Fig. 1. Distribution of gastro-intestinal pathology.

Table 1
Patient outcome[a]

Variable	Control	GI	Treatment group	
			Surgical	Conservative
Number of patients	5207	142	52	90
Operative mortality (%)	213 (4.1)	48 (34)	31 (59.6)	20 (22)
Postoperative LOS (days)	8.2 ± 1.8	26.5 ± 18	38 ± 31	19 ± 11.5

[a] GI, gastro-intestinal; and LOS, length of stay.

tension ($P = 0.053$) and diabetes ($P = 0.051$) among cases when compared to controls, but this difference did not reach statistical significance. Prevalence of peripheral vascular disease (PVD), triple vessel coronary artery disease and New York Heart association (NYHA) class IV symptoms were significantly higher in the cases when compared to the controls.

3.2. Intraoperative factors

Intraoperative variables are listed in Table 3. There were no significant differences between the two groups concerning cardiopulmonary bypass times and cardioplegia infused volumes. However, the differences in aortic cross clamp times and the need for intraoperative blood transfusion to maximize filling volume requirements achieved statistical significance between the two groups.

3.3. Post-operative factors

Early post-operative variables are illustrated in Table 4. A total of 38 (86%) patients in the GI group were given autologous blood transfusion versus 32 (21%) patients in the control group ($P < 0.001$). There was a higher prevalence of post-operative complications among the GI cases when compared to controls. Univariate analysis identified nine risk factors for mesenteric ischaemia with only perioperative myocardial infarction, renal failure and the need for haemofiltration not affecting outcome. Extubation delay was significantly higher in the GI group (55.8%) when compared to control subjects (9.2%), as was the need for re-exploration of the chest for bleeding (59% versus 3.6%).

Table 2
Demographic characteristics and patient comorbidities[a]

Variable	GI cases ($n = 39$)	Controls ($n = 156$)	P value
Demographics			
Age (mean ± SD)	71.2 ± 10.8	68.9 ± 11.6	–
Gender (male/female)	25/14	100/56	–
LVEF	42.1 ± 14.7	46.5 ± 17.2	–
Comorbidities			
Smoking (%)	25 (64)	112 (71.7)	0.89
Diabetes (%)	12 (31)	68 (41)	0.051
Obesity (%)	15 (38.5)	56 (36.2)	0.92
Renal failure (%)	6 (15.3)	25 (16)	0.93
Dialysis (%)	1 (2.6)	3 (1.9)	0.81
Hypertension (%)	28 (72)	59 (37.8)	0.053
Stroke (%)	0	1 (0.6)	0.98
Peripheral vascular disease (%)	19 (48.7)	24 (15.3)	0.002
COAD (%)	2 (5.1)	17 (10.9)	0.16
Triple vessel disease (%)	26 (66.7)	79 (50.6)	0.021
NYHA class IV (%)	15 (38.4)	29 (18.6)	0.019

[a] Values presented as n (%).

3.4. Multi-variate analysis

Table 5 shows the univariate analysis of the pre, intra and post-operative variables. Logistic regression analysis identified six possible predictors of intestinal ischaemia, namely pre operative triple vessel coronary disease, peripheral vascular disease, the length of aortic cross clamp time, the need for intra-aortic balloon counterpulsation, post operative blood transfusion and the need for re-exploration for bleeding. The presence of these six risk factors were then reassessed in the 39 patients who suffered from intestinal ischaemia. In all 39 patients, at least four out of the six risk factors as identified by logistic multivariate analysis were present in different combinations.

3.5. Surgical intervention

The patients with intestinal ischaemia were then subdivided into survivors and non-survivors and time from onset of symptoms to laparotomy was investigated with the results shown in Table 6. A total of 36 (92.3%) of the 39 patients underwent laporotomy following diagnosis. In the remaining three patients, surgery was deemed unsuitable on clinical grounds and the patients died within 24 h after diagnosis

Table 3
Intraooperative factors

Variable	GI cases ($n = 39$)	Controls ($n = 156$)	P value
CPB time (min)	147.6 ± 26.8	105.9 ± 19.4	0.21
Aortic cross-clamp time (min)	86.9 ± 19.2	49.2 ± 12.5	<0.001
Cardioplegia (ml)	1705 ± 249	1505 ± 103	0.41
Volume infusion			
Crystalloid (ml)	2295 ± 304	2105 ± 205	0.78
Colloid (ml)	670 ± 102	490 ± 150	0.29
Blood cell unit (%)	45	12	<0.001

Table 4
Postoperative factors[a]

