Management of Blunt Trauma to the Spleen (Part 2)

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Received: 7 February 2009
Revised: 22 April 2009
Accepted: 18 June 2009

Abstract

Spleen is the most frequently-injured solid organ in blunt abdominal trauma. Considering its important role in providing immunity and preventing infection by a variety of mechanisms, every attempt should be made to salvage the traumatized spleen at any age particularly in children. After primary resuscitation, mandatory requirements for non-operative management include absence of homodynamic instability, lack of associated major organ injury, and admission in the intensive care unit for high-grade splenic injury and in the ward for milder types with close monitoring. About two-thirds of the patients would respond to non-operative management. In most patients, the failure of non-operative measures usually occurs within 12 hours of management. Determinant role of abdominal sonography or computed tomography, and in selected cases, diagnostic peritoneal lavage, for appropriate decision cannot be overemphasized. However, the high status of clinical judgment would not be replaced by any paraclinical investigations. When operation is unavoidable, if possible, spleen saving procedures such as splenorrhaphy or partial splenectomy should be tried. In cases of total splenectomy, autotransplantation, preferably in the omental pouch, may lead to the return of immunity, at least partially, to prevent or reduce the chance of subsequent infection. Although total splenectomy with autograft is immunologically superior to total splenectomy-only procedure, the patients should also be protected by vaccination and daily antibiotic for certain period of time. The essential steps for the prevention of overwhelming infection after total splenectomy are not only immunization and administration of daily antibiotic for up to 5 years of age or one year in older children, but also include education and information about this dangerous complication. When non-operative management is successful, the duration of activity restriction in weeks is almost equal to the grade of splenic injury plus 2.
Iran J Med Sci 2010; 35(3): 169-189.

Keywords ● Trauma ● spleen ● autograft ● Infection ● non-operative management

D- What Are The Appropriate Decisions And Options During Operation?

If splenic injury is managed properly in a well-equipped center, more than 60% of adults and about 85-90% of children with the injury can be treated successfully without requiring surgical intervention.[64,75,81-83,107,128,129] To maintain the patient's immunity, operative management of lacerated spleen should be as

conservative as possible. Depending upon the patient's general condition and vital signs, severity of splenic injury, the presence of other injured organs, the surgeon's experience, and the availability of matched-blood and facilities such as sonography, CT, etc., the decision of splenic salvage must be weighed against life saving splenectomy. Obviously, one must not jeopardize a patient's life at the expense of preserving spleen despite its invaluable importance in the provision of immunity.

For grades I and II, and sometimes III, lacerations simple sutures with pledgets of gelfoam, surgicel or teflon to prevent tearing of the splenic capsule, may often suffice.[130] Alternatively, topical thrombin, fibrin glue (Tissucol) or bio glue have been used as a sealant to achieve immediate hemostasis.[8,126,130,131] Owing to their adhesive and hemostatic properties, the latter agents have also been used laparoscopically in hemodynamically stable patients as an effective, safe, reliable and rapid option to control bleeding following splenic injury.[126,131,132] Sulfacrylate glue composition is also useful for traumatic injury to parenchymatous organs, including spleen, not only for reparative processes, but also hemostasis.[133,134] In hemodynamically stable patients, splenorrhaphy can be done in the presence of associated organ injuries including visceral perforation. However, when there is a significant peritoneal contamination, it is relatively contraindicated to repair the spleen.[135] In a case series, which hollow viscus perforations such as stomach, small bowel, or colon were present in about 15% of patients undergoing total splenectomy or splenorrhaphy, the rate of early sepsis was twice in the total splenectomy group as compared to the patients whose spleen were repaired.[135] No fatal sepsis was reported as a long-term complication of splenic repair. A decrease in the rate of intra-abdominal collection was also observed following splenorrhaphy despite hollow viscus injury.[130] Moore and coworkers performed splenorrhaphy in 85 patients, 21 of whom had hollow viscus injuries including stomach (5), duodenum (1), small bowel (5) and colon (10).[136] Only one (4.8%) of the patients developed intra-abdominal abscess.[136]

When and How to Do Partial Splenectomy

The minimum bulk of the spleen necessary to maintain immunity is one-third of a normal spleen.[2,8,137] Therefore, if lacerated part is deep and involves the upper or lower half of the spleen, specially when it is devitalized, partial splenectomy may be the best choice.[138]

To reduce the intra-operative bleeding, partial splenectomy or repair of deep lacerations should preferably be preceded by temporary control of the hilar splenic vessels by a vascular or bull dog clamp. Alternatively for the same goal, when time and circumstances permit, the splenic artery is approached through the gastrocolic omentum. It is then encircled by a vessel-loop at its course on the superior border of the pancreas. Having identified the line of demarcation, transection of the spleen should be performed on the cyanotic side by at least 1 cm apart from the line.[138] Owing to its quick adherent property, omentum would be helpful to cover the repaired site.[2,17,18,138]

Mesh As a Saving Tool in High Grades Splenic Injury

In Grade III and IV lacerations, which are extended toward the hilum, the suturing is futile. The futility is worse when the laceration is deep. In such a situation laceration is usually multiple due to the severity of the injury, and wrapping the spleen in an absorbable mesh such as Dacron or woven polyglycolic acid, may be an appropriate decision.[2,139,140] Delany and associates were the first to use absorbable mesh as an adjunct to splenorrhaphy in 1982.[141] Oxycel (oxidized cellulose), as a topical hemostatic agent, was sutured at the inside aspect of the mesh before wrapping to enhance the efficacy of dexon mesh.[142] The use of the technique causes the mesh to become bulkier, easier to suture and more hemostatic.

