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Histological study of colonic ischaemia after aortic surgery

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Background Colonic ischaemia is a well documented complication of abdominal aortic reconstruction. In this prospective study patients had routine preoperative and postoperative colonoscopy and biopsy, in order to determine the true incidence and implications.
Methods Fifty-six patients undergoing elective infrarenal aortic surgery, 28 for aneurysm and 28 for occlusive disease, had colonoscopy and biopsy before and 1 week after operation.
Results Colonic ischaemia was identified histologically in biopsies from 16 (30 per cent) of 53 patients. Almost half the patients had normal macroscopic appearances. Two factors exhibited a statistically significant association with the development of ischaemia: prolonged cross-clamp time ($P < 0{\cdot}05$) and postoperative diarrhoea ($P < 0{\cdot}001$). Co-morbidity was much higher in patients with colonic ischaemia ($P < 0{\cdot}005$). Overall morbidity was significantly greater in the aneurysm group ($P < 0{\cdot}05$).
Conclusion Colonic ischaemia is common after aortic reconstruction. When suspected, colonoscopy with biopsy is diagnostic.

Abdominal aortic reconstruction is a routine vascular procedure, but is still associated with significant morbidity and a mortality rate approaching 6 per cent for elective aneurysm repair[1–4]. First documented in 1954[5], postoperative colonic ischaemia remains a serious potential complication; the reported incidence varies from 0 to 32 per cent[6]. Important predisposing factors are listed in *Table 1*[7–19]. The commonest reported symptom is diarrhoea with or without blood, usually commencing within 48 h of surgery[19,20]. Absence of diarrhoea is documented[18] and may present diagnostic difficulty.

The aim of this study was to examine, by colonoscopy and biopsy, the incidence of overt and subclinical postoperative colonic ischaemia in an unselected group of patients undergoing elective infrarenal aortic surgery, and to identify predictive factors.

Patients and methods

All patients undergoing elective abdominal aortic surgery involving infrarenal cross-clamping were included after giving their informed consent. Ethics committee approval was obtained before commencement of the study. Exclusion criteria were: a history of previous aortic surgery, colonic disease or resection, and intraoperative diagnosis of colonic pathology.

Venous blood was taken for measurement of baseline haematology and biochemistry. Arterial blood was sampled for measurement of blood gases, and 24-h urine collection was performed to determine creatinine clearance. The night before surgery patients were given a phosphate enema to evacuate the distal colon and rectum.

Table 1 Factors predisposing to postoperative colonic ischaemia[7–19]

Inferior mesenteric arterial ligation
Severe stenosis or occlusion of the superior mesenteric artery, internal iliac arteries or other collateral channels
Aortoiliac steal syndrome
Operative damage to vital collaterals, mesentery or colon
Previous colectomy with sacrifice of middle colic artery
Prolonged hypotension with resultant hypoperfusion
Operation for ruptured aneurysm
Embolization of atheromatous debris or cholesterol
Prolonged cross-clamp time

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A standard general anaesthetic technique was used, with non-invasive monitoring of pulse, respiratory rate, tidal volume, oxygen saturation (S_{aO_2}) and end-tidal carbon dioxide. Central venous pressure and S_{aO_2} were measured directly by means of internal jugular venous and radial arterial lines, and urine output was monitored continuously.

After induction of anaesthesia, patients were placed in the left lateral position and a limited colonoscopy performed using an Olympus CF-10 L colonoscope (Olympus Optical, London, UK). Note was made of visual appearances, and biopsies were taken at 20, 30 and 40 cm from the anal verge. Specimens were immediately fixed in 10 per cent formalin solution for later examination by the same consultant histopathologist.

