# Association of Low Preoperative Serum Albumin Concentrations and the Acute Phase Response

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ABSTRACT

*Objective:* To investigate the incidence of a preoperative acute phase response and its association with low albumin concentrations.

*Design:* Prospective open study.

*Setting:* Teaching hospital, Germany.

*Subjects:* 225 patients who were to undergo major abdominal operations, and who had no acute infections.

*Interventions:* Measurements of serum concentrations of albumin, C-reactive protein (CRP), α-1 antitrypsin, and interleukin-6 (IL-6).

*Results:* Abnormal concentrations of acute phase proteins (indicating an acute phase response) were detected in 43 of 225 patients (19%). The mean (SD) albumin concentration in these patients (35[5]g/L) was lower than that of patients who did not mount an acute phase response preoperatively (40[5]g/L). High concentrations of CRP (≥60mg/L) were associated with low albumin concentrations (33[5]g/L); high α-1 antitrypsin concentrations (≥4.0g/L) were associated with low albumin concentrations (34[6]g/L); and high IL-6 concentrations (≥4pg/ml) were associated with low albumin concentrations (37[6]g/L) compared with a mean(SD) albumin concentration of 40(5)g/L in patients who had no evidence of an acute phase response.

*Conclusion:* A metabolic response to disease referred to as an acute phase response may explain low preoperative albumin concentrations. This association interferes with the association of low preoperative albumin concentrations and malnutrition. It is a new aspect of preoperative risk evaluation and may indicate a potential for prevention.

*Key words:* acute-phase-response, hypoalbuminaemia, risk-assessment, surgical-risk, malnutrition, preoperative hyperalimentation.

## INTRODUCTION

Low plasma albumin concentrations identify patients who are at risk of developing complications during their postoperative course (25). Albumin concentrations have been measured as an indicator of malnutrition, but studies to reduce postoperative morbidity by hyperalimentation were disappointing (5, 6, 13, 25).

Methods of identifying malnutrition are still controversial (11, 12, 21, 33, 34). The failure to improve outcome by giving supplementary nutrition has challenged the interpretation of the data thought to indicate malnutrition. Independently of malnutrition, the synthesis of albumin in the liver, like that of other proteins, is affected by an acute phase response (2, 14–16), and an acute phase response to the disease for which the patient needs an operation is therefore a potential explanation of low serum albumin concentrations preoperatively. Data about a preoperative acute phase response in the context of the assessment of risk are few (10), in contrast to many about the postoperative acute phase response (29). We therefore looked at the incidence of an acute phase response in patients preoperatively to investigate whether low albumin concentrations preoperatively were associated with the acute phase response.

## SUBJECTS AND METHODS

### *Subjects*

Patients admitted to the Department of Surgery, University Hospital, Erlangen, Germany, for major abdominal operations (including oesophagectomy, gastric resection, partial hepatectomy, complex biliary tract procedures, small bowel resection, colectomy, resection of the rectum, and removal of intraperitoneal and retroperitoneal tumours) were entered into this prospective study. The study was conducted according to the ethical rules, the guidelines for good clinical practice, and the Declaration of Helsinki. Patients were eligible for the study if they had no acute infections (assessed by history, clinical examination, chest radiograph, urine culture, white cell count, and body temperature). Patients were excluded if they had had radiation or cancer chemotherapy preoperatively;

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blood transfusion within the past six weeks; parenteral nutrition preoperatively, or if they were undergoing emergency procedures, exploratory laparotomy for advanced cancer; minor palliative procedures; or only unexpected minor procedures such as simple cholecystectomy and colostomy.

### *Measurements*

In addition to personal data the following variables were measured and recorded preoperatively: serum concentrations of the acute phase reactants C-reactive protein (CRP), and α-1-antitrypsin by nephelometry (Behring, Munich, Germany); and serum concentrations of interleukin-6 (IL-6, ELISA, R & D Systems, Biermann, Germany), and albumin by routine laboratory methods.

Cutoff points for reference ranges were set at 50 mg/L for CRP, at 3.5 g/L for α-1-antitrypsin, and at 35 g/L for albumin. For IL-6 the detection limit and cutoff point was 4 pg/ml.

To assess and quantify malnutrition the body mass index (BMI, kg/m$^2$)(27) was calculated. Cutoff points were set at 19 and at 25.

