Surgery for massive splenomegaly

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Background: Splenectomy for massive splenomegaly (spleen weight more than 1.5 kg) is commonly believed to be hazardous and to provide poor palliation. The aim of this cohort study was to investigate these issues and examine the many definitions of massive splenomegaly to see whether a better tool might be proposed for preoperative evaluation of these patients.

Methods: Morbidity and long-term outcomes were assessed in consecutive patients. Relief of pressure–volume-related symptoms and sustainable independence from transfusion in patients were used to ascertain the impact of splenectomy.

Results: Splenectomy was performed in 56 patients, mainly for non-Hodgkin’s lymphoma and myeloproliferative diseases. Median spleen weight was 2.3 (range 1.5–6.0) kg. Mortality at 180 days was zero, and the postoperative complication rate was 25 per cent (17 complications in 14 patients). At 2 years, relief of pain was maintained in 33 of 34 patients, with sustained independence from transfusion in 15 of 19 patients with anaemia and nine of 11 with thrombocytopenia. Spleen weight correlated negatively with BMI (P = 0.036).

Conclusion: Splenectomy for massive splenomegaly is safe and provides effective palliation. Provisional cut-off points relating to spleen size and BMI help to identify patients benefiting from a splenectomy, even those in a critical state.

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Introduction

The definition of massive splenomegaly, as proposed by Goldstone in 1978 and adopted by Bickerstaff and Morris in 1987, is a spleen weighing more than 1.5 kg, or about ten times the normal weight. Regardless of cause, splenomegaly of this magnitude may be symptomatic for physical reasons (pain caused by the weight and volume of the spleen), related to anaemia or thrombocytopenia, or follow splenic infarction. Splenectomy in these patients is widely believed to be hazardous and to provide only poor palliation. Observational studies have reported mortality rates of 1.8–15 per cent and complication rates of 9–51 per cent. Numerous case reports and small series have shown the feasibility of laparoscopic splenectomy for massive splenomegaly, but, as with open splenectomy, the criterion of a spleen weight greater than 1.5 kg has not been used consistently to refer to massive splenomegaly. Some reports regarding the safety of laparoscopic approaches have included splenic specimens of only 500 g, whereas others have included spleens of more than 600 or 1000 g. Other authors have categorized spleens weighing 600–1600 g as ‘massive’, and those weighing more than 1600 g as ‘supramassive’.

The aims of the present observational study were to examine the mortality and complications associated with splenectomy for massive splenomegaly (above 1.5 kg) and to see whether the procedure provided symptom palliation of worthwhile duration. It was hoped that these results might also identify splenic features and patient characteristics that could be used to simplify the terminology used for splenic surgery, particularly in the laparoscopic era.

Methods

Consecutive patients with massive splenomegaly who underwent elective splenectomy between January 1985 and December 2015 as part of their treatment for neoplastic or haematological disease were studied. Preoperative variables, including underlying diagnoses, signs,
symptoms, radiology and laboratory data, and transfusion information, were recorded in a prospectively developed database. Karnofsky performance status\(^\text{19}\) was measured before and 1 month after surgery.

Clinical and haematological information was recorded at 6 months, 1 year and 2 years. Long-term follow-up was also available for most patients. Informed consent for surgery and data collection was obtained from each patient.

Splenectomy was generally planned as an open procedure, predominantly through an oblique incision starting below the left costal margin at the level and in the axis of the ninth intercostal space and descending towards the umbilicus (\(\text{Fig. 1}\)). In a small number of patients, a laparoscopic approach was considered at the outset. The patient was in the supine position, turned slightly to the right, and strapped to the operating table to allow for steep changes in table position. After mobilization of the lower part of the spleen from the peritoneal cavity, the gastroplenic ligament was divided widely to gain early access to the main splenic artery above the pancreatic tail. Early ligation of the splenic artery permitted some decompression of very large spleens by transfusing the contents before ligation of the venous return. All spleens were weighed within minutes of excision. All patients received standard preoperative antibiotic prophylaxis, and were immunized against encapsulated bacteria by receiving preoperative polysaccharide vaccines against \(\text{Streptococcus pneumoniae, Haemophilus influenzae}\) and \(\text{Neisseria meningitidis}\) at least 3 weeks before elective splenectomy.

Prophylactic measures to reduce the risk of venous thromboembolism included early mobilization, antiembolism stockings and administration of low-dose low molecular weight heparin. Aspirin (100 mg/day) was used for at least 6 months in patients with reactive thrombocytosis (platelet count above \(500 \times 10^9/\text{l}\)).

For comparison of spleen weight and bodyweight/spleen weight ratio, patients were divided into four groups: those with non-Hodgkin’s lymphoma, myeloid dysplasia, chronic lymphocytic leukaemia and rare diseases.

