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## Difficult Decisions

# Upper gastrointestinal bleeding – when to operate

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### Introduction

Gastrointestinal bleeding is a dramatic clinical problem where the outcome depends predominantly on correct and timely clinical decisions and very little on pharmacological agents. Moreover, the end point of success or failure is at the highest level, being literally life or death. All other indices of outcome (such as rebleeding, transfusion requirements or surgical intervention) are of lesser importance, although often used as predictors of danger. The operation, being the most dramatic event short of death, has indeed been used as an index, but is also cited as a hazard and its correct timing and extent have been the subject of much conjecture and debate. The difficult decision is whether such a dangerous procedure should be avoided in seriously ill and often aged patients if at all possible, or would earlier surgery actually reduce hazards from circulatory disturbance. There is no substitute for a properly designed prospective trial, but much can be learnt from trends in mortality and also from an examination of the causes of death and mortality reported as associated with different policies.

### Changing mortality

In 1927 the late Ernest Bulmer reporting from this hospital in the *Lancet*[1] observed an increase in mortality for bleeding ulcers from 0% in 1902 to 16% in 1925. He commented that 'it seemed to be a reasonable supposition that cases of such severity as in the old days would have been allowed to die comfortably at home are at the present time entrusted to a fast motor ambulance with a good prospect of arriving at hospital before a fatal issue has occurred'. It is indeed difficult to believe that the true mortality from gastrointestinal bleeding early this century could have been less than 20–30%, particularly as 'at the present time, the treatment is morphine, a period of starvation with rectal salines, and later a graduated diet with alkalis'. Probably the single most important factor in improving safety was the introduction of resuscitation with blood and intravenous fluids in the 1930s, and mortality rates at about this time appeared to halve.[2] Since then rates have continued to fall though with wide variability between different centres. They have now reached approximately 10% overall and 4–5% for peptic ulcer bleeding in units committed to a careful management policy despite a steadily ageing population.

### Causes of death

Much can also be learnt from examining the causes of death, as management must address the most obvious complications. It has been argued that surgery itself could be a major contributory factor together with a wide range of vascular catastrophes.[2] Clearly a zero rate for surgery implies zero surgical complications. An Edinburgh group[3] was able to divide the causes of 64 deaths approximately equally into exsanguination, surgical complications and coincident disease, and surprisingly concluded 'how difficult it will be to reduce the mortality of upper gastrointestinal bleeding'. Severe coincident disease particularly in the older patients has always been one of the greatest hazards for these patients.[4]

On the other hand, the hazards of surgical delay were highlighted from Ottawa[5] in an analysis of 50 consecutive deaths. In 44, transfusion was deemed inadequate, and in 29, operation was carried out much too late. The incidence of repeated haemorrhage with a mean of 5 episodes per patient appeared extraordinary, but the authors reminded us that Avery Jones described these repeated brisk and short lived episodes in 1947. Perhaps we should look more vigorously at the patients' circulatory state. The similar but more sophisticated analysis from Scotland[6] gives additional support for the safety of surgical intervention. Examination of a large number of potential risk factors failed to

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reveal surgery as an independent variable. The conclusion was that 'whether or not surgery was performed had little influence on mortality ($P<0.5$)'.

A valuable retrospective audit of results in a district general hospital[7] revealed a peptic ulcer mortality of 11% with a low operation rate (16%). The authors concluded that the commonest cause of death was unchecked bleeding which should have been controlled by more frequent and earlier surgery. They also blamed surgical delay for a high operative mortality (35%). This report probably reflects a wider pattern of management and results than is generally believed, but one which should be alterable by regular audit of clinical results.

## Delayed surgery

Increasing numbers of patients with life threatening haemorrhage are aged and suffer from severe coincident disease. It is not surprising, therefore, to find clinicians reluctant to take such apparently poor risk patients to theatre with all the inherent circulatory and respiratory problems. Thus, is it better to support the circulation, delay surgery and carry more patients on to spontaneous healing?