In spite of the theoretical risk of infectious complications, mesh splenorrhaphy is not contraindicated in the presence of injury to the alimentary tract.[143] Berry et al., reviewed the clinical courses of 23 patients subjected to Dexon mesh splenorrhaphy, of whom 11 (48%) had openings of the gastro-intestinal tract during elective operations.[143] None of the patients developed intraabdominal collection, nor did they require reoperation for rebleeding. The authors concluded that mesh splenorrhaphy controlled the bleeding effectively, and could also be performed in clean contaminated peritoneum.[143]

Total Splenectomy vs Other Spleen Saving Procedures

Regardless of the grade of isolated splenic injury, total splenectomy has to be performed in the presence of hemodynamic instability following adequate resuscitation, or avulsion of the spleen from its hilum (grade V injury). In addition, in the presence of other major organ injuries such as lung, liver, kidney, pancreas,

or duodenum or colon laceration with heavy contamination *total splenectomy* is indicated, especially when the vital signs are unstable particularly when the severity of splenic injury is grade III or IV. Thus, being sometimes a mandatory option, splenectomy should *not* be considered as a failure in the management of splenic injury.

As far as early post-operative complications are concerned, there has been no significant difference between patients treated by total splenectomy, conventional splenorrhaphy or mesh wrap splenorrhaphy.[139,144] However, morbidity is more related to the presence or absence of associated multiple injuries rather than the type of splenic operation.[144] On the contrary, according to Kaseje and colleagues' findings, short-term morbidities of spleen preservation or salvage in adults is 2-3 folds higher as compared to those of total splenectomy.[70] Should the spleen be removed totally, the next step to be performed is either to terminate the operation or proceed with autograft.

E- Is There any Role for Splenic Auto-Transplantation after Total Splenectomy?

Owing to the unpredictability and uncertainty of the provision of immunity, the most controversial issue in surgery of the spleen after total splenectomy is whether to do auto-transplantation or not. It has been proven that the spleen has the capacity to regenerate. Spontaneous splenic regeneration in the peritoneum of the splenectomized dogs was described in 1883 by Griffini and Tizzoni.[145] Similar occurrence was noted few years later in the human. Buchbinder and Lipkoff in 1939 suggested the word splenosis as a replacement for "spontaneous patchy splenic regeneration following splenectomy for trauma".[146] The rate of splenosis after splenectomy due to the rupture of spleen is 50-66%.[145,147,148] It has been shown that tuftsin, a tetrapolypeptide which accelerates phagocytosis by neutrophils, activity drops dramatically after splenectomy.[149] However, this activity decreases less when splenectomy is due to trauma as compared to elective total splenectomy.[149] Therefore, the low incidence of over-whelming post-splenectomy infection in such patients might be, at least to some extent, related to this phenomenon. Consequently, auto-transplantation of the spleen is rational since it may, at least partially, provide and maintain patients' immunity.

Appropriate Sites for Autograft:
The spleen has the ability to regenerate in any part of the body.[145] In autograft the nourishment of the graft is based on osmosis,

therefore, the environment, in which regrowth occurs, and the dimensions of the splenic segments for transplantation must be suitable. Owing to rich blood supply, peritoneal cavity, especially the omentum, seems to be the best site for this purpose.[145,150-156] Furthermore, growth factors, generous supply of inflammatory cells and cytokines provided by the omentum may have a contributing role.[157] Moreover, several investigators showed that the omentum was superior to the subcutaneous tissue or muscle.[145,152-154] The retroperitoneal location is also an acceptable option for regeneration[158] However, since the venous drainage of omentum is through portal circulation, and there is a possibility of cooperation of the liver in antigen processing, omental pouch is preferred. Based on the latter assumption, transportal injection of splenic tissue into the liver has been used in several experimental studies with equivocal, variable and uncertain successes.[145] Patel et al. have shown that autograft by *slicing* the spleen in the omentum is the only way that may be associated with some benefit.[156] Moreover, they believe that the results obtained by *minced* spleen in omentum are not superior to those following total splenectomy.[159]

Being associated with variable results, using minced spleen in subcutaneous tissue is another option for splenic implant. Some investigators believe that autograft in this region is not effective,[159] while others have found it a suitable site albeit with a slower regeneration rate than intraabdominal location.[160,161] Splenic histological changes during the processes of regeneration of splenic implants have been well described by Tavassoli et al.[160]

Optimal Dimensions for Autograft
To have more chance of survival and regeneration, the thickness of an autograft piece should not exceed 2-3 mm, although thicker slices up to 5 mm have also been used.[155,162] However, their lengths and widths vary. The recommended size in most studies is 3×40×40 mm (5 pieces),[136] or 2×15×15 mm (15-20 pieces).[152,163] Three fragments of 30×40×120 mm (weighing 51 g), reimplanted in the anterior rectus compartment, have been used successfully in a four year old boy who had huge splenomegaly.[164] *Laparoscopic auto-transplantation* of 20 fragments of spleen in the omentum has been reported in a 33 year old lady after laparoscopic total splenectomy for multiple focal thromboses of the splenic arterial branches.[165]

Are regenerated splenic tissues functional?
This question should be answered on the

basis of microorganism clearance and mortality rate. Unfortunately, majority of the studies have been performed in animals, which may not reflect the processes occurring in the human. The micro-organism clearance and mortality rate are difficult to assess not only in man due to the presence of various factors such as age, history of vaccination or antibiotic ingestion, but also in animals due to the difference from each other. Secondly, the time interval between autograft and microorganism challenge will influence the end result. Alternatively, another way to confirm the presence of regenerated splenic tissue and assess its physiologic function, is to look for other parameters such as the absence of Howell-Jolly bodies in the peripheral smears, to determine serum levels of antibody (especially IgM), to determine phagocytic activity, to do scintigraphy in man, or to do second look operation for the detection of grossly visible regrown splenic tissue in animals. There are many reports showing that the presence of these immunity indices following spleen autograft in animals or humans are indicative of viable and functional splenic tissue.[154,166-173] On the contrary, some investigators found no significant difference in immunological profile after total splenectomy with or without autograft.[148,174,175]

Although declines after splenectomy, IgM serum levels returns to normal range after regeneration.[145,155,162,163,171,176-178] Other immunological profile which reduce following splenectomy, but are restored after autograft, include complement C3,[155] phagocytosis-stimulating α_2-glycoprotein, fibronectin, opsonic activity, autoantibodies, leukokinin.[145] IgM is the only proven immunological profile indicative of regeneration, while other parameters are debatable.[145]

Function of the Splenic Autograft in the Animals

In an experimental study in rabbits, not only serum concentration of IgM but those of IgG and interleukin-1 significantly increased following total splenectomy with omental autograft as compared to the respective pre-operative levels.[150] It was also shown that upon total splenectomy and splenic autograft not only was the spleen phagocytic function preserved but peripheral phagocytic activity improved.[166] This phenomenon might be related, at least to some extent, to the enhanced concentration of IgM, which facilitates opsonization of the particles.