In patients with malignant disease the presence of metastases (microscopically in the resected tissue, or macroscopically assessed during operation) was recorded.

### *Clinical follow up*

Severe septic complications were defined according to the criteria published by Bone (1). Organ dysfunction was diagnosed if the patient needed artificial ventilation together with a need for catecholamines or a urine production of less than 40 ml/hour for more than 24 hours.

### *Statistical analysis*

Data are given as means (SD). The significance of differences between groups was assessed by analysis of variance (ANOVA), and post hoc pairwise comparisons were performed to identify which group differences account for the significant overall value. Bonferroni corrections were made where appropriate. Probabilities of less than 0.05 were accepted as significant.

Table I. *Details of the study group*

Figures are number (%) of patients unless otherwise stated.

| | |
|---|---|
| Sex: | |
| • Male | 108 (48) |
| • Female | 117 (52) |
| Mean age (years): | 56 |
| • Median | 59 |
| • Range | 19–82 |
| Malignant disease: | |
| • Yes | 172 (76) |
| With metastases | 42 (19) |
| • No | 53 (24) |
| • Site of operation: | |
| • Oesophagus | 10 (4) |
| • Stomach | 37 (16) |
| • Biliary tree | 2 (1) |
| • Liver | 34 (15) |
| • Pancreas | 28 (12) |
| • Small bowel | 8 (4) |
| • Large bowel | 49 (22) |
| • Rectum | 45 (20) |
| • Miscellaneous | 12 (5) |

## RESULTS

Two hundred and twenty five patients were included in the study, and their details are shown in Table I. We found mean (SD) preoperative albumin concentrations of 40 (5) g/L, IL-6 concentrations of 19 (170) pg/ml, α-1-antitrypsin concentrations of 2.8 (0.8) g/L and CRP concentrations of 13 (22) mg/L (Table II). Twenty seven of the patients (12%) had albumin concentrations below 35 g/L. The proportion of abnormal concentrations of the different acute phase proteins was 8% to 13% (Table II) of all patients preoperatively. For most of the patients (182, 81%) concentrations of the acute phase proteins were within the reference ranges (Table III). Forty three of the patients (19%) had plasma concentrations of at least one acute phase protein outside the reference range, indicating that they had mounted an acute phase response. The response was graduated: 21 patients (9%) had concentrations of only one, 16 (7%) had two, and 6 (3%), had all three acute phase proteins outside the reference range.

Patients who mounted an acute phase response had lower albumin concentrations than the others. These

Table II. *Preoperative albumin, IL-6, α-1-antitrypsin, and CRP concentrations in 225 patients*

| | Mean | SD | Range | Reference range | No (%) outside the reference range |
|---|---|---|---|---|---|
| Albumin (g/L) | 40 | 5 | 24–61 | 35–51 | 27 (12) |
| IL-6 (pg/ml) | 19 | 170 | 0–125 | <4 | 24 (11) |
| α-1-Antitrypsin (g/L) | 2.8 | 0.8 | 0.95–6.08 | <3.5 | 29 (13) |
| CRP (mg/L) | 13 | 22 | 0–132 | <50 | 18 (8) |

Table III. *Acute phase response in 225 patients preoperatively*

| No. of acute phase proteins outside the reference range | No. (%) of patients |
|---|---|
| 0 | 182 (81) |
| 1 | 21 (9) |
| 2 | 16 (7) |
| 3 | 6 (3) |
| 1, 2, or 3 | 43 (19) |

dropped from 40 (5) g/L to 35 (5) g/L, if at least two of the variables indicating an acute phase response were abnormal (Table IV). In patients with only one acute phase protein outside the reference range the albumin concentrations (41 (5) g/L) were not affected. In patients with CRP concentrations above 60 mg/L we found lower mean albumin concentrations (33 g/L); with α-1-antitrypsin above 4.0 g/L there were also lower albumin concentrations (34 g/L), and in patients with circulating IL-6 mean albumin concentration was 37 g/L compared with patients with no evidence of an acute phase response (40g/L, Tables Va, b, and c).

Eleven of the total of 27 albumin concentrations that were below 35 g/L were associated with an increased concentration of at least one of the acute phase proteins, and eight were associated with an increased concentration of at least two of the acute phase proteins.