This policy received some support from Oxford[8] when a detailed analysis of over 2000 patients introduced a comparison of emergency versus early elective surgery. The former carried a mortality of 20%, the latter only 7%. Clearly patient selection was paramount in a non-randomized comparison, but the suggestion had some clinical influence. The place of early surgical intervention was criticized by Dronfield and colleagues,[9] who compared the results for bleeding peptic ulcers at 2 different hospitals in the Nottingham area, one with an aggressive surgical approach, the other more conservative (Table I). A total of 302 patients were studied. They found no difference in the age, sex, diagnosis and severity of bleeding in the 2 groups. One hospital had a consistently higher operation rate and earlier time for surgery than the other, and the overall mortality was higher in the more aggressively treated patients (17.7% *vs* 12.7%). A large number of deaths followed surgery (22 deaths from 110 operations, operative mortality 20%) which accounts for the different overall mortalities. The authors concluded that an early, aggressive surgical policy was unlikely to reduce the number of deaths.

A later report from the same group[10] compared the surgical and medical management of 908 patients in a 6-year period in Nottingham. They found that operation rates fell over this period, from 34% in the initial years to 21% in the later years, with no adverse effect on mortality. The overall mortality rate was 11%, with an operative mortality of 22%. In view of the high risks of surgery, they again supported conservative management, especially in elderly patients.

The most recent enthusiastic support of a conservative approach comes from Australia[11] where, of 86 sequential patients admitted to a specialist unit, only 4 received an operation. There were 3 deaths, one of which was post-operative. The contribution of this study to the problem is, however, ques-

**Table I** Incidence of surgery and mortality for bleeding peptic ulceration in recent substantial published series

| | *Conservative* | | | | *Policy* | | *Aggressive* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Reference | 9 | 10 | 17 | 11 | 7 | 13 | 9 | 10 | 15 | 16 | 17 |
| Number of patients | 206 | 417 | 71 | 86 | 159 | 49 | 96 | 491 | 380 | 376 | 71 |
| Mean age (yrs) | 62 | 65 | 64 | 52 | 60 | 70 | 64 | 61 | ? | 55 | 64 |
| Operation rate (%) | 32 | 21 | 21 | 5 | 10 | 71 | 46 | 34 | 43 | 27 | 59 |
| Surgical mortality (%) | 20 | 24 | 40 | 25 | 35 | 3 | 20 | 21 | 10 | 19 | 5 |
| Overall mortality (%) | 13 | 11 | 11 | 3.5 | 11 | 3 | 18 | 11 | 6 | 7 | 2.8 |
| Origin of Study | Nottingham 1979 | Nottingham 1982 | Birmingham 1984 | Newcastle (Australia) 1985 | Newport (Wales) 1986 | Kansas (USA) 1977 | Nottingham 1979 | Nottingham 1982 | Melbourne 1979 | Melbourne 1987 | Birmingham 1984 |

tionable, as patients regarded as 'unsalvageable' were excluded, and 8 were recorded as having died from upper gastrointestinal haemorrhage with no diagnosis.

### Early surgery

Exsanguination is a common cause of death in the literature of gastrointestinal bleeding, and the alternative approach of early surgical intervention has had many advocates. Tanner[12] reviewed the results of surgery in bleeding peptic ulcer disease over a 10-year period which involved 622 admissions with chronic peptic ulceration. In the latter part of this period he was able to demonstrate a reduction in the overall mortality from 10% to 7% in patients treated with early surgery compared with patients treated earlier when operation was avoided. The rate of surgical intervention increased from 5% to an alarming 60%, but despite a marked increase in the average age of the patients, the overall mortality fell. This study, though impressive, was uncontrolled and involved a policy change. Tanner correctly attributed part of the success to a dedicated team of medical and nursing staff. The policy involved surgical intervention on admission for patients with known peptic ulceration and for rebleeding.

Chang and colleagues[13] reported their experience of an aggressive policy for so called massive upper gastrointestinal haemorrhage, reporting on 66 patients over the age of 60. They included only patients who required an initial transfusion of 3 or more units of whole blood to restore blood volume; their group included 49 patients who bled from peptic ulceration. They operated on 35 (71%), with only one post-operative death (operative mortality 3%). They concluded that their results supported a policy of early and aggressive resuscitation, diagnosis, and surgical intervention, but the paper contains very limited detail.

