What are the Particularities of Splenic Surgery in Cirrhotic Patients?

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Rezumat

Care sunt particularitățile chirurgiei splenice la pacienții cirofici

Obiectivul acestei lucrări este de a trece în revistă întreaga literatură chirurgicală splenică cu scopul de a defini în mod adecvat indicațiile chirurgicale și specificul managementului lor terapeutic. Am efectuat o trecere în revistă a literaturii internaționale publicată între ianuarie 1995 și august 2015.

Cuvinte cheie: splenectomie, ciroză, anevrism, radiologie intervențională, embolizare, OPSI

Abstract

The aim of this work was to review the entire literature on splenic surgery in cirrhotic patients in order to best define the surgical indications and their management specifics. A review of the international literature published between January 1995 and August 2015 was thus carried out.

Key words: splenectomy, cirrhosis, aneurysm, interventional radiology, embolisation, OPSI

Introduction

The objective of this chapter is to define the place of splenectomy

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(SP) in the cirrhotic patient. The following points will be successively addressed: indications for MS, the necessary perioperative measures, the technical characteristics linked to the field, as well as the results and alternatives to MS.

Research Carried Out

A review of the international literature published between January 1995 and August 2015. However, for the sake of clarity, the articles relating to MS carried out in the context of oesogastric devascularisation (interventions by Hassab and Sugiura, not practiced in Europe), were not retained. MS performed in the context of liver transplantation was also excluded from this work. Articles in full, prospective or retrospective texts in French or in English were selected. Clinical cases were also included in the selection. For each of the articles selected, a manual review of the references mentioned was carried out to identify possible additional studies not referenced in the databases (*Table 1*).

Main Indications for Splenectomy in Cirrhotic Patients

Splenic Trauma

There is no specific recommendation regarding

the management of spleen trauma in cirrhotic patients. The series reported in the literature are retrospective studies based on registry data (level of evidence 4, *Table 1*). However, an analysis of these data leads to the conclusion that conservative treatment of spleen trauma in cirrhotic patients is often a failure and is associated with high mortality (1). The latter depends on the stage of liver disease (MELD score, albuminemia, prothrombin level) and the severity of the splenic involvement (2). In these patients in whom conservative treatment is most often attempted, probably due to the increased operative risk, it is difficult to determine a priori whether this strategy is harmful or not. The American registry study found no significant difference in mortality according to the choice of an immediate surgical treatment or a conservative treatment (35% vs 46%) (2). However, teams reporting their experience on an individual basis tend rather to quickly consider surgical treatment in view of the high risk of failure of the conservative strategy (3, 4). The MELD score could serve as a decision factor with a threshold value of 16. The place of radiological embolization is therefore particularly important in this group of patients and will be discussed below (*Table 2*).

Hypersplenism

One of the main indications for cold MS in cirrhotic patients and which has been the subject of the greatest number of publications is MS for correction of hypersplenism. Hypersplenism represents a (pan-) cytopenia of which cirrhosis can be one of the causes, via portal hypertension and splenic sequestration of blood lines. The threshold value for thrombocytopenia used to define hypersplenism is not consensual and varies from 50 to 80 Giga/L according to the authors. If this indication has long prevailed in order to allow the introduction of hepatitis C treatment with interferon-ribavirin (5,6), it is likely that this indication will become obsolete since the recent introduction of pan-genotypic inhibitors of non-hemato RNA polymerases -toxic.

Table 1. Level of evidence of studies included in the literature review

Level of Scientific Evidence Provided by the Literature	Number of articles analysed
<i>Level 1</i>	
High-power randomized controlled trials	
Meta-analysis of randomized controlled trials	
Decision analysis based on well-conducted data	0
<i>Level 2</i>	
Low-power randomized controlled trials	
Well-conducted non-randomized comparative studies	
Cohort studies	1
<i>Level 3</i>	
Control case study	2
<i>Level 4</i>	
Comparative studies with significant biases	
Retrospective studies	
Case series	87
Descriptive epidemiological studies	
Meta analyses of retrospective studies	
Clinical cases	5
Books	0
Conferences / Consensus	6

Table 2. Retrospective studies evaluating the results of the management of spleen trauma in the cirrhotic patient

1st author	n cirrhotic patients/ N total	Conservative treatment rate	Conservative treatment failure rate	Death rate	Level of evidence
Bugaev (2)	289 / 77 754	86%	7%	22%	4
Fang (1)	12 / 487	100%	92%	50%	4
Lin (16)	34	35%	33%	44%	4
Matar (17)	1 / 1	100%	100%	100%	4

Splenic Artery Aneurysm

A splenic artery aneurysm is present in 7 to 17% of cirrhotic patients, and of hilar location in 50% of cases (7). Although MS can be indicated in the event of hilar aneurysm of more than 20 mm in prevention of the risk of rupture, there is no specific recommendation on cirrhotic ground and the data reported in the literature mainly relate to the management in peri-transplantation (8). The current trend is rather to favour radiological treatment of splenic aneurysms, a less morbid approach than MS.

