

## ORIGINAL ARTICLE

REDEFINING THE ROLE OF SPLENECTOMY IN PATIENTS WITH  
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Medical Sciences, Lucknow, India***Background:** Despite extensive work-up to establish the cause of splenomegaly, splenectomy may be required for diagnosis in certain situations. The aim of this study was to find out the role of diagnostic splenectomy in the current era.**Methods:** Between January 1989 and June 2004, 211 patients underwent splenectomy for indications other than trauma. In 41 (19%) patients, splenectomy was carried out for diagnostic purposes. Retrospective analysis of these patients was done for the purpose of the study.**Results:** All patients who underwent diagnostic splenectomy had a complete haemogram, biochemical tests for liver and renal function, bone marrow biopsy and abdominal ultrasonography before splenectomy. There were 28 (68%) men and 13 (32%) women with median age of 37 years (range, 6–62 years). The median duration of symptoms was 12 months (range, 1–180 months). Common presentations were fever ( $n = 27$ ; 66%), malaise ( $n = 26$ ; 63%), pallor ( $n = 33$ ; 80%) and gross splenomegaly ( $n = 27$ ; 66%). Thirty-two (78%) patients had hypersplenism. Splenic lesions were shown in 14 (34%) patients on ultrasonogram and in 16 (39%) patients on contrast-enhanced computed tomography scan of the abdomen. Open splenectomy was carried out in all patients. Seventeen (41%) patients had postoperative complications. Among these, three (7%) patients had postoperative bleeding. One patient died because of acute respiratory distress syndrome. Final histopathology of the spleen showed lymphoma in 15 (37%), tuberculosis in five (12%) and other lesions in five (12%) patients. Sixteen (39%) patients had only congestive splenomegaly.**Conclusion:** A high proportion of patients presenting with idiopathic splenomegaly will have underlying haematological malignancies even in tropical countries. The clinical presentation, laboratory profile and imaging findings were not helpful in differentiating between patients with haematological malignancies and non-malignant conditions. Splenectomy still has an important role in establishing the pathology in patients presenting with idiopathic splenomegaly.**Key words:** diagnostic splenectomy, splenic lymphoma, undiagnosed splenomegaly.

Abbreviations: CECT, contrast-enhanced computed tomography scan; ELISA, enzyme-linked immunosorbent assay; FNAC, fine-needle aspiration cytology; ITP, idiopathic thrombocytopenic purpura; OGD, oesophago-gastro-duodenoscopy; USG, ultrasonography; WHO, World Health Organization.

## INTRODUCTION

In patients presenting with enlargement of the spleen, a definite diagnosis is easily established with the modern array of invasive and non-invasive diagnostic tests. Bone marrow examination with immunophenotyping, abdominal contrast-enhanced computed tomography scan (CECT) and transabdominal fine-needle aspiration cytology (FNAC) or biopsy of the enlarged lymph nodes has significantly helped in identifying the cause of splenomegaly in most patients. Patients in whom no obvious cause could be isolated after detailed investigations, surgical removal of the spleen is considered as an option for both diagnosis and therapy. The proportion of diagnostic splenectomy ranges from 3 to 36% in centres with significant experience with splenectomies for indi-

cations other than trauma.<sup>1–5</sup> Splenectomy for diagnostic purpose has been strongly recommended in syndromes associated with hypersplenism because of the opportunity in getting a diagnosis of the primary condition that causes splenomegaly.<sup>6</sup> The range of patients subjected for diagnostic splenectomy in a tertiary referral centre will be different from that in other hospitals because of the availability of advanced investigations and the expertise for the diagnostic work-up. The purpose of this study was to find out the pathological range of diseases in patients subjected to diagnostic splenectomy and to redefine the role of diagnostic splenectomy in patients with isolated splenomegaly.

## MATERIALS AND METHODS

All patients who underwent splenectomy between January 1989 and June 2004 at our hospital were included in this study. Splenectomies carried out for trauma or as part of other surgical procedures such as polyvisceral resection for malignancy, portal hypertension surgery were excluded from the study. Patients who underwent splenectomy for diagnostic purpose were further analysed for the purpose of the study. Information regarding the clinical presentation, results of investigations and surgical