Functional splenic lymphoid compartments including intact marginal zone is restored following total splenectomy and autograft in rats.[171] Moreover, there is a significant humoral immune response to pneumococcal polysaccharide vaccine.[171] Omental autograft of the spleen in dog has also revealed the maintenance of certain functional splenic parameters comparable to those in dogs with normal spleen, while being significantly different from those in dogs after total splenectomy without implantation.[179] Thus, the restoration of the splenic function is to be expected after regeneration.[150,171,179] Consistent with such a view, several studies have shown that bacterial phagocytic function would be preserved in regenerated spleen in rats.[167-169] Moreover, total splenectomy in rats causes diminished phagocyte oxidative burst response, while splenic autograft returns this function to its normal level.[173] The degree of return to normal is not correlated to the amount of the splenic autograft.[173]

In terms of bacterial clearance and survival, several studies have shown no significant difference between splenectomized animals with or without autograft, or splenosis.[175,180] Cooney et al. found that there was a significant difference in the survival rate of the implanted and control groups following bacterial challenge during the first 24 h, but not after 72 hours.[181] Nonetheless, significant improvement was observed in the survival at 12th week after total splenectomy in animals with autografts as compared to 6- and 9-weeks old implants or total splenectomy-only group.[175] Furthermore, phagocytic function was found to reduce after auto-transplantation in rats,[174,182] Also, a substantial reduction in the percentage of T lymphocyte subsets (CD4+ and CD8+) was demonstrated in the regenerated splenic tissue as compared with the normal spleen in rats.[183]

The Function of the Splenic Autograft in the Human

Although positive and partial protective effects of the auto-transplantation have been shown in animal studies,[156,184-186] human studies are limited. There was no significant difference between the immunological and hematological patterns, and blood bodies of patients who had autograft after total splenectomy and individuals with intact spleen. However, splenectomized patients without implantation had higher numbers of Howell-Jolly bodies and lower serum IgM levels than those of splenectomized patients with implantation.[170] In addition, more viability and filtering function of the splenic remnant was seen in patients with autograft after total splenectomy.[170]

Leeman et al. studied the immune response in human after total splenectomy for trauma with or without autograft.[172] Ten patients

undergoing total splenectomy followed by autograft were compared with 14 consecutive patients subjected to total splenectomy alone. Six months after the operation, all patients were vaccinated by 23-valent pneumococcal vaccine followed by antibody titer measurement. Scintigraphy was also performed to detect regrowth of the spleen. The IgM and IgG (anti-pneumococcal capsular polysaccharides) titers were significantly higher in auto-transplant patients at 3 and 6 weeks after the vaccination, while no evidence of viable spleen, as indicated by negative scintigraphy, or significant change in Ig levels was observed in total splenectomy-only patients.[172] On the other hand, total splenctomized patients with positive scintigraphy, indicative of either previously present accessory spleen or splenosis due to trauma, showed some rise in Ig levels, which was less than that in autograft patients. Accordingly, these authors concluded that following autograft of the spleen after total splenectomy, the patients obtained protection against over-whelming post-splenectomy infection as there was adequate humoral response to pneumococcal infection.[172] Similarly, others have shown that regenerated spleen can, to some extent, synthesize antibody.[163,176] Other investigators have also shown that the immuno-protective effects of the autograft will be enhanced remarkably following vaccination against micro-organisms commonly responsible for over-whelming post-splenectomy infection such as *S. pneumoniea.*[145,152,158,175,184] In contrast, Kiroff and associates observed no difference in the antibody (IgM and IgG) responses to subcutaneous injection of Pneumovax between patients with or without splenosis, or even those with different degrees of splenosis.[148]

The effects of splenectomy on the lymphocyte number and function, and the ability of regenerated spleens to function normally are not clear. In other words, it is not clear whether lymphocyte function is normal after autograft. Dürig et al. compared leukocyte and lymphocyte subpopulation, and serum immunoglobulins in 23 patients after total splenectomy due to trauma (9 with and 14 without autograft) with those of 23 age- and sex-matched healthy people.[178] They found that, in the presence of splenic autograft, IgM level was normal. There was also a tendency for most white blood cells (such as T suppressors), if not all, to be preserved almost within the normal range.[178]

Moore et al. have reported a five-fold enlargement of the autografted spleen in a 30-year old man 7 years after total splenectomy for trauma, when he had survived an episode

of pneumococcal infection 3 years earlier (4 years after total splenectomy).[187] Therefore, neither regenerated splenic tissue nor its quantity is a guarantee to prevent overwhelming post-splenectomy infections. Moreover, there are several case reports of overwhelming post-splenectomy infection with fatal outcomes in the presence of regenerated spleen or splenosis as proven at autopsy.[145,188] Surprisingly, the majority of these patients were adults, who died within 36 h of their symptoms. In spite of these reports, protective effect of splenosis or regeneration cannot be denied nor excluded. Overall, the chance of overwhelming post-splenectomy infection is fortunately low, being 0.23-0.42% per year and its lifetime risk is 5%.[12,14,189] In fact, the low chance of overwhelming post-splenectomy infection in splenectomized patients for traumatic rupture of the spleen might probably be due to splenosis or regeneration occurring in about 50-66% of patients who are otherwise healthy individuals with normal reticulo-endothelial system.[145,147]

The concept of immuno-protective effect of the autograft is supported by an extensive body of work not only in animals but also in humans.[152,154,158,163,165-173,179,184-186,190,191] Therefore, when total splenectomy is un-avoidable following trauma, auto-tranplantation, at least to some extent, helps maintain immunity. The efficacy and physiologic function of the splenic autograft depends on the amount of successfully regenerated tissue.[192] Although the immunity provided by autograft is inferior to that of normal state or following partial splenectomy,[191] it is definitely superior to total splenectomy without autograft, particularly when supplemented with vaccinations.[145,151,158,172,175,184,191] Part of this superiority may be related to reticuloendothelial system phagocytic cells in the liver.[181] However, the main reason is probably an acceptable vaccination-induced concentration, often within normal range, of IgM, which facilitates opsonization and thereby phagocytosis of the microorganisms. It may also be related to partial restoration of reticuloendothelial system function by the regenerated tissue.