In a study on 211 peptic ulcer patients managed according to a specific protocol,[14] the results were compared with historical controls. The policy included early endoscopy and surgery for all patients with gastric ulcers, and for older patients with duodenal ulceration. Surgery was also indicated in patients requiring an initial transfusion of 5 or more units of whole blood. Overall mortality was reduced from 7.3% to 2.4% and transfusion requirements were halved. Although this study has all the defects of the use of historical controls, the improvement in results is impressive. One of the staunchest advocates of the policy of tight management and early surgery is Hunt who described the results achieved by his unit in Melbourne.[15] The policy was of early endoscopy with surgery to follow clearly defined criteria. Over a 6-year period there was a mortality for peptic ulcer bleeding of 6%, an operation rate of 43% and an associated surgical mortality of 10%. Curiously when the study period was broken into 3 two-year periods, mortality in the last of these was significantly lower at 1.5%, although the operation rate and case mix remained the same. Any suggestion that a permanent change had been effected was unfortunately refuted by a subsequent report,[16] when the mortality had returned to 7.4% with an operation rate of 27% (surgical mortality 19%).

In Birmingham, we believed that a prospective randomized study was necessary to answer this question. This was carried out at the Birmingham General Hospital between 1980 and 1983.[17] Patients with proven peptic ulcers were stratified by age (above and below 60 years) and randomized to receive either early or delayed surgical intervention according to defined criteria. Endoscopy was carried out within 12 hours of admission and patients were managed in a designated unit. In younger patients mortality was negligible, no advantage was found from early operation, and the operation rate of 50% in the early group was excessive. In the older group, however, mortality in the patients receiving early surgery was significantly lower (5% *vs* 15% in delayed group); most of this difference was accounted for by patients with gastric ulcers. For practical and ethical reasons the trial was stopped at this stage.

It was deduced that minimal mortality was associated with urgent and skilled surgical intervention when the following criteria were satisfied: (1) exsanguinating haemorrhage or a spurting vessel at endoscopy. (2) In patients aged 60 years or older. One rebleed, 4 units for initial resuscitation, or 8 per 48 hours during recovery. (3) In patients aged less than 60. Two rebleeds, 8 units for initial resuscitation, or 12 per 48 hours during recovery.

This policy was adopted for the 5-year period 1984–1988, and the results carefully audited.[18] At Bath, a similar audit was carried out 1986–1988 in a non-teaching district general hospital using almost identical criteria.[19] The results of these two studies are summarized in Table II. In both of these studies there were no exclusions even on the basis of advanced inoperable malignant disease, and, at least in the Birmingham census, treatment was withdrawn in several patients. Mortality was low in both, totalling 25 of 559 available for study (4.5%). There is a remarkable similarity in the mortality rate at different ages, which for the over 60s was 6% in both and for the over 80s, 10% in Bath and 8% in Birmingham. The age distribution in Bath presumably reflects demography in a spa town. Both studies give excellent results, reflecting the importance of the integrated 'bleeding unit'. The only notable clinical difference lay in the surgical mortality, 15% in Bath and 3% in Birmingham.

**Table II** Results currently achieved applying a clear aggressive surgical policy

| | *Bath*[19] | | *Birmingham*[18] | |
|---|---|---|---|---|
| | *Patients* | *Mortality %* | *Patients* | *Mortality %* |
| GU/DU | 109/108 | | 124/218 | |
| Deaths | | | | |
| Surgical | 7 | 15 | 2 | 3 |
| Non-surgical | 5 | | 11 | |
| Total | 12 | 5.5 | 13 | 3.8 |
| Surgery | | | | |
| Operation rate | 21% | | 20% | |
| V & P* | 26 | | 33 | |
| Resection | 13 | | 27 | |
| Minimal† | 7 | | 9 | |
| Age | | | | |
| <60 | 42 | 2 | 128 | 1 |
| 60–70 | 48 | 2 | 94 | 3 |
| 70–80 | 66 | 6 | 84 | 7 |
| 80+ | 61 | 10 | 36 | 8 |
| Total | 217 | 5.5 | 342 | 3.8 |

*V & P = vagotomy and pyloroplasty; †minimal = under-running of vessel or ulcer excision.