**Statistical analysis**

All data are displayed as means or medians with ranges depending on data distribution for continuous variables, and as frequency or percentages for categorical variables. When indicated, categorical variables were compared using the \(\chi^2\) test. Kaplan–Meier analysis was undertaken to estimate the postoperative cumulative survival probability for the whole series.
Table 1  Baseline patient characteristics

| No. of patients (n = 56)* | Age (years)† | Sex ratio (M:F) | Bodyweight (kg)† | BMI (kg/m²)† | ASA fitness grade | Co-morbidity (≥2) | Other abdominal surgery at time of splenectomy | Preoperative chemotherapy | Preoperative steroid treatment | Preoperative transfusion of red cells | Spleen weight for entire series (kg)† | Non-Hodgkin’s lymphoma (n = 27) | Myeloid metaplasia (n = 15) | Chronic lymphocytic leukaemia (n = 7) | Other (n = 7) |
|--------------------------|-------------|----------------|-----------------|-------------|-----------------|-----------------|-----------------------------------------------|----------------------------|-------------------------------|-----------------------------------|----------------------------------|-------------------------------|----------------|-------------------------------|--------------------------|----------------|
| Age (years)              | 25 (28–83)  | 32:24          | 64 (36–140)     | 23 (12–43)  | 1 (2)           | 18 (32)         | 33 (59)                                       | 4 (7)                      | 10 (18)                       | 32 (57)                           | 2·3 (1·5–6·0)                   | 2·1 (1·5–5·0)                 | 2·8 (1·8–6·0)              | 2·3 (1·7–3·5)                 | 1·6 (1·5–2·5)     |
| Co-morbidity (≥2)        | 31 (55)     |                |                 |             |                 |                 |                                               |                            |                               |                                   | 2·9 (6–66)                     | 34 (12–48)                    | 25 (6–36)                   | 2·3 (16–52)                  | 48 (28–66)    |
| Other abdominal surgery  | 10 (18)     |                |                 |             |                 |                 |                                               |                            |                               |                                   |                                 |                               |                             |                             |                           |
| Preoperative chemotherapy| 32 (57)     |                |                 |             |                 |                 |                                               |                            |                               |                                   |                                 |                               |                             |                             |                           |
| Preoperative steroid     | 16 (29)     |                |                 |             |                 |                 |                                               |                            |                               |                                   |                                 |                               |                             |                             |                           |
| Preoperative transfusion | 26 (46)     |                |                 |             |                 |                 |                                               |                            |                               |                                   |                                 |                               |                             |                             |                           |
| Spleen weight            | 2·3 (1·5–6·0)|                |                 |             |                 |                 |                                               |                            |                               |                                   |                                 |                               |                             |                             |                           |

*Unless indicated otherwise; †values are median (range).

As the persistence of a favourable outcome for pain relief, control of anaemia and thrombocytopenia could be biased by patient death during long-term follow-up, the analysis considered the effects of death during follow-up as a censoring or competing risk event on the inference made for these three outcomes.

Bodyweight and height were measured to derive the BMI, and the bodyweight/spleen weight ratio was correlated with BMI to take the patient’s morphology into account. As there was a common component (bodyweight), mathematical coupling of data was considered and also taken into account.

Results

Baseline characteristics of the 56 patients are summarized in Table 1 and pathological diagnoses in Table 2. More than two-thirds (71 per cent) of the patients were 60 years of age or older. With one exception of idiopathic left-sided portal hypertension, all patients had some form of haematological disease. Mean duration of disease before surgical involvement was 60 (median 24, range 9–164) months. Spleen weights and bodyweight/spleen weight ratios for the entire series and for each of the four disease groups are shown in Table 1.

The mean duration of surgery was 128 min, and ten patients (18 per cent) required intraoperative blood transfusion (2–5 units of packed red cells). Platelet concentrate was generally infused after early ligation of the splenic artery in those with severe preoperative thrombocytopenia. The weight distribution of the removed spleens is shown in Fig. 2; 12 patients had a spleen weight greater than 3·0 (mean 3·2; median 3·4, range 3·1–6·0) kg. The scatter plot of bodyweight/spleen weight ratio against BMI with the corresponding regression line is shown in Fig. 3.