Importance of an Intact Blood Supply to the Retained Spleen

The clearance of pneumococci is minimally reduced when hemisplenectomy with preserved blood supply is compared to sham operated controls in experimental studies,[161,175,182] It was shown that hemisplenctomy not only reduced the mortality rate from pneumococcal infection, but also was remarkably

superior to autograft in terms of blood clearance of micro-organisms and survival.[161,175,182] The most crucial and determinant factors in this regard are probably an intact blood supply and normal microvascular anatomy of the spleen.[145] Thus, a small segment of a spleen with its intact blood supply is superior to equivalent mass of regenerated splenic tissue because blood flow in the latter is not proportional to its weight. In other words, filtering function and polysaccharide antigenic response of the regenerated spleen are less than those of an equivalent mass of normal splenic tissue with intact blood supply.

It is interesting to know that splenic fragments fail to grow when a part of a spleen with intact vasculature is left in situ. The reason for this phenomenon may be the probable existence of an inhibitory humoral factor synthesized in the native spleen,[161] or inadequacy of the blood (1.5% of total splenic blood flow) supplying the transplanted tissue.[161]

How Much Splenic Tissue Is Required to Have an Immuno-Protection: Autograft vs Part of the Native Spleen?

It is believed that the minimum size of autograft to provide immuno-protection against experimental pneumococcal infections is about 50% of the original spleen.[153,190] Autografts of roughly 50 gm in 10 patients (age range 8-34 years), who received pneumococcal vaccination postoperatively, was associated with normal splenic function indices.[154] On the other hand, autografts of one-third the original spleen was associated with poor immuno-protection.[193] In contrast, adequate antibody production could be provided by 30% of the spleen in the presence of an intact splenic vascular supply in animals.[137] Moreover, it is believed that more than 75% of the spleen can be removed and the remaining, which will hypertrophy, can prevent bacteremia.[194] Therefore, depending on the presence or absence of splenic blood supply, it seems that about 30% of the native spleen,[2,8,137] and an autograft of 50% of original spleen [153,154] are adequate for immunoprotection.

Is There Any Sequel Afterward?

Although implants in the presence of gross contamination due to bowel laceration are not recommended, they have not been a problem according to Moore and colleagues.[136] They showed that hollow viscus perforations did not precluded splenorrhaphy or splenic implantation.[136] They performed splenorrhaphy in 85 patients, of whom 21 had viscus perforations,

and only one of them (4.8%) developed intra-abdominal abscess.[136] In addition, they did splenic autograft in the omentum after total splenectomy for trauma in 43 patients, of whom 13 had concomitant hollow viscus injuries including stomach (4), small bowel (2) and colon (7).[136] Although different complications including intra-abdominal abscess, not at the site of implantation, occurred after the operation in 3 patients, none was attributed to the splenic implantation.[136] Therefore, in spite of the ischemic nature of splenic slices and rare possibility of abscess formation in the presence of contaminated environment, autotransplantation of the spleen can be safely performed after total splenectomy in the absence of hemodynamic instability.

Some patients may develop signs and symptoms of abdominal collection following autograft. CT scan of these patients may be confusing and even similar to abscess. To avoid a diagnostic dilemma, Cothren et al. have described CT scan criteria of splenic auto-transplantation after total splenectomy.[195] Accordingly, in splenic implants, surrounding omental fat stranding or other inflammatory changes, which are typical indicators of an abscess, are not present.[195] Moreover, the sterile implants has time-related radiologic changes such as early rim enhancement and also late shrinkage.[195] Furthermore, air is not present in the sterile implants while the infected ones may contain air.[195]

F- What Are the Necessary Measures or Steps Following Non-Operative Management vs Partial Splenectomy or Total Splenectomy before or after Hospital Discharge?

Duration of Hospitalization and Activity Restriction In Relation To the Extent of Splenic Injury

Once non-operative management is successful, the patient should have complete bed rest for a certain period of time. Recommendations for the length of hospitalization, bed rest and timing of activities varies, and depend on the grade and mechanism of splenic injury, degree of response to non-operative management, age of the patient, and associated organ injuries. A retrospective analysis of 243 children admitted with blunt splenic and/or liver injury during 10 years (1996-2005) showed that in the absence of clinical signs of ongoing blood loss, for grades I and II splenic injuries one night, and for higher grades 2 nights of observation would suffice.[95] Similarly, others have followed the policy of discharge after a short period of hospitalization (48 h) provided that there is no

abdominal tenderness, diet is tolerated, and hematocrit is stable.[65]

A retrospective cohort study on 182 adult patients sustaining splenic injuries subjected to non-operative management examined the association of *mobilization* with delayed bleeding requiring operation using uni- and multivariate analyses.[114] Thirty one (17%) patients were mobilized on the first hospital day while the majority (77%) within 72 h of admission. In 13 (7.1%) patients non-operative management was failed, and in 10 (5.5%) of them delayed rupture of the spleen occurred.[114] According to the study, the chance of delayed hemorrhage from an injured spleen was *not* related to the duration of bed rest nor the timing of mobilization.[114] In other words, early mobilization was *not* associated with higher chance of splenic rupture. However, splenic rapture occurred more frequently in higher grades splenic injuries and in higher Injury Severity Scores.[114] Therefore, the incorporation of a policy of early mobilization in the conservative therapy of splenic injury reduces hospital stay and overall hospital costs without affecting the failure rate of non-operative management. Furthermore, the rate of bed rest-related complications such as pneumonia, deep vein thrombosis or pulmonary embolus would decline.[114]