Splenectomy Associated with Partial Hepatectomy in Cirrhotic Patients

The results of MS in the treatment of hepatocellular carcinoma (HCC) on cirrhosis are mainly reported by Asian teams and this is an exceptional indication in Europe. The published series are retrospective (level of evidence 4) and summarized in *Table 2*. MS is performed before or during the hepatectomy period (1 or 2-stage surgery). These studies highlight the feasibility of this strategy and its low morbidity (9). The pathophysiological hypotheses mentioned to explain the benefit of MS (synchronous or deferred) are the

correction of thrombocytopenia allowing 1/ to limit post-operative haemorrhage, 2/ to improve hepatocellular function (and limit the risk of hepatocellular decompensation), 3 / to improve hepatic regeneration by mechanisms mediated by serotonin (10) and 4/ to obtain better haematological tolerance to chemotherapies or antiviral treatments. Other hypotheses concerning immuno-modulation have been put forward and will need to be confirmed (11).

Splenic Tumours

These are exceptional indications. To our knowledge, only a few clinical cases of MS for splenic metastasis of CHC (12,13) or for ruptured haematoma (14) have been reported. It is therefore not possible to establish a recommendation for this situation which requires an individual assessment.

In total, in cirrhotic patients, an interventional attitude (radiological and/or surgical) should be favoured in the event of splenic trauma, the more so as there are signs of active haemorrhage and that cirrhosis is advanced (Child B, MELD > 16, branch routes). Endovascular therapy should be very early in these patients at high risk of failure of conservative therapy. In case of failure, surgical treatment should be quickly considered. There

Table 3. Retrospective studies evaluating the impact of neoadjuvant or simultaneous splenectomy with hepatectomy for hepatocellular carcinoma

1 st author	n simultaneous resection	Morbidity	Mortality	Survival (* if significantly different vs hepatectomy alone)
Cai (81)	57	29,8%	1,7%	OS 5 years: 41,8% *
Chen (11)	94	16%	0%	DFS 5 years: 30% *
Oh(82)	12	50%	8%	NS
Wu(41)	41	15%	3%	DFS 5 years: 58%*

DFS: disease-free survival, OS: overall survival

is no specific recommendation for the prevention of rupture of splenic artery aneurysms in cirrhotic patients. In the case of a diameter > 2 cm, an endovascular prophylactic treatment may be proposed as a first intention. Splenectomy was performed for or in association with hepatectomy for hepatocellular carcinoma. It could increase the number of patients treated surgically but cannot be recommended outside of trials.

Technical Features

Before Surgery

Vaccination

The objective is the prevention of post-SP septic syndrome (Overwhelming Post-Splenectomy Infection [OPSI]) which progresses to death within 48 hours in 50 to 70% of cases. The risk of OPSI concerns 5% of children and 0.9% of adults with splenectomy, with an incidence of 0.2% per year post-MS. The most common manifestations are pneumonitis and meningitis. Encapsulated pathogens are most often involved with, in decreasing order of frequency, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*. The actual incidence of OPSI in cirrhotic asplenic patients has not been evaluated but appears to be very low (<1%) (15).

The published series reporting cases of MS in cirrhotic patients does not allow the development of recommendations with a high level of evidence because the impact of vaccination has not been specifically evaluated. Most of the authors do not detail the vaccination schedule applied, some do not perform any systematic vaccination (5, 16) and others carry out an exclusive pneumococcal vaccination (15, 17,18) or associated with meningococcal and *Haemophilus* vaccines (19).

Very little data is available on the incidence of long-term infectious complications after MS in the cirrhotic patient. Akaoshi et al. (15) reported a fatal case of pneumococcal meningitis among 100 patients followed for an average period of 33 months. This patient had not received preventive vaccination. After this death, all splenectomized patients received

vaccination and no case of meningitis was subsequently reported by the authors. Conversely, Kedia et al. (5) reported no severe infectious complications among 33 splenectomized cirrhotic patients who had not received any preventive vaccination (median follow-up of 27 months).

Several French recommendations are available concerning the vaccination of the asplenic patient or the cirrhotic (immunosuppressed) patient. No specific recommendation exists for splenectomized and cirrhotic patients. Official recommendations for infectious prophylaxis should therefore be applied in patients with non-cirrhotic splenectomy even if the immunization of patients with liver disease appears to be lower (20,21). There are no contraindications or special precautions for the use of live attenuated vaccines in asplenic patients except in the event of an associated immune deficiency.

In total, there is no specific recommendation regarding prophylactic vaccination in the cirrhotic asplenic patient. The recommended vaccines are therefore those in the current vaccination calendar (22). Vaccinations against influenza and invasive pneumococcal, meningococcal and *Haemophilus influenzae* type b infections are specifically recommended (23). A booster every 5 years for pneumococcal and meningococcal vaccines is recommended.

Two situations differ:

- In case of planned MS: vaccination must be carried out at least 15 days before the intervention in order to allow an optimal response (24).
- In case of emergency MS: vaccination is conventionally recommended 30 days after MS but its effectiveness has been described from the 14th day on post-traumatic splenectomized patients. Regarding pneumococcal prevention, the High Authority for Health (25) confirms the vaccination schedule recommended by the High Council for Public Health (22):
 - patients not previously vaccinated receive a dose of vaccine 13 worth pneumococcal conjugate, followed 8 weeks later by a dose of vaccine 23 worth pneumococcal unconjugated.