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pathology was collected from the computerized hospital information system and medical records. The decision for diagnostic splenectomy was taken by the primary referral departments. Complete haemogram, biochemical tests for liver and renal function and abdominal ultrasonography (USG) were carried out in all patients as part of the diagnostic work-up. Bone marrow biopsy was also carried out in all patients. Immunophenotyping for haematological disorders by flow cytometry was started at our centre only from January 2004. CECT scan of the abdomen was carried out if USG showed any focal lesion in the spleen or if the clinical suspicion of malignancy was high. FNAC of the splenic lesion was carried out only in selected patients with easily accessible lesions and no risk of bleeding. Enzyme-linked immunosorbent assay (ELISA) for HIV was carried out in all patients presented in the past 6 years of the study period. Serological tests for hepatitis B and C viruses were carried out in patients with a history of jaundice. Oesophago-gastro-duodenoscopy (OGD) was carried out to rule out portal hypertension. Doppler ultrasonogram of the abdomen (Doppler USG) was carried out in patients who had varices on OGD. Splenomegaly was graded based on the enlargement of the spleen in centimetres below the left costal margin (mild, up to 5 cm; moderate, between 5 and 10 cm and gross, more than 10 cm).<sup>7</sup> Hypersplenism was defined as the presence of at least two cytopenia (anaemia as defined by haemoglobin <6.2 mmol/L, leucopenia as defined by total leucocyte count <4 × 10<sup>9</sup>/L and thrombocytopenia as defined by platelet count <150 × 10<sup>9</sup>/L) along with a normal or a hypercellular bone marrow. Reversal of hypersplenism was defined as the normalization of all three cytopenia above the upper limits defined for hypersplenism within 1 month of splenectomy.<sup>8</sup> All the patients received pneumococcal vaccine before splenectomy. Three doses of i.v. ceftizoxime were given as the perioperative antibiotic. Splenectomy was carried out with a midline or a left subcostal incision. Liver tissue was taken for biopsy if there was a suspicion of a lymphoproliferative disorder. Lymph nodes were taken for biopsy if found enlarged. Major postoperative morbidity was defined as any complication that prolonged the hospital stay beyond 7 days. Statistical analysis was carried out using SPSS 10.0 software (SPSS for Windows; SPSS Inc., USA). Values of haematological parameters were calculated as median and range. Univariate analysis was carried out using  $\chi^2$ -test, Fisher's exact test or Student's *t*-test.

## RESULTS

Two hundred and eleven patients underwent splenectomy between January 1989 and July 2004 at our centre for various indications other than trauma. These indications were idiopathic thrombocytopenic purpura (ITP; *n* = 71, 34%), thalassaemia (*n* = 51, 24%), hereditary spherocytosis (*n* = 36, 17%), autoimmune haemolytic anaemia (*n* = 6, 3%) and miscellaneous conditions (*n* = 6, 3%). Forty-one patients (28 men and 13 women) underwent splenectomy primarily as a diagnostic procedure. The median age was 37 years (range 6–62 years). Clinical features of these patients are summarized in Table 1.

Fourteen (34%) patients showed splenic lesions on USG. Overall, 20 patients underwent CECT. Of the 20 patients, 16 had splenic lesions on CECT including all patients who had demonstrable lesions on USG. CECT additionally showed intra-abdominal lymphadenopathy in four patients. OGD showed grade

**Table 1.** Clinical features in patients with idiopathic splenomegaly (*n* = 41)

Symptoms and signs	<i>n</i> (%)
Fever	26 (63)
Malaise	26 (63)
Abdominal pain	14 (34)
Weight loss	10 (24)
Bleeding manifestations	10 (24)
History of jaundice	10 (24)
Gross splenomegaly	27 (66)
Hepatomegaly	21 (51)
Anaemia	36 (88)
Leucopenia	23 (56)
Thrombocytopenia	37 (90)
Hypersplenism	32 (78)

1 gastric varices in six (15%) patients. None had oesophageal varices. Among these patients, four (10%) showed collaterals confined to the splenic hilum on Doppler USG. Hepatitis B surface antigen was positive in one patient. This patient had history of multiple blood transfusions for anaemia. None of the patients had a positive ELISA test for HIV.

Fine-needle aspiration cytology from the splenic lesion was carried out in five patients. Aspirate was suspicious of lymphoproliferative disorder in one patient and showed granulomatous inflammation in another. Two aspirates yielded normal splenic tissue, and in fifth patient, the aspirate showed only necrotic tissue.