## Discussion

A novice to this field could be forgiven for feeling that the results available are so different, the patient mix so variable, and the policies of management often so poorly defined that no conclusions are possible. It is entirely unhelpful to compare studies across a time scale of 50 years and then attempt to draw conclusions as to optimal management for the 1990s. In examining causes of death, most retrospective analyses have pointed to exsanguination, inadequate resuscitation and surgical delay, although these factors are difficult to assess in reading case records written by others. Certainly exsanguination features repeatedly and is a consequence of continued and repeated bleeding. In the absence of widespread availability of proven endoscopic methods of control, surgery must for the moment remain the preferred option in most hospitals. The question is, therefore, one of its timing and extension. The precise reasons for the danger of exsanguination and fluctuating blood volume are for the present unclear, but are less important than the real link with mortality. It is possible that repeated hypovolaemia results in a tendency to small vessel thrombosis with or without embolism, and sometimes to irreversible shock. Other complications also follow, such as infection, failure of wound healing, and the acute respiratory distress syndrome. We believe that the maintenance of a stable circulation is the prime aim of therapy.

The hazards which may follow an operation can be serious and life threatening, and it is reasonable to ask whether they are increased with early surgery and high operation rates. The evidence in favour of this view is sparse, and centres mainly on the studies from Oxford[8] and Nottingham.[9,10] The former was a retrospective comparison of records spread over 6 years, and the group receiving early elective surgery must have been entirely different from those operated upon as an emergency. It is not possible to draw meaningful conclusions from this comparison. The study from Nottingham was more satisfactory, being a parallel examination of the results from 2 hospitals with different policies. From its nature it was not randomized, different populations were involved, and different surgeons carried out the operations. In addition, mortality in both groups was much higher than is now achievable by standard care, largely invalidating the conclusions. If both mortality figures carry deaths avoidable more simply, then even in a properly randomized study, the issue would still have remained clouded. The study from Australia[11] gives low mortality, but its small numbers and extensive exclusions make its contribution dubious.

Similarly, most of the data which support early surgery are also uncontrolled, with higher mortality than is now acceptable. Nonetheless, several groups have achieved mortality rates of approximately 5% for bleeding peptic ulceration, often for quite large study numbers. The major reservation must remain that these good figures all come from

enthusiastic teams with an evident attention to detail. Both Hunt[15] and Tanner[12] give appropriate tribute to their supporting teams and most recently Sanderson and colleagues[20] have re-emphasized the importance of specialized GI units. There is indeed no substitute for devoted and skilled care. One wonders for instance whether the 1.5% mortality achieved briefly in Melbourne[15] represented a peak of clinical vigilance, and a subsequent fall off to 7.4%[16] some change in the management team. It is unfortunate for this argument that the Birmingham study stopped when its data had reached bare statistical significance, but the difficulties of running such a prolonged randomized trial are self evident. The results achieved in the 5 years following this trial[18] do, however, strongly support the conclusions from the randomized study and are supported by the study from Bath.[19] The overall mortality for peptic ulcer bleeding of 4.2% from 400 patients was still 6% for those over 60 and 9% for those over 80.

These figures must stand as a target for alternative policies. It is encouraging and supportive of the general argument that the only other comparable figure in a large study comes from the use of laser therapy to both stop and prevent further bleeding.[21] The conclusion must be that further bleeding in these patients is the most dangerous of all complications, and the aim of management is to strenuously pursue any measure to prevent it happening. Physical endoscopic measures may in trained hands be an alternative, but in their absence early and skilled surgery on the carefully selected patients is the option of choice.

The surgical mortality in our latest audit (3% from 69 operations) is the combination of a decade of weekly audit meetings and is attainable by all. It is due partly to the correct choice of the time of surgery, partly to our policy that both surgeon and anaesthetist must be of an adequate level of seniority and training, and partly to the care of patients in a designated unit with a dedicated staff. The question only remains of the extent of surgery. It has frequently been argued that gastric resection carries greater hazard than vagotomy and local control of bleeding.[22] With the advent of more powerful drugs to heal ulcers, it is logical to propose even less surgery aimed simply at stopping the bleeding. Any remaining ulcer disease can then be treated along conventional medical lines. This question is the subject of a multi-centre study now in progress (Keighley, M.R.B., personal communication) and its results will be awaited with interest.

We believe, therefore, that the current correct approach to peptic ulcer bleeding is rapid resuscitation, early diagnosis, careful monitoring and immediate skilled surgical intervention when defined criteria are breached.

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