Variable	Cases (%)	Control (%)	*P* value
Postoperative blood transfusion	33 (86)	32 (21)	<0.001
Re-exploration for bleeding	23 (59)	5 (3.6)	<0.001
Prolonged ventilation (>24 h)	22 (55.8)	14 (9.2)	<0.001
Perioperative MI	1 (2.5)	7 (4.6)	0.112
Renal failure	3 (8.5)	17 (11.2)	0.21
Post-operative CVVH	3 (8.5)	8 (5.4)	0.35
Significant inotropic support	11 (28)	8 (5.3)	<0.001
Sepsis	16 (42)	3 (1.9)	<0.001
Multi-organ failure	11 (28)	1 (0.89)	<0.001
CVA	5 (12.8)	3 (1.9)	<0.001
Coagulopathy	4 (10.8)	1 (0.89)	<0.001
IABP	21 (54)	26 (16.7)	<0.001

[a] GI, gastro-intestinal; MI, myocardial infarction; CVA, cerebrovascular accident; and CVVH, continous veno-venous haemofiltration.

and large bowel necrosis was confirmed at autopsy. Although the mean time to laporotomy from onset of symptoms for survivors was shorter when compared to non-survivors, this did not achieve statistical significance. Table 6 also shows the outcome of patients who underwent surgical laporotomy within 6 h from onset of symptoms. A total of 21 (54%) patients were taken to theatre within 6 h and underwent appropriate bowel resection compared to 18 patients who were treated after 6 h. Early diagnosis and prompt surgical intervention resulted in a reduction in mortality from 83 to 48% ($P < 0.001$).

4. Discussion

Acute mesenteric infarction after extracorporeal circulation is an infrequent but catastrophic event that constitutes 5–27% of all intraabdominal complications occurring on an active cardiac surgical unit. Majority of the cases are the result of non-occlusive mesenteric insufficiency [14,15], as was the case in our unit; constituting 34 of the 39 cases. This diagnosis was made intra-operatively or at post mortem. The remainder was distributed between embolic and thrombotic phenomenon. Unfortunately, the prognosis of acute mesenteric ischaemia resulting in intestinal infarction after CPB has remained dismal, with mortality rates varying from 60 to 100% [2,6,12]. In our series, 25 patients (64%) of 39 patients died.

Majority of co-morbid conditions did not appear to be correlated with the development of acute mesenteric ischaemia. However, the presence of peripheral vascular and triple vessel coronary disease did confirm a statistical significant association in the development of mesenteric infarction. Results of published studies [10–12] agree on these two fundamental variables as general risk factors for the development of GI complications after cardiopulmonary bypass.

Clinical parameters have been identified that are capable of precipitating visceral hypoperfusion after CPB. These include emergency surgery, failed percutaneous coronary angioplasty requiring emergency surgery, IABPs, prolonged cardiopulmonary bypass time, dependence on high doses of inotropes, and advanced age [16–18]. Logistic multivariate analysis of intra and post-operative variables of our patient series identified four parameters as predictors of mesenteric ischaemia: (1) duration of cardiopulmonary bypass; (2) post-operative blood transfusions; (3) significant use of vasopressor inotropes; and (4) use of IABP. No correlation was demonstrated for cross-clamp time or emergency cardiac surgery as only one patient in our series was an emergency. As in other reports [1,19] vasopressor support was prevalent in our patients before the development of acute mesenteric ischaemia. In general, patients requiring pharmacologic and mechanical support after prolonged CPB are the high risk group.

A high index of clinical suspicion should be the initial step in any algorithm proposed for the diagnosis and subsequent surgical intervention of acute mesenteric ischaemia after CPB. Difficulties in the diagnosis of mesenteric ischaemia resulted in an average delay of 17 h before surgical intervention was instituted in the non-survivors in our series. Similar delays have been noted by others [20,21] and have been attributed to ventilator support and heavy sedation, making communication and physical examination difficult. Certainly, in our series, the delay to extubation was significantly more prevalent when compared to controls and by all

Table 5
Risk factors

Risk factor	Relative	95% Confidence interval	*P* value
Triple vessel disease	2.35	1.11–5.56	<0.05
NYHA class IV	2.1	0.82–3.12	>0.2
PVD	8.1	5.2–9.7	<0.05
Diabetes	0.79	0.31–1.69	0.28
Cardiopulmonary bypass	1.68	0.92–2.0	0.06
Cross clamp time	2.18	1.01–4.21	<0.05
IABP	2.29	1.16–6.09	<0.05
Inotropic support	3.9	2.1–7.0	<0.05
Post-operative blood transfusions	12	5.9–29	<0.05
Re-exploration for bleeding	2.34	0.68–2.59	0.09