All operations were performed using a standard technique of aortic graft insertion. Aortic aneurysms were replaced by inlay of straight or bifurcated grafts as necessary. Aortic occlusive disease was bypassed using an end-to-side proximal anastomosis. At operation, note was made of the patency of the superior mesenteric artery (SMA), inferior mesenteric artery (IMA) and marginal arteries. Cross-clamp time was documented together with whether or not the IMA or internal iliac arteries were ligated. All patients except one had preservation of at least one internal iliac artery. The incidence of significant hypotension, defined as systolic blood pressure less than 85 mmHg lasting longer than 10 min, was documented for the intervals before, during and after cross-clamping, and after operation.

Fluid administration was governed by anaesthetic staff, losses being replaced by colloid, crystalloid and blood, as required. Routine postoperative management included intravenous fluids, analgesia using intravenous morphine via a patient-controlled administration pump, and monitoring of pulse, blood pressure, central venous pressure, urine output and peripheral pulses. The incidence of postoperative diarrhoea was documented, as were cardiac, respiratory, renal and circulatory complications.

Haematology and serum biochemistry were measured on days 1, 2, 3 and 7 after operation; 24-h urine collections were also made for the purpose of measuring creatinine clearance.

Colonoscopy with biopsies was repeated under sedation 1 week after surgery.

Results

Fifty-six patients were studied (male:female ratio 3:1, mean age 64 (range 46–80) years). The mean age of those

undergoing surgery for aneurysm was significantly greater than that of patients having an operation for occlusive disease (67 *versus* 60 years; $P < 0{\cdot}005$, two-tailed unpaired *t* test).

Preoperative arteriography was available in 35 patients (63 per cent), seven with an aneurysm and 28 with occlusive disease. The SMA was patent in all patients. Seven had an occluded or stenosed IMA; 27 had at least one occluded or stenosed common iliac artery; and 19 had at least one occluded or stenosed internal iliac artery.

At operation the IMA was ligated in significantly more patients in the aneurysm group (all patients *versus* ten of 28; $P < 0{\cdot}05$, two-tailed Fisher's exact test). Ligation of both the IMA and an internal iliac artery was necessary in five patients.

Cross-clamp time ranged from 20 to 87 (mean 38) min, and was almost 5 min longer in the aneurysm group (40 *versus* 35 min, $P = 0{\cdot}06$, two-tailed unpaired *t* test).

Significant hypotension occurred in ten patients (18 per cent), significantly more in the aneurysm group (nine of 28 *versus* one of 28; $P = 0{\cdot}01$, Fisher's exact test). Mild to moderate diarrhoea occurred in 19 patients (34 per cent); three had associated bleeding, one of whom progressed to frank necrosis. The incidence was similar in aneurysm and occlusive groups (11 of 28 *versus* eight of 28). Stool culture for pathogens including *Clostridium difficile* was negative in all patients who had diarrhoea.

Colonic histology (Fig. 1)

All patients had normal macroscopic and microscopic appearances of colonic mucosa before surgery. Post-operative ischaemia was suggested on macroscopic appearances in 13 patients (25 per cent); however, four of these had oedema or pallor of the mucosa but normal histology. Ischaemia was diagnosed by microscopy in 16 patients (30 per cent). Of these, seven patients had normal mucosa macroscopically. There was no significant difference in the incidence of ischaemia between patients with aneurysm or occlusive disease (ten of 26 *versus* six of 27; $P > 0{\cdot}05$, Fisher's exact test). In each patient, histological appearances of biopsies taken at the specified levels showed no differences in the distribution of ischaemia.