Open splenectomy was performed in 55 patients; hand-assisted laparoscopic splenectomy was attempted in four patients, with conversion to open surgery in three of these. The oblique left upper quadrant incision was used in 32 patients (57 per cent), mainly for spleens weighing more than 2·5 kg. A subcostal incision was used in 13 patients (23 per cent). Of 30 patients (54 per cent) who had early intraoperative ligation of the main splenic
Massive splenomegaly
Died in first postoperative year (n = 9)
Laparoscopic splenectomy attempted (n = 4)

Fig. 3 Scatter plot of bodyweight/spleen weight ratio against BMI in 56 patients with massive splenomegaly. The left lower quadrant delineated by dotted lines (BMI less than 24 kg/m² and bodyweight/spleen weight ratio below 40) includes 35 of the 42 patients who had excellent pain relief after splenectomy (Karnofsky performance score increased from 20–50 to a postoperative score of 70–90). The regression line with its 95 per cent c.i. is shown. $R = 0.69$, $P < 0.001$

Fig. 4 Kaplan–Meier survival estimate with 95 per cent c.i. for 56 severely compromised patients with massive splenomegaly

artery, none required intraoperative or postoperative blood transfusion.

All 56 patients were discharged from hospital, and there was no death within 180 days of operation. Mean duration of stay from surgery to hospital discharge was 12 (median 10, range 5–21) days. Fig. 4 shows Kaplan–Meier survival estimate with 95 per cent c.i.

A total of 17 postoperative complications occurred in 14 of the 56 patients (25 per cent): eight chest infections that responded rapidly to treatment; four pleural effusions (1 required drainage); two cases of early bleeding from the splenic bed that required surgical operation; one incisional hernia after median laparotomy; one case of severe epistaxis in a patient with chronic lymphocytic leukaemia and severe preoperative thrombocytopenia (platelet count $2.8 \times 10^9/l$); and one portal vein thrombosis.

Factors that were significantly associated with postoperative complications were ASA grade above II ($P = 0.015$) and bodyweight/spleen weight ratio less than 20 ($P = 0.044$) (Table 3). Of 37 patients classified as ASA grade III or IV, 13 developed postoperative complications, compared with only one of the 19 patients with ASA grade I or II. The use of short-term high-dose steroids, prescribed before surgery in 16 patients (29 per cent) as part of the medical management of their haematological disorder, was not associated with postoperative complications when compared with patients who had not received steroids.

Palliation was effective in 42 patients in whom splenectomy was performed primarily for pain relief. Analysis of BMI and the bodyweight/spleen weight ratio indicated that 35 of these 42 patients had excellent pain relief, and moved from preoperative Karnofsky performance score of 20–50 to a postoperative score of 70–90 (Fig. 3). To overcome the problem of mathematical coupling, spleen weight alone was compared with BMI (Fig. 5). Spleen weight correlated negatively with BMI. This still allowed the identification of 25 patients who moved from a Karnofsky score of 20–50 to a score of 70–90 after splenectomy. The provisional cut-off points adopted for good pain relief were bodyweight/spleen weight ratio below 40, spleen weight greater than 2.0 kg, and BMI below 24 kg/m². Determination of these provisional cut-off points was based on the tentative delineation of the quadrant of the scatter plot encompassing a maximum of patients who had good pain relief in the face of a low preoperative bodyweight/spleen

Table 3 Factors significantly associated with postoperative complications

| No. of complications | $P^*$ |
|----------------------|------|
| Preoperative need for blood transfusion |      |
| Yes                  | 12 of 26 | 0.001 |
| No                   | 2 of 30  |      |
| Presence of $\geq$ 2 co-morbidities |      |
| Yes                  | 13 of 31 | 0.001 |
| No                   | 1 of 25  |      |
| ASA fitness grade $> II$ |      |
| Yes                  | 13 of 37 | 0.015 |
| No                   | 1 of 19  |      |
| Bodyweight/spleen weight ratio $< 20$ |      |
| Yes                  | 5 of 10  | 0.044 |
| No                   | 9 of 46  |      |

$^*$ $\chi^2$ test.
The present study, there was no correlation between the incidence of complications and age, preoperative chemotherapy, steroid treatment, volume and/or weight of the spleen, nature of the underlying disease or intraoperative blood loss. These findings differ from those of at least one other study, which concluded that increased age and underlying illness were the predominant factors associated with morbidity and mortality following splenectomy for massive splenomegaly. In another study, the preoperative categorical variables that significantly correlated with postoperative complications were preoperative need for blood transfusion and the presence of more than two co-morbidities.

The zero mortality rate achieved in the present study was also shown in 1987 by Bickerstaff and Morris. Complications after splenectomy for massive splenomegaly include bleeding, respiratory infection, subphrenic abscess, and splenic or portal vein thrombosis, especially in patients with myeloproliferative disorders. In a large series published in 2013 involving 222 consecutive patients, the 30-day mortality rate was 1.8 per cent and the complication rate 20 per cent. The most common complications were bleeding (9 per cent) and portal venous thrombosis (9.9 per cent), as detected by postoperative imaging. This rate suggests that postoperative portal vein thrombosis is underestimated because postoperative imaging is not performed routinely, being reserved for patients with persistent symptoms. If there were other patients in the present series with portal vein thrombosis, they were not symptomatic.