- people vaccinated for more than 3 years with the 23 equivalent pneumococcal vaccine, receive a dose of 13 equivalent pneumococcal vaccine followed 8 weeks later by a dose of 23 equivalent pneumococcal vaccine.

This vaccination sequence must be respected in order to avoid the risk of hypo-reactivity observed when vaccination is carried out in the reverse order. The 23 valent unconjugated pneumococcal vaccine, although less immunogenic, remains the only protection against the 10 serotypes not present in the 13 valent vaccine, in particular against the currently emerging serotype 12F.

Meningococcal B vaccine is recommended (two doses at least one month apart) as well as quadrivalent conjugate vaccines A, C, Y, W with two-dose schedule six months apart. If the subject previously received an unconjugated polysaccharide vaccine, a minimum period of three years is recommended before vaccinating him with the meningococcal tetravalent conjugate vaccine. A 5-year booster for pneumococcal and meningococcal vaccines is recommended.

For *Haemophilus influenzae b* prophylaxis, a single injection is recommended. In this population, the duration of protection conferred by the vaccine is unknown and to date there are no recommendations for booster administration.

Vaccination against seasonal influenza with the inactivated vaccine is recommended every year because of the increased risk of infection with bacteria encapsulated in the course of infection with the influenza virus.

For other inactivated or subunit vaccines, the entire current vaccination schedule applies.

Before Surgery

Approach

The choice of the first route for achieving MS in the cirrhotic patient only arises in the context of scheduled surgery. Any MS of haemostasis meets the classic rules of emergency surgery and a laparotomy (if need be shortened) remains the rule in order to perform a rapid gesture and manage any

associated lesions.

Only the recommendations published in 2008 by Habermalz et al. (26) are currently available and it was stated that portal hypertension was a contraindication to the laparoscopic route (Grade C). It is not currently possible to make any further recommendations because a prospective randomized series has not been published since. However, several series suggest that laparoscopy is feasible despite portal hypertension (levels of evidence 3 or 4).

- In their systematic review of laparoscopic MS series, Chen et al. (27) evaluated the mortality rate at 0.6% and the conversion rate to laparotomy at 4.4% (21/478). Compared to the open route, the laparoscopic route resulted in a longer operating time but a reduction in blood loss, the length of hospital stays, the rate of complications and the risk of hepatocellular decompensation.
- Hashizume et al. (28) reported in 2002 a series of 73 splenectomized cirrhotic patients with a conversion rate of only 4.1% and blood loss of 375 ± 352 mL, recommending the laparoscopic approach as a reference.
- Cobb et al. (29) reported a retrospective series of 18 splenectomized cirrhotic patients and concluded that the laparoscopic approach was feasible in cases of Child-Pugh A or B cirrhosis, allowing a shorter hospital stay and morbidity and mortality.
- Cai et al. (30) retrospectively compared 24 laparoscopic SP to laparotomy 24 SP by laparotomy for hypersplenism and showed that the laparoscopic approach allowed a reduction of the blood losses, the duration of hospitalization and the morbidity, concluding that the laparoscopic approach is safe and achievable.
- Hama et al. (31) showed that postoperative follow-up after laparoscopic MS was comparable in cases of hypersplenism ($n = 17$) or idiopathic thrombocytopenic purpura ($n = 17$).
- Finally, Kawanaka et al. (32) recently reported a series of 390 laparoscopic SPs

without mortality. Between 2008 and 2013 (n = 125), they had a conversion rate of 3.2% and a significantly lower complication rate than at the start of the experience (notably no severe Dindo-Clavian complication ≥ 4).

- Conversely, Ohta et al. (33) showed that portal hypertension and the Child-Pugh score were significant risk factors in multivariate analysis of massive bleeding (> 800mL) during laparoscopic MS. Kawanaka et al. (34) also suggested that the conversion rate was correlated with the severity of liver failure and spleen weight.

In addition to the classical laparoscopic approach, many authors have reported the hybrid technique ("hand-assisted laparoscopic splenectomy"), that is to say the realization of a short laparotomy [usually mid-umbilical (35)] for introduce the non-dominant hand of the operator through a device allowing the maintenance of the pneumoperitoneum. Habermalz et al. (26) recommended this technique in case of massive splenomegaly (splenic weight > 1000 grams or volume > 1000 mm³, largest splenic axis between 15 and 17 cm depending on the series) (Grade B). Other authors have also recommended this technique in the case of voluminous perisplenic varicose veins on preoperative imaging (15,36) in order to control possible intraoperative bleeding, in the event of a Child-Pugh score ≥ 9 (37). Recently, Kawanaka et al. published a series of 390 laparoscopic SPs and the authors now use the 600 mL limit as an indication for a hand-assisted route (32).

The open road remains the benchmark approach in emergency situations. Routine laparoscopic use cannot be recommended for performing a splenectomy in a cirrhotic patient. In expert centres, this approach can nevertheless be considered and the hybrid technique must be considered as a useful device in case of splenomegaly or perisplenic varicose veins (Grade C).

Whatever the indication for a laparoscopy in the cirrhotic patient, the usual precautions should be recalled concerning the verification of

the absence of parietal varicose veins or of re-permeabilization of the umbilical vein (venous bypass pathway) before the introduction of the optical trocar to avoid serious bleeding. The open technique (mini-laparotomy allowing introduction under visual control) is highly recommended in cirrhotic patients in order to limit the risk of bleeding. The analysis of the injected scanner is essential preoperatively.