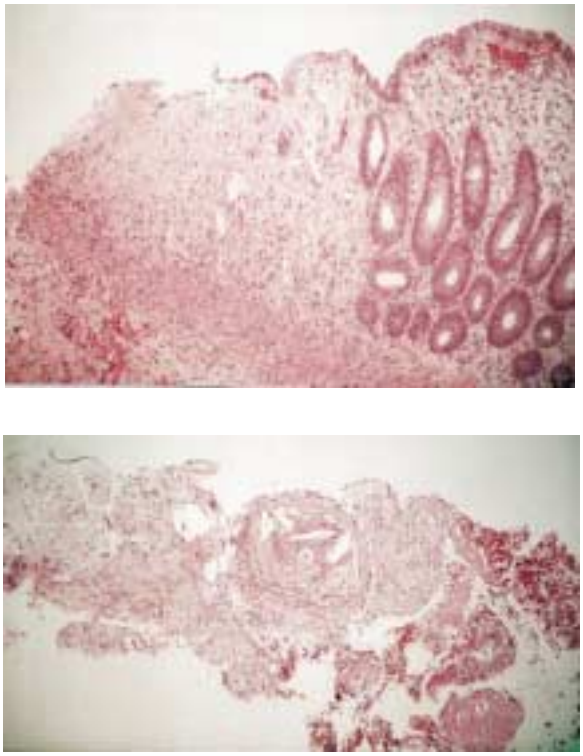

Fig. 1 a Colonic mucosa in which there is superficial ulceration and granulation tissue (to the left) along with acute inflammation of the adjacent epithelium (to the right). b Section from the base of the ulcer in a showing cholesterol emboli in the arteriole. Haematoxylin and eosin stain, original magnification ×40

Complications

Overall morbidity, excluding colonic ischaemia, was 34 per cent, significantly greater following aneurysm repair (13 of 28 *versus* six of 28 patients; $P < 0{\cdot}05$, Fisher's exact test). Cardiac complications occurred in five patients (myocardial infarction, two; heart failure, two; significant dysrhythmia, one); three of these were fatal. Respiratory complications occurred in three of 56 patients (5 per cent). Three patients experienced major vascular morbidity: two had critical ischaemia of one foot which recovered, and in one patient one limb of a bifurcated graft was occluded at 24 h, requiring further surgery. There were no haemorrhagic complications. Gastrointestinal complications included one fatal colonic infarction on the ninth postoperative day and one perforated gastric ulcer on day 10, with recovery after partial gastrectomy. Most renal complications were subclinical and were diagnosed on the basis of changes in serum creatinine or creatinine clearance (30 per cent rise in the former or decrease in the latter sustained for a minimum of 2 days); all but one patient recovered within 1 week. No patient required dialysis, nor were any deaths directly attributable to renal failure.

Patients with colonic ischaemia

Comparing patients with and without colonic ischaemia, there were no differences in age, sex and preoperative arterial patencies (*Fig. 2*). At operation, a palpable pulse was noted in the IMA in nine of 16 patients who developed colonic ischaemia compared with 33 of 40 who did not ($P < 0{\cdot}05$, Fisher's exact test). All patients had pulsatile marginal arteries. Although IMA ligation was performed more frequently in patients who developed

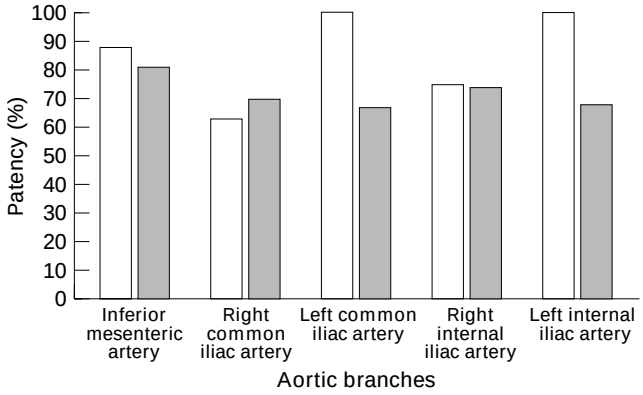

Fig. 2 Patency of aortic branches at preoperative angiography in patients with (□) and without (▨) colonic ischaemia. There were no significant differences in patency between the two groups