Table 6
Surgical outcome

	Survivors ($n = 14$)	Non-survivors ($n = 25$)	P value
Mean time to laporotomy (h)	6.4 ± 3.8	16.9 ± 10	0.519
	Mean time to laporotomy		
	Early (<6 h)	Late (>6 h)	
n	21	18	
Mortality (%)	10 (48)	15 (83)	<0.05

accounts would play a significant role in the delay to accurate diagnosis. Establishing an early diagnosis is difficult. Apart from abdominal pain, there are usually no abdominal signs till established bowel infarction has occurred. Classically, the pain is described to be out of proportion to the physical signs. In our series, only 18 patients (62%) of the 29 that were already extubated before the development of mesenteric ischaemia had pain and tenderness as an early prominent feature in their clinical presentation. In the plain abdominal film, apart from non-specific dilated loops, there are no other signs until pnuemotosis, frank perforation or portal venous gas develop. 'Thumb-printing' and formless loops of small bowel can sometimes be seen due to mucosal oedema and haemorrhage. However, this usually signifies infarction. Persistent metabolic acidiosis, hyperkalemia and leucocytosis are often associated with intestinal ischaemia; their presence in a ventilated patient undergoing CPB who is not improving should alert one to the possibility of underlying mesenteric ischaemia. In view of the lack of characteristic clinical symptoms and signs and bedside investigations in the early phase of bowel ischaemia, the only way to come to a diagnosis is to have index of awareness.

Laporotomy should not be delayed out of trepidation of intervening after cardiac surgery, particularly because missed mesenteric ischaemia results in 100% mortality. Concerns have been raised about the reluctance of GI surgical colleagues to operate on patients in the early post-cardiac surgery phase due to supposed instability of the cardiovascular system [12,22]. Clearly, in our series, patients who underwent laporotomy early (within 6 h) had a mortality rate of 48%. Majority of cardiac patients have improved cardiac function after open-heart surgery, but are unable to compensate much further for the considerable demands of severe ischaemic intestinal complications. It is therefore of supreme importance that early diagnosis and immediate surgery is undertaken if the greatest benefit from the cardiac reserve is to be made. A negative laparotomy, as seen in five patients in our series, does not seem to upset recovery of cardiac patients as the trauma of the procedure is limited in absence of life threatening abdominal pathology.

Significant risk factors identified for the development of intestinal ischaemia after cardiac surgery include presence of co-morbid peripheral vascular disease, triple vessel coronary disease, prolonged pump time, use of an IABP, need for post-operative blood transfusions and use of significant inotropic support. In consideration of these risk factors, a heightened suspicion may decrease diagnostic delay and promote prompt surgical intervention resulting in improved clinical outcome.

Acknowledgements

We wish to thank Dr N. Taub for his help with the statistical analysis in this paper.

References

[1] Ohri SK, Desai JB, Gaer JA, Roussak JB, Hashemi M, Smith PL, Taylor KM. Intraabdominal complications after cardiopulmonary bypass. Ann Thorac Surg 1991;52(4):826–831.
[2] Fitzgerald T, Kim D, Karakozis S, Alam H, Provido H, Kirkpatrick J. Visceral ischaemia after cardiopulmonary bypass. Am J Surg 2000;66(7):623–626.
[3] Moneta GL, Misbach GA, Ivey TD. Hypoperfusion as a possible factor in the development of gastro-intestinal complications after cardiac surgery. Am J Surg 1985;149(5):648–650.
[4] Krasna MJ, Flancbaum L, Trroskin SZ, Fitzpatrick JC, Scholz PM, Scott GE, Spotnitz AJ, Mackenzie JW. Gastro-intestinal complications after cardiac surgery. Surgery 1988;104(4):773–780.
[5] Christenson JT, Schmuziger M, Maurice J, Simonet F, Velebit V. Postoperative visceral hypotension the common cause for gastro-intestinal complications after cardiac surgery. J Thorac Cardiovasc Surg 1994;42(3):152–157.
[6] Lazar HL, Hudson H, McCann J, Fonger JD, Birkett D, Aldea GS, Shemin RJ. Gastro-intestinal complications following cardiac surgery. J Cardiovasc Surg 1995;3(3):341–344.
[7] Aouifi A, Pirou V, Bastien O, Joseph P, Blanc P, Chiari P, Diab C, Villard J, Lehot JJ. Severe digestive complications after heart surgery using extracorporeal circulation. Can J Anaesth 1999;46(2):114–121.
[8] Ojeda GA, Mosqueda OA, Zepeda BL, Orozco FC, Gonzalez AJ, Alarcon HF, Carlo PCO, Adame VO. Abdominal complications after cardiopulmonary procedures. Rev Gastroenterol Mex 1999; 64(2):61–69.
[9] Yilmaz AT, Arslan M, Demirkilic U, Ozal E, Kuralay E, Bingol H, Oz BS, Tatar H, Ozturk OY. Gastro-intestinal complications after cardiac surgery. Eur J Cardiothorac Surg 1996;10:763–767.
[10] Perugini RA, Orr RK, Porter D, Dumas EM, Maini BS. Gastro-intestinal complications following cardiac surgery. Arch Surg 1997;132: 352–357.
[11] Egleston CV, Gorey TF, Wood AE, McGovern EM. Gastro-intestinal complications after cardiac surgery. Ann R Coll Surg Engl 1993;75: 52–56.
[12] Zacharias A, Schwann TA, Parenteau GL, Riordan CJ, Durham SJ, Engoren M, Fenn-Buderer N, Habib RH. Predictors of gastro-intestinal complications. Tex Heart Inst J 2000;27:93–99.