Vascular control procedures

European recommendations published in 2008 (26) recommended the use of tissue thermofusion or ultrasonic dissection forceps and mechanical staplers during laparoscopic MS (Grade B). Since these recommendations, many authors have reported their experience of laparoscopic MS in the cirrhotic patient using this type of equipment, without rigorous evaluation of the interest or benefit provided (15,30,35-38). Only Yao et al. (39) published a level 2 randomized study comparing the use of Ligasure® (n = 30) with manual ligation (n = 30) for performing MS with oesogastric devascularisation in cirrhotic patients (open route). Ligasure® reduced blood loss and length of hospital stay, with no impact on morbidity (including drainage rate) or length of hospital stay. This instrument was therefore recommended by the authors.

The use of self-suturing equipment would limit intraoperative blood loss during an open or laparoscopic splenectomy in cirrhotic patients. No high-grade recommendation can be made regarding its systematic use. However, a rigorous evaluation, particularly on the financial impact, seems desirable (Grade C).

Drain

In 2008, Habermalz et al. (26) recommended not to drain after MS (Grade C), based on a single retrospective series (40). The authors specified that drainage could be proposed in the event of a pancreatic wound.

To our knowledge, no series has specifically evaluated the interest or the specific morbidity of drainage after MS in cirrhotic patients. Rare retrospective series report the placement of a

drain in the MS cell in cirrhotic patients, by open or laparoscopic route, without specifying the indications for drainage (5,30,31,41-43). The drain ablation criteria also appeared to be empirical and usually corresponded to an ascites flow rate < 500 ml/day (5) and a negative amylase assay (15,44).

In total, no recommendation can be made on the interest of systematic drainage of the left hypochondrium after splenectomy in the cirrhotic patient. A case-by-case evaluation should be carried out according to the operator's habits, local conditions (pancreatic trauma, perisplenic varicose veins, digestive wound) or general (scheduled or emergency intervention). Particular attention should be paid to the absence of parietal varices which can be responsible for bleeding that is difficult to control when installing the drain.

After Surgery

Antibiotic prophylaxis

No study has specifically evaluated the impact of antibiotic prophylaxis in cirrhotic asplenic patients. The same recommendations should therefore be applied as those available for asplenic patients without underlying liver disease (45). This antibiotic prophylaxis is based on the use of a narrow spectrum molecule covering the bacteria involved in the infections of asplenic patients. Thus, phenoxymethylpenicillin (Oracillin®: 1 million units, twice a day) has had marketing authorization since 2001 in this indication. In case of allergy it is replaced by erythromycin (Erythrocin®: 500 mg in one take). Phenoxymethylpenicillin has shown its effectiveness in children with sickle cell disease since it reduces in this population up to more than 80% the incidence of infectious complications and the carriage of pneumococci, without there being any benefit in continuing it after 5 years old (46). In adults, the level of evidence of its effectiveness is lower, but given the epidemiological data and the reduction in the risk of infection in the event of good compliance (47), antibiotic prophylaxis remains recommended. In total, there are no specific recommendations regarding antibiotic prophylaxis

in the cirrhotic asplenic patient. Antibiotic prophylaxis must be started immediately postoperatively with amoxicillin (Clamoxyl®: 500 mg, twice a day) if the oral route is impossible with a secondary oral relay. In adults or children over 5 years of age, it is recommended during the 2 years post-splenectomy and may be prolonged in the event of immunosuppression or signs of persistent hyposplenism (Jolly body, thrombocytosis).

In addition to antibiotic prophylaxis, some advice should be remembered (48,49) and education can be considered the most important preventive measure for OPSI. It must be emphasized that the risk remains, even in the case of vaccination and antibiotic prophylaxis which do not confer absolute protection. Specialized medical management is recommended in the event of the appearance of symptoms that may suggest an infection in order to start antibiotic therapy in an emergency. The patient should always carry amoxicillin with him or her immediately in case of fever if prompt contact with a doctor is not possible (for example during travel). Supervision by a referring doctor should be indicated to him in order to carry out in particular the booster shots.

Preventive anticoagulation

MS causes a decrease in the speed of circulation of the portal blood, responsible for the formation of a portal thrombus at the level of the splenic venous stump with possible extension to the portal trunk (50). There have been more than 40 publications since 1990 reporting portal thrombosis after MS. Its incidence is variable depending on the definition adopted (mural or complete, splenic vein or portal vein). Portal thrombosis can have important consequences for survival and the possibility of subsequent transplantation. After MS and without prophylactic anticoagulant treatment, in the cirrhotic patient, the incidence of thrombosis was 36% in a study by Kawanaka et al (47), 34.2% in a study by Ushitora et al. (51). The identified risk factors for door thrombosis after MS in cirrhotic patients are: 1/ the rate of white

blood cells $< 2000 / \text{mm}^3$ (52), 2/ the rate of antithrombin III $< 60\%$ (37) and 3/ the size of the spleen and the diameter of the splenic vein. Threshold values have been identified for the diameter of the splenic vein. These [9 mm thresholds for Kinjo et al. (52) 10 mm for Kawanaka et al. (37)] are used in Asia to decide whether to start anticoagulant therapy.