All the patients underwent open splenectomy. Fifteen (37%) patients had platelet count persistently below 40 × 10<sup>9</sup>/L and were at high risk for bleeding at surgery. Twenty-six (63%) patients were operated by a midline incision, and 15 (37%) were operated by a left subcostal incision. Additionally, cholecystectomy was carried out in five patients with gallstones. At operation, ascites was present in five patients and accessory splenic tissue in four. In all patients who had splenic lesions on preoperative imaging, the same was confirmed at operation. One additional patient showed splenic lesion at operation, which was not detected on preoperative CECT. In 13 (32%) patients, enlarged lymph nodes were seen at the splenic hilum. Preoperative imaging failed to show splenic hilar lymphadenopathy in any of the patients. Para-aortic lymphadenopathy was confirmed in four (10%) patients at operation. All these patients had splenic hilar lymphadenopathy also. At operation, liver was grossly normal in all patients, except in one who showed multiple, small, white nodules on the surface. Liver tissue was taken for biopsy in 18 patients.

Seventeen (41%) patients had postoperative complications. Post-splenectomy fever was seen in 12 (29%) patients. Nine (22%) patients had major morbidities. Of these patients, three (7%) had postoperative haemorrhage, in whom one required re-exploration and packing. Pleural effusion developed in three (7%) patients and lobar pneumonia in two (5%). Three patients developed intra-abdominal collection and all were treated by aspiration. One patient who underwent cholecystectomy with splenectomy developed bile leak from the subvesical duct, which resolved spontaneously. There was one mortality (2.4%). This patient had severe thrombocytopenia (platelet count 26 × 10<sup>9</sup>/L) at the time of splenectomy and required re-exploration for bleeding; however, he developed ARDS and died on the fourth postoperative day. Final histopathology of the spleen in this patient showed congestive splenomegaly.

**Table 2.** Pathological diagnosis in patients with idiopathic splenomegaly (*n* = 41)

Pathology	<i>n</i> (%)
Congestive splenomegaly	16 (39)
Lymphoma	14 (34)
Lymphoma + tuberculosis	1 (2)
Tuberculosis	5 (12)
Tropical splenomegaly	2 (5)
Pyogenic abscess	1 (2)
Haemangiosarcoma	1 (2)
Littoral cell angioma	1 (2)

Histopathology of the spleen was suggestive of congestive splenomegaly in 16 of the 41 (39%) patients. Haematological malignancy was the cause of splenomegaly in 15 of the 41 (37%) patients (Table 2). Tuberculosis was seen in five (12%) patients. Another patient has tuberculosis with diffuse large cell lymphoma. The lymphomas (*n* = 15) were further divided into various subtypes according to the World Health Organization classification (Table 3). Splenic hilar lymph node biopsy showed tuberculosis in three patients and lymphoma in another. In the remaining patients, lymph nodes were not affected with the disease. Intraoperative liver biopsy showed lymphomatous infiltration in three patients and tubercular granuloma in two. In other patients, liver tissue was normal on histopathology. Among the various factors analysed to predict haematological malignancy before splenectomy (presenting signs and symptoms, incidence and degree of cytopenias, presence of splenic lesions and lymph nodes on imaging and presence of varices), except for a low proportion of polymorphs (median 43% in lymphoma and 61% in others; *P* = 0.01), none was found to be significant.

Cytopenia was reversed after splenectomy in all patients who had hypersplenism. Splenectomy thus resulted in additional therapeutic benefits apart from reaching a diagnosis of the underlying pathology.

### DISCUSSION

This study examines the effectiveness of splenectomy as a diagnostic procedure in a tertiary referral centre with significant experience in dealing with various haematological disorders with the aid of modern diagnostic methods. Undiagnosed splenomegaly still remains a challenge to physicians and haematologists. In tropical countries, malaria, infections and anaemia constitute

**Table 3.** Subtypes of lymphoma according to WHO classification (*n* = 15)

Subtypes of lymphoma	<i>n</i>
Hodgkin's disease	2
B-cell lymphoma	10
Follicular	1
Marginal zone	3
Diffuse large cell	4
High grade	2
T cell	3
Anaplastic large	1
Hepatosplenic	1
Other T cell	1

WHO, World Health Organization.

majority of cases of splenomegaly.<sup>9,10</sup> Pattern of splenomegaly in tertiary care centres will be different from those found by general practitioners. A study of 2505 patients with splenomegaly in a university medical centre showed that haematological disorders were the cause of splenomegaly in 57% of cases and of massive splenomegaly in 81%.<sup>11</sup> Improvements in haematological evaluation methods, increased use of CECT in abdominal imaging and better experience with percutaneous radiological diagnostic interventions have drastically reduced the number of diagnostic splenectomies in the current era. A small number of patients still require diagnostic splenectomy even in centres with vast experience in haematological and oncological diseases. Reported experience of splenectomy carried out for idiopathic splenomegaly showed a high incidence of malignancy ranging from 39 to 80% in the pathological specimens.<sup>1,3,5,12,13</sup> Majority of these were lymphomas. Our study also reports similar findings.