[13] Waspe SR, Agrawal NK, Spyt TJ. Acute abdomen after cardiac surgery: three cases, one fatal. J R Soc Med 2001;94(1):30–31.
[14] Pinson CW, Alberty RE. General surgical complications after cardiopulmonary bypass surgery. Am J Surg 1983;146:133–137.
[15] Wilson C, Gupta R, Gilmour G, Imrie W. Acute superior mesenteric ischaemia. Br J Surg 1987;74:279–281.
[16] Klempnauer J, Grothues F, Bektas H, Wahlers T. Acute mesenteric ischemia following cardiac surgery. J Cardiovasc Surg 1997;38:639–643.
[17] Christenson JT, Schmuziger M, Maurice J, Simonet F, Velebit V. Postoperative visceral hypotension the common cause for gastrointestinal complications after cardiac surgery. Thorac Cardiovasc Surg 1994;42:152–157.
[18] Tsiotos GG, Mullany CJ, Zietlows S, Van Heerden JA. Abdominal complications following cardiac surgery. Am J Surg 1994;167:553–557.
[19] Welling RE, Rath R, Albers JE, Glaser RS. Gastro-intestinal complications after cardiac surgery. Arch Surg 1986;121:1178–1180.
[20] Leitman IM, Paull DE, Barie PS, Isom OW, Shires GT. Intra-abdominal complications of cardiopulmonary bypass operations. Surg Gynecol Obstet 1987;165:251–254.
[21] Wallwork J, Davidson KG. The acute abdomen following cardiopulmonary bypass surgery. Br J Surg 1980;67:410–412.
[22] Sakorafas GH, Tsiotos GG. Intra-abdominal complications after cardiac surgery. Eur J Surg 1999;165:820–827.

Appendix A. Conference discussion

Dr D. Wheatley (*Glasgow, Scotland*): I think we would all recognize this as a serious complication. One of the problems is that some of the predictors you have mentioned are so common, like three-vessel disease and poor left ventricular function, that it is very difficult to see this coming ahead of time. I would also note that splanchnic constriction is a reaction to shock. Does this modify your use of inotropes or the use of vasodilators in these high risk patients?

Mr Ghosh: I don't think it actually modified our use, to be fair. The difference in the way we have approached this is that we have started to alert our general surgeons early in the sense that once somebody develops some sort of complication, we look back now and look at these risk factors, and we have tried to promote them to try and open the belly up sooner rather than later if these predictors are present in our patients.

Dr B. Podesser (*Innsbruck, Austria*): I have two questions. Question number 1: did you see any metabolic differences of markers, e.g. lactate, between the operative and the non-operative group or between the group that was operated earlier than the other one?

And the second question: as the postoperative number of blood transfusion is a predictor in our study, don't you think that blood transfusions change rheology? We all know data from Messmer when he started promoting hemodilution in coronary bypass surgery?

Mr Ghosh: Can I answer your second question? I think you are right, I think that the postoperative blood transfusion does converse rheology and that may well have some difference in splanchnic microcirculation.

With regard to your first question, this is something we are looking at. The problem is that we don't routinely measure markers like lactate in our past experience. I looked at things like negative acid base balance and all the rest of it, and because the numbers are actually quite small, I couldn't really infer with any statistical surety that there was any discrete factor that could tell us this.