There is no unanimous agreement among surgeons in regards to the duration of strict bed rest, avoidance of normal activity following splenic injuries and the timing of light or strenuous activity. A survey of EAST (Eastern Association for the Surgery of Trauma) members regarding the duration of activity restriction and recommendations following splenic injury recommends that for mild splenic injuries *all activities* should be restricted for 2 weeks and return to *full activity* is allowed after 6 weeks. There was no agreement among respondent in regards to more severe splenic injuries with approximately 50% advising avoidance of *light activity* for 4-6 weeks and *full activity* for 2-3 months, and about one-third advising resumption of *full activity* after 4-6 months.[128]

There is no objective data in adults regarding the time of return to normal activity. Some authors believe that 2-3 weeks for grade I or II and 6-8 weeks for higher grade injuries would probably be adequate.[8] An evidence-based guidelines defined by the American Pediatric Surgical Association suggest that, when non-operative management is successful, duration of activity restriction, in weeks, in children is approximately equal to the grade of splenic injury plus 2.[67,68] Thus, almost similar to adults, for a grade III splenic injury 5-week, and for a grade IV 6-week activity restriction is advised.[66-68,95] Part of this period must be absolute bed rest, while the remaining time not beyond limited activities with avoidance from competitive and contact sports. According to the same guideline the recommended duration of absolute bed rest, in days, in a hemodynamically stable pediatric patient is equal to the grade of splenic injury plus one.[66-68,95] Therefore, 4 days bed rest is enough for a patient with grade III splenic injury.

Healing Process and *Imaging*

The evolution, resolution and progression of blunt splenic injuries were studied by Savage et al. on 894 adult patients in a 5-year period from Jan. 2002 to April. 2007.[63] The excluded patients were those who died (161) or underwent total splenectomy (96) before being discharged from the hospital. The remaining (637) patients (mean age 32.8 years, age range 15-83), who underwent non-operative management with mild (grade I-II; 63.9%) to severe (grade III-V; 36.1%) splenic injury were analyzed.[63] While still in hospital (average 10.5-10.9 days), 480 (75.4%) patients had at least one follow-up CT scan before discharge. Although, the majority of injuries were unchanged (73.6%) as compared with the original CT, improvement and healing were observed in 26 (5.5%) and 51 (10.6%) patients, respectively. However, worsening of the injuries occurred in 49 (10.3%) patients with mild (27) and severe (22) injuries. In-patient course of the lesion revealed that the rate of healing in mild group was higher than those with severe splenic injuries (15.8% vs 3.1%). After discharge as outpatients, 97 had at least one abdominal CT within 90 days from their initial injuries.[63] Improvement and healing were demonstrated in 52.6% and 34% of the patients, respectively, while injuries were unchanged in 5.2%. On the other hand, the extent of injury in 9 (9.3%) patients worsened to the extent that total splenectomy had to be performed in one patient with mild and one with severe splenic injuries. The latter two patients had grade II and V injuries, respectively, and were splenctomized on the 35th and 34th post-injury days. The remaining 7 patients who were asymptomatic had no documented intervention.[63]

Seventy two (57 with mild and 15 with severe splenic injuries) of 637 patients (11.3%) whose injuries healed as in-patient or outpatient were eligible for Time-to-Healing Analysis.[63] Thirty three out-patients could be followed-up to complete healing. As expected, the mean healing time in mild splenic injury

was significantly shorter than that of severe splenic injury (12.5 *vs* 37.2 days; *P*<0.001). Complete healing was confirmed in 80% of mild and severe splenic injuries by 50th and 75th days, respectively.[63] Thus, the majority of patients would have complete healing in *2-2.5 months* regardless of initial severity of splenic injuries. On the other hand, healing was not complete in 20% of patients with mild or severe injuries after 3 months. The authors concluded that splenic injuries, with whatever grade, may get worse in 10% of patients being followed.[63] Therefore, all patients sustaining splenic injuries, even those with mild degrees, should be followed until healing is confirmed by imaging.[63]

There are, however, a number of studies suggesting that routine follow-up imaging is not necessary in majority of cases, since the management plan would not be usually changed.[95,104,196-198] They suggest that management plan should preferably be individualized, and other factors including grades of splenic injuries, the presence of other intra-abdominal organ injuries, the patients' age and mechanisms of injuries should be considered. In addition, they believe that the integrity of tissue is not necessarily correlated with the sonography or CT findings. Therefore, it offers little help in determining the period of physical activity restriction. In another study,[128] majority of surgeons who replied (78.1%) relied on the clinical judgment alone for low grades (I and II) splenic injuries, while 50% of them believed that CT was necessary as a decision making tool for high grade (IV and V) injuries. In a prospective application of a proposed guidelines on 312 patients, Stylianos showed that, compared with his previous study on 832 patients, there was a significant *reduction* in ICU and hospital stays, restriction of physical activity, and follow-up imaging.[68] No adverse sequelae occurred in 87% of the patients in the absence of the follow-up imaging, therefore, it should mostly be requested based on clinical signs or symptoms rather than as routine work-up[68]. However, some authors believe that it is on the safe side to use CT to evaluate the gross anatomy of the spleen in patients sustaining high grade splenic injuries, who are hospitalized longer than usual, before discharge from the hospital, and as out-patient before returning to full physical activity.[8,128]

General Information Regarding Overwhelming Post-Splenectomy Infection

There are a number of points, which may be considered in regards to overwhelming post-splenectomy infections

1- There is an *inverse* relationship between the chance of overwhelming post-splenectomy infection and the age of a patient; the younger the patient, the more the chance of overwhelming post-splenectomy infection. Thus, it is highest in infants and children under 5 years, and lowest in adults.[10,15,16,199,200]

2- There is a *direct* relationship between the patient age at the time of total splenectomy and the time to infection. Therefore, the younger the patient, the shorter the time to infection.[16]

3- The rate of overwhelming post-splenectomy infection is highest during the first 2-3 years following total splenectomy, and declines dramatically afterwards.[10,189,199,201,202] About 30% of infectious episodes occurs during the first year, while 50% occurs within two years after total splenectomy.[189] However, Waghorn and Mayton-White reported that 60% and 4.76% of overwhelming post-splenectomy infection occurred 10-30 and more than 50 years, respectively after total splenectomy.[202] Therefore, although prophylactic antibiotic and immunization against *S. pneumoniae, H. influenza* type b and *N. meningococcus* have significantly reduced the chance of overwhelming post-splenectomy infections, the risk is still higher than that in general population and never reaches zero even after a long period of time.[14] For instance, overwhelming post-splenectomy infection with fatality was reported in an 87 year-old man 65 years after total splenectomy.[14] On the other hand, overwhelming post-splenectomy infection may occur as early as 24 days following total splenectomy.[14]