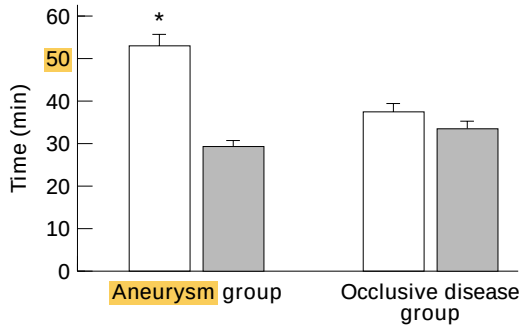

Fig. 3 Aortic cross-clamp time in patients with (□) and without (▨) colonic ischaemia. $P < 0{\cdot}05$ *versus* patients without colonic ischaemia (Mann–Whitney *U* test)

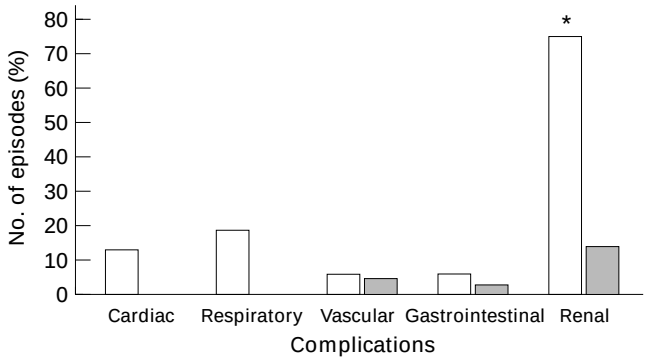

Fig. 4 Morbidity in patients with (□) and without (▨) colonic ischaemia. $P < 0{\cdot}05$ *versus* patients without colonic ischaemia (Fisher's exact test)

colonic ischaemia (13 of 16 *versus* 25 of 40), this did not reach statistical significance.

Cross-clamp time was significantly longer in patients who developed ischaemia (mean 45 *versus* 35 min; $P < 0{\cdot}05$, Mann–Whitney *U* test). This difference occurred in the patients with aneurysm (mean 53 *versus* 29 min; $P < 0{\cdot}05$) (*Fig. 3*). Significant hypotension occurred more often in patients who developed colonic ischaemia (five of 16 *versus* five of 40), although this difference was not significant. Postoperative diarrhoea occurred more often only in patients with ischaemia (14 of 16 *versus* five of 40; $P < 0{\cdot}001$, Fisher's exact test). Mortality and overall morbidity rates were also greater in the ischaemia group (13 of 16 *versus* six of 37; $P < 0{\cdot}005$, Fisher's exact test) (*Fig. 4*).

Discussion

The majority of reports about postoperative colonic ischaemia following aortic surgery are anecdotal or retrospective. Ernst *et al.*[8] colonoscoped 50 consecutive patients within 4 days of aortic surgery, noting macroscopic changes of ischaemia; Zelenock *et al.*[21] performed colonoscopy in 100 consecutive patients within 48 h of surgery. The incidence of ischaemia in these studies was 6 and 3 per cent respectively, but they relied on visual assessment by the endoscopist and these values were almost certainly inaccurate.

A more scientific method of diagnosing ischaemia is by histological examination. Marston *et al.*[22] described three patterns of ischaemic colitis: infarction of the colon, ischaemic stricture and 'transient ischaemic colitis'. Bicks *et al.*[23] also agreed with the concept of 'transient' ischaemia: diarrhoea which occurred 6–8 days after operation, with a spectrum of proctoscopic findings varying between normal, pallor, non-specific oedema, granularity, friability and punctate ulceration. Others have reported non-specific sigmoidoscopic appearances similar to those of ulcerative colitis[24,25]. Macroscopic signs of transient mucosal ischaemia may include non-specific diffuse hyperaemia with multiple submucosal haemorrhagic spots, oedema, or small erosions or ulcers[26]. It was felt that such lesions had no clinical significance. However, patients with subclinical ischaemia may develop mucosal disruption at macroscopic and microscopic levels, and may be susceptible to development of sepsis from enteric organisms and multiple organ failure.