The association of malnutrition referred to as BMI below 19, low albumin concentrations, and the acute phase response is shown in Table VI. All patients with albumin concentrations below 35g/L and a BMI below 19 had at least one of the acute phase proteins out of the reference range, giving evidence of an acute phase response. Most of the reduced albumin concentrations ($n = 25$, 93%) were found in patients with a normal or raised BMI of ≥19 or of ≥25, respectively. Albumin concentrations of 36(5)g/L were lower in patients with BMI below compared with 40(5)g/L in those patients who had a BMI of ≥19. Fourteen of the reduced albumin concentrations were associated with neither a low BMI nor an acute phase response.

Thirty-one (18%) of the 172 patients with cancer showed an acute phase response, compared with 26% of the patients with benign disease. Albumin concentrations of 40(5) g/L compared with 40(6) g/L did not differ in these groups. An acute phase response was evident in 10% of the patients with metastatic cancer and in 21% of the patients with non-metastatic cancer (not significantly different).

Four (11%) of the 27 patients with low preoperative albumin concentrations developed complications associated with a severe systemic inflammatory response syndrome and organ dysfunction during their postoperative course. Another 11 (6%) severe septic complications developed in 198 patients with preoperative serum albumin concentrations within the reference range.

## DISCUSSION

Hypoalbuminaemia in patients before major operations is a risk factor for postoperative morbidity (7, 9, 17, 29). Low concentrations were usually attributed to malnutrition, and in consequence studies have been undertaken to improve nutritional state before operation. However, despite adequate nutritional support there were no convincing results, either because the methods used did not truly identify malnutrition, or a metabolic disorder made the patients resistant to nutritional support. The acute phase response is an example of a systemic reaction that modulates protein synthesis in the liver, including that of albumin, and alters the patient's condition (32) and various aspects of the immune system at the same time. Despite low albumin concentrations during the postoperative course being attributed to an acute phase response, sufficient data were not available about such a correlation preoperatively.

An acute phase response is a consequence of various stimuli, including operations and infections (8, 30). The response (24) is mediated through cytokines like IL-1 and IL-6 (3, 4, 23, 24), which are released after activation of the immune system (19). However, patients with cancer have also been found to have

Table IV. *Mean (SD) preoperative serum albumin concentrations in patients with and without an acute phase response*

| | No acute phase response ($n = 182$) | Acute phase response, concentration of one of the acute phase indicators outside the reference range ($n = 21$) | Acute phase response, concentrations of two or more of the acute phase indicators outside the reference range ($n = 21$) |
|---|---|---|---|
| Albumin (g/L) | 40 (5) | 41 (5) | 35 (5)* |

* $P < 0.01$, compared with patients who had no acute phase response (column 1) or only one of the acute phase indicators outside the reference range (column 2).

Table Va. *Mean (SD) albumin concentrations in patients with normal, intermediate, and high serum CRP concentrations*

| | CRP < 30 mg/L (*n* = 203) | CRP ≥ 30–59 mg/L (*n* = 9) | CRP ≥ 60 mg/L (*n* = 13) |
|---|---|---|---|
| Albumin (g/L) | 40 (5) | 37 (2)* | 33 (5)** |

* $P < 0.01$, ** $p < 0.001$ compared with patients who had CRP concentrations <30 mg/L (column 1).

Table Vb. *Mean (SD) albumin concentrations in patients with normal, intermediate, and high serum α-1-antitrypsin concentrations*

| | α-1-antitrypsin <3.3 g/L (*n* = 186) | α-1-antitrypsin ≥3.3–3.9 g/L (*n* = 20) | α-1-antitrypsin ≥4.0 g/L (*n* = 19) |
|---|---|---|---|
| Albumin(g/L) | 40 (5) | 40 (6)* | 34 (6)* |

* $P < 0.001$, compared with patients who had α-1-antitrypsin concentrations <3.3 g/L (column 1).