4- Degree of involvement of the reticuloendothelial system in the disease process is also a determining factor in the prevalence of overwhelming post-splenectomy infection.[13,16] For this reason, the chance of overwhelming post-splenectomy infection is high in thalassemia where the reticuloendothelial system is involved in hemosiderosis.[13,16] On the other hand, the chance is the lowest in healthy individuals, presumably with normal reticuloendothelial system, whose spleen has to be removed due to trauma. Another reason contributing to the low rate of overwhelming post-splenectomy infection in the latter group is splenosis, which starts at the commencement of splenic laceration.[145,147,148]

The Incidence and Rate of Overwhelming Post-Splenectomy Infection

A review of 59 case series, published between 1952-1987, showed that the incidence

of infection and mortality in splenectomized children aged less than 16 years were 4.4% and 2.2%, respectively. The corresponding figures for adults were 0.9% and 0.8%.[16] The lowest incidence of infection belonged to otherwise healthy individuals who had undergone total splenectomy for trauma (1.5%), while the highest incidence was for patients whose reticulo-endothelial system had been involved in a disease process such as thalassemia (7%) or Hodgkin's disease (7.1%).[16]

Bisharat and his colleagues determined the incidence of post-splenectomy infection and mortality using a MEDLINE search and review articles performed in the English literature during 30 years (1966-1996).[13] Among 78 papers comprising 19680 patients with total splenectomy, 28 had full documentation of 6942 patients splenectomized for different reasons including trauma. Two hundred and nine (3.3%) of such patients developed invasive infections, which led to the death of half of them.[13] Similar to Holdsworth et al.[16] findings, the lowest incidence of infection was for individuals splenectomized for trauma (2.3%).[13]

A study in Western Australia between 1971-83 on trauma-related splenectomy (n=628) to determine the incidence of overwhelming post-splenectomy infection and its mortality showed 3922 person years exposure.[203] In other words, the total length of time during which 628 splenectomized patients were exposed to the infection and were susceptible to developing bacteremia or septicemia was equivalent to 3922 years. Severe late post-splenectomy infection occurred in 8 patients resulting in an incidence of 0.21 per 100 person year exposure. One of those with severe late post-splenctomy infection developed overwhelming post-splenectomy infection giving an incidence of 0.03 per 100 person years exposure.[203] Therefore, the incidence of severe post-splenectomy infection in 100 patients is 0.21 each year, while the rate of death subsequent to overwhelming post-splenectomy infection in each 100 patients is 0.03 per year (or 3 death each year among 10000 patients). The study also showed that, compared to the general population, there was an 8.6-fold increased risk of late septicemia in those splenectomized for trauma *vs* 12.6-fold increased risk after total splenectomy for other reasons.[203] Accordingly, because of the low incidences of late and overwhelming post-splenectomy infections after total splenectomy for trauma, the assessment and evaluation of efficacy of vaccination and chemoprophylaxis is statistically difficult.[203]

Approaches To Increase the Immunity and

Decrease the Chance Of Infection After Total Splenectomy

a- Vaccination

For patients undergoing operation with more than 30% of the spleen remaining neither vaccination nor daily antibiotic is necessary, since splenic tissue is adequate for maintaining immunity.[2,8,137] If any doubt exists regarding the viability of the retained spleen, the absence of Howell-Jolly bodies in the peripheral smear, normal serum level of IgM, and visualization of the retained spleen by isotope scan may prove its normal physiologic functions.[9,17,18,25,154,170,204]

The immuno-protective effects of autograft are enhanced remarkably following vaccination.[145,152,158,175,181,184] Therefore, following total splenectomy, whether or not autograft is performed, daily antibiotic therapy (see below) and vaccination against encapsulated organisms (mostly *Strep. pneumoniae*, *H. influenza* type b and *Neisseria meningiditis* types A and C) are recommended to prevent overwhelming post-splenectomy infection.[189,204,205] The most efficient time for vaccination in elective splenectomy is about 2 weeks prior to the operation.[8,10,199-201,204,205,206] Although vaccination in the absence of spleen is less effective than in its presence, it is still advocated following total splenectomy for any reason including trauma.[10,204,205] The best time for this purpose is day 14 compared to days 1, 7 or 28 after total splenectomy.[10,201,205,207,208] However, because some of the patients may be lost to follow-up, it is advisable to vaccinate them soon after total splenectomy or before being discharged,[204] and not to wait for 2 weeks. Early vaccination has been shown to be associated with adequate antibody response.[8,201,209]

Although boosters of all 3 common bacterial vaccines are recommended by some practitioners after total splenectomy for trauma,[199,210] owing to lack of underlying disease, revaccination in immuno-competent patients is not necessary , particularly if they have received 23-polyvalent pneumococcal vaccine (PPV23).[11] On the contrary, some authors have advised a repetition of PPV23 5-6 years later.[199,205] Current recommendation for revaccination is 3 to 5 years after total splenectomy for trauma in children, depending on whether the patient is younger than or beyond 10 years of age respectively.[10,199] For adults, it is 5-6 years after total splenectomy.[205] Revaccination in adults 3-5 years after the initial vaccination has also been recommended by some investigators.[11] Some others have suggested that before revaccination 3 and 5 years after the

initial one, a measurement of antibodies be preferably performed. .[202] It was shown that revaccination 2 years after total splenectomy led to the doubling of antibody titers in about half of the patients.[209] Therefore, owing to variable responses in different individuals, revaccination can also be performed as early as 2 years after the initial one.