There is little evidence that splenectomy has an impact on subsequent thromboembolic complications. Reactive thrombocytosis occurred in 27 patients (48 per cent) in the present series. Administration of antiplatelet agents such as aspirin (100 mg/day) for at least 6 months before surgery. A single patient with myelofibrosis developed portal vein thrombosis, diagnosed 2 months after splenectomy, and died 8 months after the operation.

**Discussion**

Experience with splenectomy for massive splenomegaly is often limited because this operation concerns only a small proportion of patients who undergo splenectomy as treatment for their haematological disease. Laparotomy is usually required to remove a massive spleen. Pioneers of laparoscopic splenectomy concluded that spleens weighing more than 3.2 kg required conversion to open surgery. Others have suggested a limitation of a splenic size greater than 27 or 30 cm.

In the present study, there was no correlation between the incidence of complications and age, preoperative chemotherapy, steroid treatment, volume and/or weight of the spleen, nature of the underlying disease or intraoperative blood loss. These findings differ from those of at least one other study, which concluded that increased age and underlying illness were the predominant factors associated with morbidity and mortality following splenectomy for massive splenomegaly. In another study, the preoperative categorical variables that significantly correlated with postoperative complications were preoperative need for blood transfusion and the presence of more than two co-morbidities.

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as aspirin for prevention of complications related to post-
splenectomy thrombocytosis may be of benefit in patients
presenting with additional cardiovascular risk factors.
General prophylactic measures such as early mobilization
and antemembolism stockings combined with low-dose low
molecular weight heparin are also indicated to reduce the
risk of thromboembolism. Policy in the present series
was routine application of these measures in all patients
during the perioperative period, and to continue aspirin
(100 mg daily) for at least 6 months if reactive thrombo-
cytosis (platelet count above 500 x 10⁹/l) occurred.

The use of short-term high-dose steroids as part of the
medical management of haematological disorders did not
constitute a potentially higher risk of postoperative com-
inations than haematological disorders requiring a shorter
duration of steroid treatment (median 6 months) at higher
doses (median 1-20 mg per kg per day).

Splenectomy appeared to offer durable palliation for
the correction of haematological cytopenia in the present
study, as shown in earlier reports. Symptom pallia-
tion and need for transfusion were excellent in the present
series, along with advantageous survival in terms of both
duration and performance status. The threshold to per-
form splenectomy for massive splenomegaly should remain
low, because the benefits are significant for the majority of
patients. Janus kinase 2 inhibitors are new potential ther-
apeutic options for splenomegaly associated with primary or
secondary myelofibrosis. If these inhibitors reduce the
size of the spleen and improve quality of life, the need for
splenectomy could diminish, along with the risk of portal
vein thrombosis.

The literature relating to splenic surgery contains an
inconsistent terminology that seems to have worsened with
the introduction of laparoscopic surgery. In addition, sub-
sets of spleens weighing 600–1600 g or more have been
classified as massive or supramassive. This problem
might be overcome with the wider assessment of splenic
size by three-dimensional reconstruction of CT images to
calculate spleen volume.

Adjustment of spleen size and weight to the patient’s
morphology and habitus seems a logical step that might
influence the surgical decision-making process, such as the
use of a laparoscopic approach. The scatter plot of
bodyweight/spleen weight ratios versus BMI demonstrated
that the lower the ratio, the lower the BMI. In general
the very large spleen is more likely to cause anorexia and
weight loss. In this study, a bodyweight/spleen weight ratio
below 20 was significantly associated with the occurrence
of postoperative complications (P=0.044).

The relationship between bodyweight/spleen weight
ratio and BMI was further explored by comparing spleen
weight alone with BMI to overcome mathematical
coupling. The relationship was still significant. This
relationship was also effective in identifying 60 per cent
of patients (25 of 42) who had excellent pain relief, con-
formed by an improvement in their Karnofsky performance
score. The provisional cut-off points for good pain
relief are spleen weight greater than 2.0 kg and BMI
below 24 kg/m². In general, the implication is that the
larger the spleen, the greater the improvement following
splenectomy.

The adjustment of spleen weight and volume (by pre-
operative 3-dimensional CT reconstruction) to BMI could
offer a potentially useful estimate of a patient’s preopera-
tive condition and morphology. This should be confirmed
by independent studies, in the hope of defining practical
cut-off points for BMI and spleen weight that could inform
surgical decision-making. These data could lead to a more
practical definition of massive splenomegaly rather than a
simple weight of more than 1.5 kg, a measurement that is
only really available after operation.

Disclosure

The authors declare no conflict of interest.

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