Table Vc. *Mean (SD) albumin concentrations in patients with normal, intermediate, and high serum IL-6 concentrations*

| | IL-6 < 4 pg/ml (*n* = 201) | IL-6 ≥ 4–19 pg/ml (*n* = 10) | IL-6 ≥ 20 pg/ml (*n* = 14) |
|---|---|---|---|
| Albumin (g/L) | 40 (5) | 37 (6) | 37 (6)* |

* $P < 0.05$, compared with patients who had IL-6 concentrations <4 pg/ml (column 1).

increased concentrations of IL-6 (26). In a proportion of our patients the underlying disease may have activated the immune system and subsequently triggered an acute phase response; our data support this hypothesis. Low albumin concentrations were detected in 12% of our patients. In addition, 19% of the patients showed evidence of an acute phase response. Hypoalbuminaemia was associated with the acute phase response if it was indicated by abnormal concentrations of at least two of the acute phase proteins. In addition, altered plasma albumin concentrations correlated with abnormal concentrations of acute phase proteins. Our series contains a relatively large number of patients in whom preoperative albumin concentrations were related to other acute phase variables including IL-6, a central trigger of the acute phase response (20, 28). From the data we conclude that in a small proportion of patients low preoperative albumin concentrations were associated with alterations of other acute phase proteins. This was a potential consequence of a metabolic process that may have an important effect on the postoperative complication rate in such patients. The question of whether the acute phase response was a risk factor for postoperative complications has been answered in a previous paper (18). The fact that the acute phase response was associated with a low albumin concentration, which is an accepted risk factor, would have suggested this. However, it has previously been suggested that an acute phase response may also have beneficial effects (10). The data provide a link between a well known independent risk factor for postoperative complications (low albumin concentration), and a new approach to elucidate the nature of the underlying regulatory events. This new approach included the investigation of preoperative monocyte activation, which may have triggered the acute phase response (24). The association of low preoperative albumin concentrations and an acute phase response interferes with the association of low preoperative albumin concentrations and malnutrition reported in many previous papers.

Table VI. *Association of the body mass index (BMI[kg/m²]), low albumin concentrations, and a positive acute phase reaction in 225 patients before major abdominal operations*

Figures are number (%) of patients unless otherwise stated.

| | BMI < 19 | BMI 19 - ≤ 25 | BMI > 25 |
|---|---|---|---|
| Proportion of patients | 12 (5) | 112 (50) | 101 (45) |
| Albumin <35 g/L | 4 (2) | 9 (4) | 14 (6) |
| APR-positive (at least one of the acute phase proteins outside the reference range) | 4 (2) | 25 (11) | 14 (6) |
| Mean (SD) Albumin (g/L) | 36 (6)* | 40 (4) | 40 (6) |

* $P = 0.05$, compared with patients with BMI from 19 - ≤ 25 (column 2) and BMI > 25 (column 3).

Our data offer an option to explain the development of malnutrition in addition to the fact that some of the patients cannot or do not eat. Identification of cachectin/tumour necrosis factor-α, a cytokine that can induce an acute phase response (31) and cachexia in patients with cancer (22), supports our conclusion. The potential preventive approach that is required to reduce the risk related to low preoperative albumin concentrations in such patients from that point of view cannot include hyperalimentation, which is not adequate to treat a metabolic disorder like the acute phase response. This may have already been shown by previous studies on preoperative hyperalimentation. Separating patients without an acute phase response from patients with an acute phase response may be useful to identify patients who can metabolise the nutrients for preventive nutritional support, and to separate others who might be better off with an approach directed towards reversal of the catabolic metabolism induced by the underlying disease. The data may also be useful to improve the classification of patients at risk and help to adjust the planned procedure to avoid complications, which is of benefit to the patient and cost-saving for the community.

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## RÉSUMÉ

*But:* Etudier l'incidence des stigmates préopératoires d'un état inflammatoire et son association à des concentrations basses d'albumine.
*Type d'étude:* Prospective, ouverte.
*Provenance:* Hôpital universitaire, Allemagne.
*Patients:* Deux cent vingt cinq patients devant subir une intervention abdominale majeure et qui n'avaient pas d'infection.
*Méthodes:* Les mesures des concentrations sériques d'albumine, de protéine C réactive (CRP), d'α-1 antitrypsine, et d'interleukine-6 (IL-6)
*Résultats:* Des concentrations anormales des protéines de la phase aiguë (témoignant d'une réponse à un état inflammatoire) ont été détectées chez 42 des 225 patients (19%). La concentration moyenne (ET) d'albumine chez ces patients (35 (5) g/l) était plus basse que chez ceux qui n'avaient pas de stigmates préopératoires d'un état inflammatoire (40 (5) g/l). Des concentrations élevées de CRP (≥60 mg/L) étaient associées à des concentrations basses d'albumine (33 g/L); des concentrations élevées d'α-1 antitrypsine (4 g/L) étaient associées à des concentrations basses d'albumine (34 g/L); et des concentrations élevées d'IL-6 (≥4 pg/ml) étaient associées à des concentrations basses d'albumine (37 g/L) contre une concentration d'albumine moyenne (ET) d'albumine de 40 (5) g/L chez les patients qui n'avaient pas de stigmates préopératoires d'un état inflammatoire.
*Conclusions:* Une réponse métabolique à une maladie considérée comme une réponse à un état inflammatoire peut expliquer des concentrations préopératoires basses d'albumine. Cette association interfère avec la conjonction de concentration basse d'albumine et de malnutrition. C'est un nouvel aspect de l'évaluation du risque préopératoire et pourrait déboucher sur des mesures préventives.
*Mots-clés:* réponse à un état inflammatoire, hypoalbuminémie, évaluation du risque, risque chirurgical, dénutrition, hyperalimentation préopératoire.