No high-grade recommendation can be made regarding the best thrombotic prophylaxis regimen for MS in cirrhotic patients because no high-level study is available. Most of the Asian series which have compared thromboprophylaxis protocols have included eso-gastric devascularisation procedures which are no longer performed in Europe and which therefore cannot be directly extrapolated to Western practices. In addition, certain series have reported treatments not usually used in the west for first-line anti-thrombotic prophylaxis [danaparoid sodium (53), aspirin (54), clopidogrel (55), warfarin (18, 55)].

- However, it appears that the risk of port mesenteric thrombosis after MS in cirrhotic patients seems particularly high due to:
- imbalance of pro- and anticoagulant factors resulting from a global state of hypercoagulability despite a fall in the prothrombin and INR levels (reduction in synthesis of anticoagulant factors such as proteins C and S and antithrombin III, increase synthesis of procoagulant factors such as factors VIII and Willebrand),
- the decrease in portal flow after MS and the risk of extension of the thrombus of the stump of the large splenic vein (52),
- thrombocytosis which usually appears after MS.

Several series have established that the risk of bleeding is not increased when prescribing low molecular weight heparin in the cirrhotic patient (56,57), notably in the randomized study by Villa et al. (58). In 2008, Habermalz et al. (26) published recommendations on antithrombotic prophylaxis in laparoscopic MS (without underlying hepatopathy), recommending peri-operative prevention with subcutaneous heparin, continued for 4 weeks postoperatively

(grade C). Despite procedures that go beyond the recommendations (SP associated with oesogastric devascularization), Cheng et al. (55) and Lai et al. (54) seemed to confirm the interest of an early prophylaxis based on low molecular weight heparin in prevention of portal thrombosis (grade C). Kawanaka et al. have shown in a prospective non-randomized series of 50 patients that the preventive administration of antithrombin III during the first three postoperative days significantly reduced the incidence of portal thrombosis after MS in cirrhotic patients (versus no prophylaxis, grade B) (59). The same group reported in 2014 a preoperative staging of the risk of post-SP port mesenteric thrombosis according to the dosage of anti-thrombin III activity and the diameter of the splenic vein in cirrhotic patients (Child-Pugh A to C) (53). Depending on the risk, prevention based on anti-thrombin III, low molecular weight heparin, danaparoid sodium or warfarin was prescribed. This prospective study does not allow definitive validation of the authors' algorithm (grade B) but opens the way to other prospective randomized series.

Except for a particularly high perioperative haemorrhagic risk (thrombocytopenia $< 30\text{-}50$ Giga/L) or specific contraindication (renal failure or history of heparin-induced thrombocytopenia in particular), it seems that heparin-based thromboprophylaxis Low molecular weight limits the incidence of post-splenectomy portal thrombosis in the cirrhotic patient. The place of the other alternatives (danaparoid sodium, antiplatelet agents or oral anticoagulants) must be specified. Other measures not specific to the cirrhotic terrain should also be applied, if possible: elastic compression of the lower limbs and early lifting.

Short-term Surgery Results: Morbidity and Mortality

Consequences for hepatic hemodynamic

MS suppresses a significant part of the portal flow, directly proportional to the volume of the spleen. Imura et al. (60) reported an average decrease of 4.7 mmHg in portal pressure after MS. Kawanaka et al. (37) found a 25% drop in the cellular-cellular gradient after SP and a 12%

drop in gate flow. In patients with significant splenomegaly (weight of the spleen > 500g), the authors noted a decrease in the porto-cave gradient of 33% and a decrease in portal flow of 15.4%. We can therefore conclude that MS in the cirrhotic patient reduces the pressure and the flow rate.

Consequences on Liver Function

The liver function seems to improve after MS in the cirrhotic patient (level 4), except in a situation of decompensated cirrhosis. Yamamoto et al. (61) demonstrated an improvement in the Child score in Child B patients (from 7.4 points to 6.3 points) and an aggravation in the score in Child A patients (from 5.5 to 6.3 points) 1 year after MS. Kawanaka et al. (37) found a stable Child score in Child A patients and an improvement in Child B patients (8.3 to 6.6 points) 1 month after surgery. The incidence of ascites fell from 62% to 18% in the latter group. Anegawa et al. (36) published similar results with an improvement in Child's score one month after MS (from 6.8 to 6.3 points).

In total, MS in cirrhotic patients reduces portal pressure and door flow. Improvements in liver function have also been reported but cannot, by themselves, be an indication of MS.

Early Complications after Splenectomy in Cirrhotic Patients

- Certain complications are common to any surgery for cirrhotic patients: onset of ascites, wall infections, bleeding, encephalopathy. Other complications are more specific: portal vein thrombosis, pancreatic fistula and fulminant infections.
- General complications: ascites de novo and encephalopathy seem rare after MS, their reported rates remaining below 2% (15,30,32,44,61-63). Wall infections have comparable rates (3-12%) with other interventions in the cirrhotic patient, and their frequency is increased in case of laparotomy or Child B cirrhosis (22, 96) (level 4). The rate of postoperative haemorrhage requiring resumption is low (0-4%) and appears to be further

reduced in the case of laparoscopic approach (27-30) (level 4).