It is mandatory to re-immunize high-risk patients 3-6 years after the first vaccination.[8] For those with underlying diseases and the involvement of the reticuloendothelial system, who have higher chance of overwhelming post-splenectomy infection, vaccination may be repeated every 4-6 years for a maximum of 4 times.[211] Moreover, regardless of the underlying cause of hyposplenism or asplenia, some authors advocate re-immunization of such patients every 5-6 years.[9,189,206] Annual influenza vaccination to reduce the chance of secondary bacterial infections has also been suggested by many physicians.[10,204,210,206,211]

b- Antibiotics

Owing to the high frequency of pneumococcal organisms in overwhelming post-splenectomy infection, most authors recommend oral phenoxymethylpenicillin or amoxicillin on a daily basis as the best prophylactic agent unless there is hypersensitivity to the drug.[199,200,204,206] In the latter situation, erythromycin or trimethoprim-sulfamethoxazole, although less effective because of a higher rate of pneumococcal resistance, are the drugs of choice.[200,204,206] Other prophylactic antibiotics with broader activity include cefuroxime and amoxicillin/calvulanic acid (co-amoxiclave).[204] Once used, monthly injection of benzathin penicillin is no longer advised for the following reasons: a) duration of antimicrobial activity of penicillin benzathin in the serum is about 26 days.[212] Therefore, the patient is left without adequate serum antibiotic for about 5 days or more each month, b) the intramuscular injection of the drug is painful, which causes psychological trauma especially in children, and c) intra-muscular abscess may develop at the site of injection.

The duration of chemoprophylaxis, especially in otherwise healthy individuals, is a matter of debate varying from one to several years, until the patients reach age 21, and even for rest of the life after total splenectomy.[10,199,202,204,206,213] American Association of Pediatrics recommends that after total splenectomy of children less than 5 years old, prophylactic antibiotic therapy should continue up to the end of 5th year provided that the patient is immunized and there has not been an episode of pneumococcal infection.[10] If such conditions are not met, antibiotic therapy should be continued for several years. Canadian Pediatric Society has also advised that for children under 5 antibiotics should be administered up to the end of 5th year, and if older it should be continued up to one year after total splenectomy.[10] Furthermore, it advises that according to individual clinical circumstances antibiotic may be continued for a longer period of time. [10] However, many pediatricians advocate daily oral penicillin until the age of 10 for children splenectomized before the age of 5.[214] Others have also advocated chemoprophylaxis, particularly in children over 5, in the first 2-3 years after total splenectomy.[8,10,199,204] However, considering the minimal chance of overwhelming post-splenectomy infection after total splenectomy for trauma in children older than 5 years and adults, the efficacy of chemoprophylaxis has not been proven yet for this age group.[189,199]

In spite of the occurrence of overwhelming post-splenectomy infection 50-60 years after total splenectomy,[14,202] there is no convincing data to support long-term penicillin prophylaxis in asplenic adults.[8,199] Furthermore, it may not be followed or accepted by many patients. Nonetheless, American Association of Pediatrics recommends that asplenic patients be treated for about one year if beyond 5 years of age.[10]

While receiving oral penicillin, if the patients develop fever or conditions such as sore throat, toothache, urinary tract infection, or even common cold, the drug is replaced temporarily by a broad spectrum antibiotic, such as amoxicillin, to cover not only pneumococcal organisms but also H. influenza. Thus, *empirical antibacterial therapy* of fever and/or suspected infection *should be started immediately* in all splenectomised patients *without* considering the time elapsed from total splenectomy, patients' vaccination status, and patients' situation in terms of antibacterial prophylaxis. Obviously, penicillin-resistant pneumococci require broad spectrum antibiotics, such as cefotaxime or ceftriaxone, as empiric treatment for symptomatic patients.[204]

Considering the rare possibility of overwhelming post-splenectomy infection many years after total splenectomy due to trauma in an otherwise normal person, and the reports of failure of antibiotic prophylaxis to prevent sepsis,[8,14,199,202,204] another option is the policy of *starting treatment immediately*. Accordingly, beside early referral to a Medical Center, the patients start treatment with broad spectrum antibiotics immediately at the commencement

of suggestive symptoms. This option requires that the patient is informed and educated in regards to the risks involved and has always available a supply of a broad spectrum antibiotics, preferably amoxicillin, co-amoxiclave or cefuroxime.[8,14,199,204] It was shown in an experimental model that penicillin given at the beginning of the infection was equally effective as regular daily consumption in the prevention of overwhelming post-splenectomy infections.[215] Nevertheless, it is recommended that immuno-compromised patients receive daily antibiotic indefinitely beside revaccination(s).[10,200] Similarly, those with poor or absent responses to immunization, or following booster doses, as identified by very low antibody titers, could be candidates for life-long chemoprophylaxis.[201]

c- Education and Knowledge about Overwhelming Post-Splenectomy Infection

Unfortunately, the best and effective preventive measures have not been applied to prevent overwhelming post-splenectomy infection. This has been related to a number of reasons. First, the necessary recommendations and guidelines are not often given and their importance is not emphasized to the patients or his/her parents by the Medical Staff. Secondly, the patients/parents do not frequently consider the preventive measures as serious,[14,202] and thirdly, many patients have compliance difficulties and do not follow the guidelines.[216] M*ale sex* and *older age* are considered risk factors as they have been associated with poor compliance and non-adherence to the guidelines for the prevention of overwhelming post-splenectomy infection.[216] General information, and the education of a patient and his/her family members about signs and symptoms of overwhelming post-splenectomy infection is more important than receiving prophylactic antibiotic or vaccination.[10,14,189,217,218] In a study performed by El-Alfy and El-Sayed on 318 splenectomized patients over a period of 17 years, the incidence of overwhelming post-splenectomy infection in those with complete knowledge and those with minimal information about overwhelming post-splenectomy infection were 1.4% and 16.5%, respectively (P<0.001).[217] Moreover, the incidence of overwhelming post-splenectomy infection in those receiving antibiotic regularly or irregularly was 2.7% and 10%, respectively (P<0.01).[217] In addition, the incidence of overwhelming post-splenectomy infection after vaccination against pneumococcal infection reduced from 7.3% to 3.2% (P<0.05).[217] Thus, knowledge about the nature of overwhelming post-splenectomy infection and ways to tackle the infection when it occurs are among the most important determinant factors in reducing the prevalence of morbidity and mortality of the infection.

d- Other Recommendations

Aside from the education of patients and raising their information and knowledge, antibiotic therapy and vaccination, a number of other preventive measures have been recommended. Such measures include wearing Medic-Alert bracelet, avoiding travel to areas with endemic diseases such as malaria and tick-born diseases, and taking prophylactic medications.[10,204]

G- Functional (Non-Anatomical)-Related Complications after Total Splenectomy Other Than Overwhelming Post-Splenectomy Infection

Description of anatomical-related complications following partial splenectomy or total splenectomy such as iatrogenic injury to the tail of pancreas, stomach and colon is not within the scope of this review article. However, some of the physiologic and functional-related sequelae after total splenectomy will be mentioned.