## ZUSAMMENFASSUNG

*Ziel:* Untersuchung der Inzidenz präoperativer Akut-Phasen-Antwort und deren Assoziation mit erniedrigten Konzentrationen des Serum-Albumins.
*Studienanordnung:* Offene, prospektive Studie.
*Studienort:* Akademisches Lehrkrankenhaus, Deutschland.
*Patienten:* 225 Patienten, vorgesehen für größere abdominalchirurgische Eingriffe, ohne Zeichen akuter Infektionen.
*Methoden:* Bestimmungen der Serum-Konzentrationen des Albumins, C-reaktiven Proteins (CRP), α-1-Antitrypsin sowie des Interleukin-6 (IL-6).
*Ergebnisse:* Bei 43 von 225 Patienten (19%) wurden Konzentrationen von Akute-Phase-Proteinen außerhalb des Normalbereichs nachgewiesen (hinweisend auf eine Akute-Phase-Antwort). Die präoperativen, mittleren Serum-Albumin-Konzentrationen dieser Patienten waren niedriger als die derjenigen Patienten, die keine Akute-Phase-Antwort aufwiesen (35 ± 5 g/l vs. 40 ± 5 g/l). Hohe Serum-Konzentrationen an CRP (≥60 mg/l) waren mit niedrigen Serum-Albumin-Konzentrationen assoziiert (33 g/l); hohe Konzentrationen von α-1-Antitrypsin (≥4 g/l) waren assoziiert mit ernied-rigten Konzentrationen an Serum-Albumin (34 g/l); und hohe IL-6-Konzentrationen (≥4 pg/ml) waren ebenfalls assoziiert mit erniedrigten Serum-Albumin-Konzentrationen (37 g/l) jeweils verglichen mit den Serum-Albumin-Konzentrationen von im mittel 40 ± 5 g/l in denjenigen Patienten, die keine Hinweise für eine Akute-Phase-Antwort hatten.
*Schlußfolgerung:* Die als Akute-Phase-Antwort angesprochene metabolische Reaktion auf Erkrankungen kann präoperativ erniedrigte Serum-Albumin-Konzentrationen erklären. Dieser Zusammenhang überschneidet sich mit der bekannten Assoziation erniedrigter präoperativer Serum-Albumin-Konzentrationen und Fehlernährung. Dieser neue Aspekt der präoperativen Risikoabklärung hat möglicherweise präventiven Nutzen.
*Schlüsselwörter:* Akute-Phase-Antwort, Hypalbuminämie, Risiko-Abklärung, chirurgisches Risiko, Fehlernährung, präoperative Hyperalimentation.

## РЕЗГОМÉ

*Цель:* Изучить процент развития острой ответной реакции в предоперативном периоде, а также ее ассоциацию с низким уровнем концентрации сывороточного альбумина.
*Характер исследования:* Проспективное открытое исследование.
*Клиника:* Учебный госпиталь, Германия.
*Пациенты:* 225 пациентов, подвергшихся большим абдоминальным операциям, у которых не было острых воспалительных заболеваний.
*Методы:* Измеренная концентрация сывороточного альбумина, С-реактивного протеина, α-1 антитрипсина и интерлейкина-6 (IL-6).
*Результаты:* Изменения концентрации протеинов в острой фазе указывала на развитие острого ответного синдрома и определялась у 43 из 225 пациентов (19%). Средняя концентрация альбумина у этих пациентов была 35 г/L, что было меньше, чем концентрация альбумина у пациентов, у которых не было развития острой защитной реакции в предоперативном периоде (40 г/L). Повышенная концентрация С-реактивного протеина (>60 мг/L) ассоциировалась с низкой концентрацией сывороточного альбумина (33 г/L); повышенная концентрация α-1 антитрипсина (>4 г/L) ассоциировалась с низкой концентрацией альбумина (34 г/L), высокая концетрация IL-6 (>4 рг/мл)