- Portal thrombosis: the risk is increased after MS (see chapter on thrombotic prophylaxis).
- Pancreatic fistulas remain rare, whether after laparoscopy or laparotomy, with an incidence of between 2 and 5% and a generally favourable course (63).
- Fulminant infections are very rare in adults with cirrhosis (<1%) (15, 64). Prophylactic treatment is recommended, by vaccination and antibiotic prophylaxis (see specific recommendations).

Results of long-term surgery

Long-term survival (Table 4)

Few series have reported long-term follow-up after MS in cirrhotic patients and most authors associated another gesture with MS, in particular a liver resection for the management of CHC nodule (s) or oesogastric devascularisation. It is therefore difficult to assess the specific impact of MS since survival was also dependent on the underlying liver disease and the course of the tumour disease. It should be noted, however, that the four series that compared the survival of splenectomized and non-splenectomized patients (after hepatectomy or oesogastric devascularization) did not highlight any statistical difference in overall survival (11,16,41,65). No deaths were directly attributable to a post-MS complication.

In total, no conclusion can be offered regarding the impact on the survival of splenectomy in the cirrhotic patient.

Long-term Evolution of the Platelet Rate (Table 5)

The short-term correction of thrombocytopenia after MS in the cirrhotic patient has been widely evaluated, and compared with other techniques [notably radiofrequency (66, 67) and splenic embolization (17, 68, 69)]. The effectiveness of MS on the platelet count is widely recognized but the sustainability of its action has, on the other hand, been little studied. Some

Table 4. Main series reporting the long-term follow-up of splenectomised cirrhotic patients.

1st author	n	Child-Pugh Score	Approach	Associated Gesture	Follow-up in months (median)	Survival
Chen (11)	94	A/B	Ouverte	Hepatectomy for HCC	41	5 years: 56%
Imura (60)	18	B/C	Ouverte	Hepatectomy (n = 3) or radiofrequency (n = 9) for HCC	NS	1 year: 83.3% 2 years: 62/7%
Kim (65)	19	A	Ouverte	Hepatectomy for HCC	NS	5 years: 74.5%
Ogata (18)	46	B/C	Ouverte (n=37) Hybrid (n=9)	Hepatectomy for CHC oeso-gastric devascularization (n = 1)	52 months	1 year: 93.5% 3 years: 76% 5 years: 37.9%
Sugawara (83)	48	NS	Ouverte	Hepatectomy (n = 27, CHC) Hepatectomy + oeso-gastric devascularization (n = 21, CHC)	48 months	3 years: 72.3% 5 years: 38.9%
Tomikawa (16)	31	A/B	Ouverte	Oesophageal transection (n = 31)	92 months (average)	5 years: 77.4% 10 years: 37.7%
Wu (41)	41	A/B/C	Ouverte	Hepatectomy for HCC	38 months (average)	3 years: 71% 5 years: 42% (approx.)

authors have reported a correction of persistent thrombocytopenia for several years. Note that there seems to be a gradual decrease in the platelet count in the long term, but this probably does not call into question the value of this treatment in cases of severe thrombocytopenia since the rates observed remained higher than the pre-SP rate.

In total, splenectomy has a major, rapid and lasting positive effect on thrombocytopenia secondary to hypersplenism. However, drug alternatives are now available and can act directly on platelet progenitors with a lower risk than MS.

Place of Alternatives to Splenectomy

Partial Splenectomy (Table 6)

Partial MS is an intervention rarely performed because of its difficulty in performing and the risk of bleeding. In the context of cirrhosis, very rare cases have been published (*Table 5*) for hypersplenism associated with other stigmas of portal hypertension (ascites, oesophageal varices) in young patients with cystic fibrosis complicated by cirrhosis. This MS technique was proposed in order to preserve the immunological function of the spleen. The published experience is limited to

Table 5. Main series reporting the evolution of the long-term platelet count of splenectomised cirrhotic patients.

1 st author	n	Pre-splenectomy plates (G/L)	Post-splenectomy plates (G/L)
Akahoshi (15)	21	56	M6: 105 1 year: 100
Amin (17)	20	47	M3: 260 M6: 322
Anegawa (36)	70	53	M3: 184
Feng (66)	19	34	M6: 120 1 year: 115 3 years: 97 5 years: 75 (approx.)
Kedia (5)	33	44	1 year: 250
Tomikawa (16)	31	78	1 year: 243 5 years: 193
Zhou (42)	34 (coelio) 29 (open surgery)	38 41	M6: 244 M6: 251

Table 6. Cases of partial splenectomy in cirrhotic patients

1 st author	n (context)	Indication	Efficacy	Morbidity
Feigelson (112)	1 (9 years, cystic fibrosis)	HTP	Disappearance of the OV	0
Thalhammer (84)	3 (12 to 19 years, cystic fibrosis)	HTP	Regression of thrombocytopenia and disappearance of OV	1 totalisation for hilum hematoma
Chazalotte (85)	11 (children, cystic fibrosis)	HTP	Lasting regression of thrombocytopenia, Disappearance of OV in 9 cases	3 segment hematomas 2 inexplicable pain
Louis (86)	19 (7 to 23 years, cystic fibrosis)	HTP	PH regression in 16 cases. Recurrence in 2 cases	3 cases of right ascites and pleural effusion treated with medication 3 segment hematomas 4 events

(HTP: portal hypertension, OV: oesophageal varices)

23 cases. The intervention was carried out by left subcostal laparotomy and the pedicle vessels were ligated in contact with the spleen from bottom to top while respecting the superior polar vascularization. The parenchymal transection was performed with a monopolar electrosurgical unit and by digitoclasis. Haemostasis of the slice was achieved by multiple ligations with non-absorbable wire. In more than 85% of cases, the intervention reduced thrombocytopenia and other stigmas of PH for at least 5 years. Morbidity was low. No cases of hemoperitoneum or spleno-portal thrombosis have been described.