It is important to exclude patients with splenomegaly because of portal hypertension by OGD, Doppler USG and liver function tests before subjecting these patients for splenectomy. Liver biopsy can be carried out in suspected cases to examine for cirrhosis. Grade 1 gastric varices in the absence of oesophageal varices along with collaterals confined to the splenic hilum in six of our patients can be explained by the massively enlarged spleen. Final histopathology showed lymphoma in two of these patients and the other four had congestive splenomegaly.

Sixteen (39%) of our patients showed splenic lesions on preoperative imaging, and five (31%) of them had only haemorrhage and necrosis as a result of the venous congestion and repeated ischaemia and infarction in the grossly enlarged spleen (Table 4). Although malignant splenic lesions are hypoechoic on USG in 97% of cases, infarcts can also produce a similar picture.<sup>14</sup> Computed tomography findings alone are not helpful in the differentiation of different low attenuation lesions.<sup>15</sup> Our study shows that overemphasis on the presence or nature of splenic lesions seen on abdominal imaging for therapeutic decisions may lead to missing of malignancy in a significant proportion of patients presenting with undiagnosed splenomegaly. FNAC of the splenic lesions has a reported diagnostic accuracy of 63–100%.<sup>16,17</sup> But because of the need for typing, many centres still prefer to have a histological specimen in suspected malignant splenic lesions. Risk of bleeding may be a deterrent in carrying out FNAC from the spleen in patients with thrombocytopenia. Histopathology of the removed spleen helped us to characterize lymphomas in all our patients. Absence of any preoperative factors associated with malignancy apart from a low polymorph count also favours splenectomy after an exhaustive diagnostic work-up. Our series had only 5% incidence of tropical splenomegaly, which is contrary to what is expected from tropical countries. This may be partly because of referral bias. Our study shows that with aggressive diagnostic

**Table 4.** Final diagnosis of patients with splenic lesions shown on CECT scan (*n* = 16)

Pathological diagnosis	<i>n</i>
Lymphoma	6
Haemorrhage and infarcts	5
Tuberculosis	2
Haemangiosarcoma	1
Littoral angioma	1
Pyogenic abscess	1

CECT, contrast-enhanced computed tomography.

work-up, the proportion of patients labelled as idiopathic splenomegaly can be reduced to a minimum.

The incidence of major postoperative complications (41%) and mortality (2.4%) in our series correlates to the reported experience of splenectomy for haematological diseases. Various series have quoted a 14–48% incidence of postoperative complications and a 2–5% mortality after elective splenectomy.<sup>2,18,19</sup> The significant proportion of patients with cytopenia and resultant immunosuppression may be a possible explanation for the higher incidence of haemorrhagic and infectious complications after splenectomy.

The additional therapeutic advantage of diagnostic splenectomy is evident from the fact that all our patients with cytopenia had reversal of hypersplenism. The published report shows that the reversal of cytopenia following splenectomy occurs in 75–100% of patients.<sup>1,8,20,21</sup> The improvement in cell counts further facilitates early institution of chemotherapy in patients with haematological malignancies.

The 100% overall diagnostic yield and the 39% incidence of malignant diseases in our series show that a subset of patients with splenomegaly may still require splenectomy for diagnosis even in this era of spleen-conserving diagnostic procedures. Although some patients may be found to have congestive splenomegaly, the difficulty in getting the diagnosis of primary hypersplenism without splenectomy and the therapeutic benefit of the reversal of hypersplenism prompt the haematologist to opt for splenectomy in cases of idiopathic splenomegaly. Our department has recently started to carry out laparoscopic splenectomy mainly for diseases with small spleens (ITP, hereditary spherocytosis etc.), and we do not have any experience in carrying out splenectomy for diseases with large spleens. Increasing usage of laparoscopic methods even in massive splenomegaly may become an additional consideration for diagnostic splenectomy, but with increased morbidity.<sup>22</sup>

## CONCLUSIONS

Our study shows that a high proportion of patients presenting with idiopathic splenomegaly will have underlying haematological malignancies even in tropical countries. The clinical presentation, laboratory profile and imaging findings are not helpful to differentiate between patients with haematological malignancies and nonmalignant conditions. Because of the high diagnostic yield and the added therapeutic advantages, diagnostic splenectomy should be considered as the procedure of choice in patients with undiagnosed splenomegaly.

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