ассоциировалась с низкой концентрацией альбумина (37 г/L) по сравнению со средней концентрацией альбумина (40 г/L) у пациентов, у которых не развилась острая ответная реакция .
*Выводы:* Метаболические нарушения, относящиеся к острой защитной реакции можно объяснить низкой предоперативной концетрацией альбумина. №та связь может комбинироваться с низкой предоперативной концентрацией альбумина и неправильным питанием. №тот новый аспект оценки предоперативного риска может быть использован для предотвращения развития тяжелых осложнений.
*Ключевые слова:* Острая ответная реакция, гипоальбуминемия, оценка риска, хирургический риск, мальнутриция, предоперативная гипералиментация.

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# Reconstruction of the Supra-aortic Trunks

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ABSTRACT

*Objective:* To review our 10-year experience of recontruction of the supra-aortic trunks.
*Design:* Retrospective study.
*Setting:* Teaching hospital, The Netherlands.
*Subjects:* 47 patients who required reconstruction of the supra-aortic trunks for stenotic or occlusive disease between April 1987 and May 1997.
*Interventions:* Right-sided bifurcation graft through a sternotomy ($n = 25$), left-sided thoracotomy ($n = 1$), and extra-anatomic bypass ($n = 21$).
*Main outcome measures:* Morbidity, mortality, and long term patency.
*Results:* 3 patients died (6%); 7 (15%) developed major complications (leak from the brachiocephalic stump, $n = 2$, and acute occlusion of the bypass graft, $n = 5$) all of which were successfully treated by immediate reoperation; and 9 (19%) developed minor complications, all of which resolved within 3 months. The median follow up was 36 months (range 1–108), and the 3-year patency rate was 80%. No patient died during the follow up period, but a further 3 were lost to follow up. The remaining 41 were all assessed by duplex scanning or angiography, and 3 required further operation for recurrent symptoms; 33 remained completely free of symptoms.
*Conclusion:* Symptomatic stenotic or occlusive lesions of the supra-aortic trunks can be treated with acceptable morbidity and mortality, giving long term benefit to patients.

*Key words:* aortic arch trunks, occlusive disease, reconstruction, anonyma artery, brachiocephalic artery, subclavian artery.

## INTRODUCTION

Clinical signs of occlusive or stenotic lesions of the supra-aortic trunks depend on the vessels affected, the degree of obstruction, and also the systemic signs associated with a particular disease, such as arteritis. The stage and onset of vascular occlusion together with the extent of development and collateral circulation also influence the severity of symptoms.

The selection of treatment depends on the severity of symptoms, the natural history of the disease, and the morbidity and mortality of the treatment. Surgical intervention is indicated when the lesions are responsible for neurological or ischaemic symptoms in the arm (16). Although reconstruction of brachiocephalic arterial occlusive disease was introduced in the early 1950s (8, 15), the optimum operation remains controversial.

The aim of this report is to review our 10-year experience of recontruction of the brachiocephalic, carotid, and subclavian trunks.

## PATIENTS AND METHODS

The hospital records of all patients who underwent revascularisation for occlusive or stenotic disease of the supra-aortic trunks between April 1987 and May 1997 were reviewed. Patients with aneurysmal disease or those with acute occlusion were excluded. Forty-seven consecutive patients were involved in the study. There were 27 men and 20 women, age range 36 to 79 (mean 61).

Cardiovascular risk factors, initial symptoms, non-invasive and arteriographic findings, type of revascularisation, operative techniques, and early and late results were recorded as well. Follow up information was obtained from review of the out-patient charts and telephone contact with patients' families and family doctors. Patency was diagnosed by Duplex scanning, brachial pressure measurements, or angiography.

Patency of bypass grafts was calculated by life table analysis.

## RESULTS

The main presenting features are summarised in Table I. Forty patients (85%) presented with more than one symptom. Among the risk factors that are usually associated with arterial disease, smoking was encountered in 16 patients (34%), hypertension in 10 (21%),

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