In total, partial splenectomy has not been evaluated in cirrhotic adults and no recommendation can be made in this area.

Embolization of the Splenic Artery (EAS)

This therapeutic option has been used since the 1970s and flourished from the 1990s due to a reduction in post-interventional morbidity and mortality (70). It is now the preferred route in Western countries and may be indicated for the management of splenic trauma and splenic artery aneurysms. The main effects of this therapy have been studied in the treatment of complications of portal hypertension in Asian patients (*Table 7*).

The EAS consists of a percutaneous arterial embolization after femoral approach. The embolization implants were variable depending on the centres: non-absorbable microspires (coils), non-absorbable particles (PVA, acrylic polymer), gelatine sponges (Gelfoam). Embolization can be partial or total (71).

Hemodynamically, splenic embolization has an impact on portal hypertension by reducing splenic venous return. The consequences are mainly a correction of hypersplenism. The reported effect is maximal at D15 but can last several months, even several years. A decrease in the risk of bleeding from ruptured oesophageal varices or gastropathy of portal hypertension, and a decrease in ascites, have also been described. The serious and frequent complications reported are:

- portal thrombosis (approximately 10 to 15% of cases) by slowing down the portal flow. It is the most feared complication, at risk of acute liver failure and death. It is favoured by preexisting partial thrombosis, broad splenic embolization and severe portal hypertension preoperatively. Its diagnosis must be made early by doppler to be able to introduce a curative anticoagulant treatment,
- splenic abscess (approximately 5 to 10% of cases) which develops on an infarcted area, probably by digestive translocation or per-procedure contamination. Antibiotic prophylaxis is therefore necessary to limit this risk,
- splenic infarction (less than 5% of cases) is the consequence of extensive splenic embolization and is manifested by severe pain, fever, abscess, portal thrombosis or left pleural effusion. Full embolization of the splenic artery are therefore not recommended. However, a prospective non-randomized Chinese study shows a

Table 7. Main studies on the effects of splenic arterial embolization in cirrhotics

1 st author	n	Indication	Embolization extent	Efficacy	Complications
Sakai (87)	17	HTP	50-70%	Correction of thrombocytopenia in 90% of patients	1 death from liver failure 1 peritonitis due to abscess rupture prolonged fever (5 cases) pleural effusion G (3 cases) post-embolization syndromes (100%)
Palsson (88)	26	HTP	30-40%	Decrease in the frequency of haemorrhages Correction of thrombocytopenia: +120,000	2 deaths (portal thrombosis, pneumonia) Portal thrombosis (4 cases) Splenic abscess (2 cases) Complications at the puncture site (2 cases) Post-embolization syndrome (100%)
Xu (89)	41	HTP	30-60%	Correction of thrombocytopenia: + 70,000 1 case of haemorrhagic recurrence Portal flow reduced by 15%	1 death from PE Abscess (1 case) post-embolization syndrome (100%) prolonged fever (1 case)
N'Kontchou (90)	32	HTP	50%	Correction of thrombocytopenia: + 70,000	2 deaths from splenic abscess portal thrombosis (2 cases) puncture site haemorrhage (1 case) post-embolization syndrome (78%) prolonged fever (2 cases)
Hayashi (91)	42	HTP	50-70%	Correction of thrombocytopenia: + 70,000	Post-embolisation syndrome (100%) Pleural effusion G (10%)
Amin (17)	20	HTP	50%	Correction of thrombocytopenia: + 200,000	1 death Pleural effusion G (10%) Portal thrombosis (1 case) Splenic abscess (1 case)
Zhu (92)	62	HTP	50-70%	Correction of thrombocytopenia: + 80,000, especially at Child A B	1 death Splenic abscess (1 case) Peritonitis (1 case) Post-embolisation syndrome (100%) Pleural effusion G (5%)
Moon (77)	7	AAS	NC	ASA control in 100% of cases	splenic abscess (1 case) portal thrombosis (1 case) splenic infarction (1 case)
Elmonem (122)	23	HTP	50-70%	Correction of thrombocytopenia: +70,000	1 death Post-embolization syndrome (91%) Pleural effusion G (9%) Portal thrombosis (1 case) Peritonitis (1 case)
Bugaev (2)	32	Trauma	NC	Haemorrhagic control: 71%	Mortality: 32% $\pm$ 3 m
Shimizu (93)	108	HTP	70%	Thrombocytopenia correction: +80,000 Decrease in splenic venous flow: -50% No decrease in portal venous flow	-
Kondo (94)	18	HTP	70-80%	Correction of thrombocytopenia: +50,000	post-embolization syndrome (100%)

(HTP: portal hypertension, ASA: splenic artery aneurysm)

decrease in morbidity and mortality after total embolization (71),

- post-embolization syndrome (90 to 100% of cases) combines pain and fever. It usually improves within a few days,
- left pleural effusion (20 to 30% of cases) is a sweating reaction to subphrenic inflammation. It can be complicated by passive atelectasis and pneumonitis.