The importance of histological assessment in the diagnosis of ischaemic colitis was emphasized by McBurney *et al.*[20]. In the present study all patients had normal macroscopic and microscopic appearances before operation. Of 13 patients (25 per cent) with abnormal postoperative macroscopic appearances, four had normal histology, therefore excluding ischaemia. However, ischaemia was diagnosed on the basis of histology in seven more patients, resulting in an overall incidence of 16 patients (30 per cent). This incidence is higher than that in any previously reported prospective study. Prospective studies that reported a high incidence of ischaemia are not comparable for various reasons: Fiddian-Green *et al.*[27] and Schiedler *et al.*[28] described incidences of 25 and 29 per cent respectively, but in selected patients considered to be at highest risk of developing colonic ischaemia. Krohg-Sorensen and Kvernebo[29] diagnosed ischaemia on the basis of symptoms in three of 16 patients (19 per cent), Meroni *et al.*[30] reported a 17 per cent incidence in only 18 patients, and a 13 per cent incidence was reported by Hagihara *et al.*[31] in a larger study.

Preoperative arteriography was not performed in most patients in this study, particularly before aneurysm repair. Although important information may be obtained[9,32] preoperative arteriography does not reduce morbidity and mortality rates[3] and in this study it failed to help predict which patients would develop postoperative colonic ischaemia.

The importance of the fate of the IMA is unknown. IMA clamping reduces colonic blood flow, particularly in patients undergoing surgery for occlusive disease[29]. Ernst *et al.*[33] described a critical IMA stump pressure of 40 mmHg, below which ischaemia would develop after IMA ligation, but in their study only one such patient had ischaemic colitis. Ernst and colleagues reported previously that colonic ischaemia may still develop when the IMA is preserved[8]. Others found that ligation of a patent IMA did not increase the likelihood of ischaemic colitis, and that IMA stump pressure measurement was unreliable[28]. Zelenock *et al.*[21] suggested that ischaemia was less likely if the IMA was reimplanted; one large retrospective study found a lower incidence of colonic infarction when a policy of routine IMA reimplantation was undertaken[6]. In the present study colonic ischaemia was more common in patients who had IMA ligation (although not significantly so). Reimplantation was never performed.

The importance of the duration of aortic clamping in the aetiology of colonic ischaemia is well recognized[19]. This is particularly important in patients with aneurysms, who do not have an adequate collateral circulation. In the present study, cross-clamp time was significantly longer in patients who developed ischaemia, mainly during

aneurysm repair. The few published prospective studies disagree whether colonic ischaemia is more likely after surgery for aneurysm than for occlusive disease[8,28]. In the present study, patients who had aneurysm repair had a longer cross-clamp time and were significantly more likely to need IMA ligation. Perioperative hypotensive episodes were more frequent, diarrhoea more common and histological ischaemia more prevalent in patients who had aneurysm repair. Mortality and overall morbidity rates were also greater. Therefore, although colonic ischaemia did not develop in significantly more patients with aneurysm, risk factors for ischaemia were more common and postoperative mortality and morbidity rates were higher in this group.

Although a high incidence of colonic ischaemia was demonstrated in this study (30 per cent), progression to colonic infarction was rare; only one patient died from this complication. In this case, the patient's clinical state did not suggest that laparotomy was required. The severity of ischaemia cannot currently be predicted by histological means alone.

While in many cases, colonic ischaemia is truly transient and is not a major clinical problem, patients who have prolonged aortic cross-clamp, or who develop postoperative diarrhoea, would benefit from investigation. Sigmoid tonometry, which can detect intramural acidosis and thus ischaemia, might help determine which patients should undergo colonoscopy. When colonoscopy is deemed necessary, biopsy and histology should be performed. Although current basic histological stains do not fulfil any predictive role, a diagnosis of ischaemia is indicative of higher risk.

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