1- Transient low grad*e fever* without apparent infectious etiology may occur following total splenectomy in some patients.[219]

2- The chance of infectious complications including pneumonia, urinary tract infection, intra-abdominal abscess, wound infection and multiple infections after total splenectomy for trauma is higher than the chance of them occurring following laparotomy for trauma but without splenectomy. However, there is no difference between the mortalities from such complications in the two group.[220]

3- Leukocytosis after total splenectomy for trauma can be either a physiologic event or sign of sepsis. White blood cell (WBC) counts in non-septic patients after total splenectomy is usually less than 15000/µL.[221,222] However, several investigators have shown that WBC greater than 15000/µL *at and beyond* the 5th postsplenectomy day, and platelet /WBC ratio of less than 20 are reliable indicators of infection.[221,222] Thus, leukocytosis in excess of 15000/µL after total splenectomy *should* be regarded as a clue to the presence of some sort of infection rather than a physiologic response.

4- Regardless of the underlying cause, *thrombocytosis* (platelet count ≥ 1,000,000 /mm^3) may occur following total splenectomy. Platelet count typically increases within the first week,[223] and sometimes within 2-3 weeks after total splenectomy.[224] It then gradually returns to normal usually within 2 months,[223] although the return to normal may last several months or even years.[224] Persistent thrombocytosis after total splenectomy for trauma is unlikely unless the patient has an unmasking of a previously unrecognized myeloproliferative disorder or some kind of hemolytic anemia.[223] If untreated in the latter situations, thrombocytosis may subsequently lead to splenic vein and even portal vein thrombosis. Fortunately, this dangerous complication *almost never occurs* after total splenectomy for trauma in an otherwise healthy individual.[225] However, to prevent any unpredictable and unexpected complications, the splenectomized patient should have platelets counted post-operatively on days 2, 7 and 14. Once thrombocytosis is detected, albeit transient, daily administration of a tablet of baby aspirin (100 mg) is recommended. In addition, the patient should also be referred to a hematologist for further management.

5- *Priapism*, which is usually a complication of hematological disorders, may rarely occur after total splenectomy for trauma.[226]

6- The spleen may also play a role in *lipid metabolism* as studies in splenectomized rabbits have revealed higher serum levels of triglyceride and cholesterol, and lower HDL associated with atherosclerosis.[227]

Conclusion

Owing to the important role of spleen in the provision of immunity and host defense against different infections, particularly bacterial ones, every possible attempt should be made to preserve it following splenic injury due to trauma. The first therapeutic option following adequate primary resuscitation in a hemodynamically stable patient, especially in the absence of concomitant major organ injury, is non-operative management. This can be done in the ward with close monitoring provided the splenic injury is mild (grade I-II) or even in selected cases of grade III. However, patients sustaining higher grades splenic inuries, particularly grades IV-V, *must be* admitted in surgical ICUs. Diagnostic measures mostly include focused abdominal sonography for trauma, or CT scan. In spite of the undeniable role of the imaging technologies in proper decision making, it can not replace the physical examination, vital signs and clinical judgment in the diagnosis of splenic injuries. Should the patient develop hemodynamic instability, which occurs mostly in the first 24 hours with the highest frequency in the first 6-12 hours, some sort of intervention such as angio-embolization or surgery may deem necessary. Depending on a patient's general condition, the extent of splenic injury, and the absence or presence of concomitant extra-splenic injuries, a variety of procedures including application of hemostatic agent, simple suturing, partial splenectomy, wrapping the lacerated spleen in an absorbable mesh, or total splenectomy may be performed. To reduce the chance of overwhelming infections after total splenectomy, especially in children, auto-transplantation in an omental pouch of about 50% of the spleen, cut in appropriate slices, is recommended.

Early mobilization does not increase chance of the splenic rupture. It is mostly related to the grade of splenic injury and Severity of Injury Score. Because of the possibility of delayed rupture of the spleen, particularly during the first two weeks after trauma and following an apparently successful non-operative management, patients are advised to refer immediately to a medical center in the event of any acute abdominal symptoms. If such a complication is suspected, early operation following a short resuscitation is advised. The duration of *absolute bed rest* and *restriction of ordinary activities* depend on the severity of splenic injury. The former in *days* equals to the grade of splenic injury plus one*,* and the latter in *weeks* equals to the grade of splenic injury plus two. Paraclinical work-ups during, before and after hospitalization should be based on the signs and symptoms of the patient and clinical judgments. The routine follow-up imaging is not recommended as it does not usually alter the treatment plan. However, when splenic injury is severe (grade IV and sometimes III), especially in those with prolonged hospital stay, follow-up CT, or sometimes sonography when CT is not available, is recommended. For high grade splenic injuries, one should avoid strenuous or full physical activities unless complete healing, which may occasionally last 3 months or more, is confirmed by appropriate paraclinical work-ups, preferably using new generation of helical or spiral CT.

Immunization against different micro-organisms, particularly pneumococci, should

be done before hospital discharge or about two weeks after total splenectomy in patients with or without autograft. Re-vaccination with PPV23 is advised 3-6 years later. Daily oral penicillin should also be given to asplenic patients, especially children, for a while. There is no agreement in regards to the duration of antibiotic therapy. Most authors advise antibiotic therapy for young children up to 5 years of age, and 1-2 years for others. Last but not the least, the education of patients about the signs and symptoms of overwhelming post-splenectomy infection and ways to tackle the problem are as important as vaccination and daily administration of oral antibiotic.

Conflict of Interest: None declared

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