Embolization of the splenic artery is a simple technique to perform. The consequences of this

gesture are usually favourable, but serious complications are to be prevented or detected early, especially on cirrhotic ground. The place of embolization in the cirrhotic patient remains to be evaluated.

Non-operative Treatment (TNO) of Spleen Trauma

Abdominal trauma in cirrhotic patients has a very poor prognosis. The excess mortality in this population is linked to the severity of liver

disease (correlation between survival and the MELD score (72,73)) and to the risk of oedemato-ascitic decompensation and haemorrhage if surgery is used. Mortality after laparotomy in the context of trauma is thus estimated at 40% in cirrhotic patients vs. 15% in the general population (74).

Since the 1990s, non-operative management of abdominal trauma has developed, particularly for spleen trauma. This strategy has enabled a reduction in morbidity and mortality in selected cases, thanks to advances in resuscitation and diagnostic and interventional radiology (75). The indications for TNO in the general population are reserved for hemodynamically stable patients with mild lesions of the spleen. In case of extravasation of contrast agent of the splenic artery or intrasplenic, the splenic arterial embolization allows haemostasis. The evaluation of the TNO strategy in cirrhotic patients has been the subject of only a few retrospective publications. The results are presented in *Table 8*.

NWT has been described in less than 300 cirrhotic patients. In 0 to 13% of cases, splenic arterial embolization was performed. The success rate defined by the absence of recourse to MS haemostasis varied widely from 8% to 71%, reflecting a heterogeneity of expertise in trauma and hepatology from the different centres. Mortality after TNO treatment was only described in one study (2), at 23% (32% after splenic embolization, 16% without interventional treatment).

TNO treatment failure factors are (1-3) coagulation disorders and severe splenic lesions (grade 4 and 5). Risk factors for mortality after TNO are: male, hypotension on admission, Glasgow admission score <13, bleeding disorders, TNO failure, MELD score,

IJ (Injury Severity Score), remedy at transfusion, failure of TNO.

The results of TNO treatment are not comparable to those of MS because the decision criteria for one or the other option are different in these studies.

In total, no recommendation can be made regarding the place of nonoperative treatment of spleen trauma in cirrhotic patients. In all cases, close monitoring in a specialized medical and surgical environment is recommended. A comparative evaluation of this strategy is recommended.

Non-operative Treatment of Splenic Artery Aneurysms (ASA)

- The treatment of ASA in cirrhotic patients remains controversial. In the event of rupture, initial in most cases (76), or after liver transplantation in 3 to 4% of cases (77), the mortality rate is 59%. The standard treatment for ASA has long been MS associated with ligation or resection of the aneurysm (7, 78), a heavy gesture in a context of cirrhosis. The alternatives to surgical treatment are:
- surveillance, in particular for small lesions of less than 2 to 3 cm, which are not progressive or in patients over 60 years of age (77, 78). It is also discussed in patients with stable lesions of less than 3 cm, awaiting transplantation, the natural evolution being towards regression after correction of portal hypertension. The risk of rupture in post-transplantation is however significant and must be taken into account in the surveillance decision.
- splenic artery ligation, often performed during liver transplantation, but burdened with a high failure rate [75% of cases in the

Table 8. Comparative studies of nonoperative treatment for splenectomy in cirrhotic patients

1 st author	n	Type of care		Success: TNO / SP	Mortality: TNO / SP
		TNO / SP	TNO: EMB / SURV		
Fang (1)	12	100% / 0%	0% / 100%	8%/-	Global: 50%
Lin (73)	20	50% / 50%	10% / 90%	Global: 30%	-
Bugaev (2)	289	86% / 14%	13% / 87%	71% / 65%	23% / 35%
Cook (3)	77	48% / 52%	8% / 92%	-	Global: 27%

EMB: splenic embolization, NO: non-operative treatment, SP: splenectomy

Seoul series (77)].

- endovascular treatment, currently the benchmark in the general population (79,80).

Only one Korean series analysed the results of the various treatments in 41 cirrhotic or recently transplanted patients (77). Non-operative treatment was performed as first-line treatment in 90% of cases, including 5 cases of radiological embolization. In only one case was SP necessary for rupture of the ASA after TH. In case of rupture, embolization allowed haemostasis in the 2 cases where the technique was used. In the same series, the mortality rate after first MS was 20% vs. 0% in the case of non-operative treatment.

In total, because of the severity of a ruptured aneurysm of the splenic artery in the cirrhotic patient, their prophylactic management is therefore essential. Endovascular treatment is currently the treatment of choice because of its lower morbidity and mortality. In patients with cirrhosis without a transplant plan, monitoring every 6 months is recommended and treatment in case of evolution or of size greater than 2 cm.

Conflict of Interest

Nothing to disclose.

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