

Sclerotherapy of Symptomatic Nonparasitic Splenic Cysts: Excellent Long-Term Treatment Response'

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Abstract

Background Splenic cysts are rare and occur in 0.5 to 2% of the population. They are usually asymptomatic and do not require therapy. In case of symptomatic nonparasitic splenic cysts, potential therapy includes partial splenectomy or laparoscopic cyst de-roofing as well as ultrasound-guided sclerotherapy with 1% polidocanol or 10% sodium chloride (NaCl) as an interventional alternative. So far, single-session sclerotherapy of symptomatic nonparasitic cysts is recommended only if clear-transparent cyst fluid is aspirated.

Materials and Methods We report a case series of 17 patients with symptomatic macroscopically turbid nonparasitic splenic cyst fluid who underwent ultrasound-guided fine needle sclerotherapy with either polidocanol ± 10% NaCl ($n = 12$) or 10% NaCl alone ($n = 5$) and a follow-up of a maximum of 12 years after first intervention. Clinical, sonographic, and laboratory chemistry data were recorded at baseline and during the follow-up.

Results The mean follow-up time was 43.65 ± 40.18 months. At the end of the follow-up, a 79% reduction of cyst size was achieved. The maximum size reduction in the polidocanol group was $76 \pm 18\%$ and $84 \pm 21\%$ in the sodium chloride group ($p > 0.05$). At the end of follow-up, 15 out of the 17 patients did not have any further symptoms. Despite the cystic fluid being turbid, it was hardly possible to detect a microbiological superinfection.

Conclusion Sclerotherapy of splenic cysts leads to a significant size regression in all patients, independent of the sclerotherapy agent used with fewer systemic toxic side effects of polidocanol treatment. It was shown that in a tertiary care center with significant experience, sclerotherapy of splenic cysts is also safe and successful and can lead to a drastic regression of cyst size and symptoms. This shows that interventional therapy is a good alternative to surgical procedures.

Keywords

- ▶ splenic cyst
- ▶ sclerotherapy
- ▶ polidocanol
- ▶ interventional ultrasound
- ▶ de-roofing

Splenic cysts are rare and occur in 0.5 to 2% of the population.¹ They are often incidental findings during abdominal sonography and include benign cysts, neoplasia, and abscesses.² They can be categorized as congenital or acquired, of parasitic or nonparasitic origin.³ Parasitic splenic cysts include echinococ-

cus granulosis, which is an important differential diagnosis, especially in endemic areas.⁴ Primary splenic cysts account for approximately 10% of all nonparasitic cysts and are found primarily in Europe and North America, mostly in children, adolescents, and young adults.⁵

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Splenic cysts are usually asymptomatic and do not require therapy. Rarely, symptoms such as localized pressure pain in the left upper abdomen, nausea, feelings of fullness, or clinical signs of infection occur.⁶ These are often associated with large cysts, signs of bleeding, or superinfection.

Standard surgical procedures for symptomatic nonparasitic splenic cysts include partial splenectomy or laparoscopic cyst de-roofing.^{7,8} Ultrasound-guided sclerotherapy with 1% polidocanol (referred to simply as polidocanol in the following) is an alternative, effective, and minimally invasive therapy for symptomatic splenic cysts and often prevents splenectomy.^{9,10} In a small series from the clinic associated with the authors, it was shown that by using this therapy the size of the cyst decreased significantly and that the symptoms improved.¹⁰ However, single-session sclerotherapy of symptomatic nonparasitic cysts is recommended only if clear-transparent cyst fluid is aspirated.¹¹

The purpose of this study was to investigate whether the response to ultrasound-guided sclerotherapy with polidocanol or 10% sodium chloride in patients with symptomatic splenic cysts is influenced by a turbid cyst aspirate.

Materials and Methods

This study was performed in compliance with the Declaration of Helsinki and with the approval of the local Ethics Committee. All patients gave written informed consent prior to the therapy.

Screening Procedure

A database search was made of all patients who were seen in our ultrasound unit of the Department of Gastroenterology, Hepatology and Endocrinology of the Hannover Medical School, Hannover, Germany. In this search, the occurrence of splenic cysts between beginning of 2008 and end of 2018 was noted. A total of 103,861 ultrasound reports were categorized and 218 patients with splenic cysts were identified. Particular interest was placed on those patients who reported symptoms of the splenic cyst like localized pressure pain in the left upper abdomen, nausea, feelings of fullness, and who had turbid cystic fluid detected during ultrasound-guided splenic cyst fluid aspiration. Seventeen patients who met these criteria were identified. The screening procedure is illustrated in ►Fig. 1.

Cyst Puncture and Sclerotherapy

Preprocedural ultrasound was performed to evaluate the best puncture position (patients were laid either on their back or on their right side) and to exclude parasitic cysts. The appearance of the following sonographic criteria has been considered to exclude parasitic cysts: irregular wall-thickening, solid intracystic structures, wall defragmentation, cyst in cyst appearance, or focal calcifications.¹² In addition, each patient received serologic testing for echinococcosis to further reduce the likelihood of a parasitic cyst.¹³ Puncture was performed under continuous monitoring of vital signs and with emergency medication prepared in case of helminth-associated anaphylactic shock. The puncture was usually performed by two

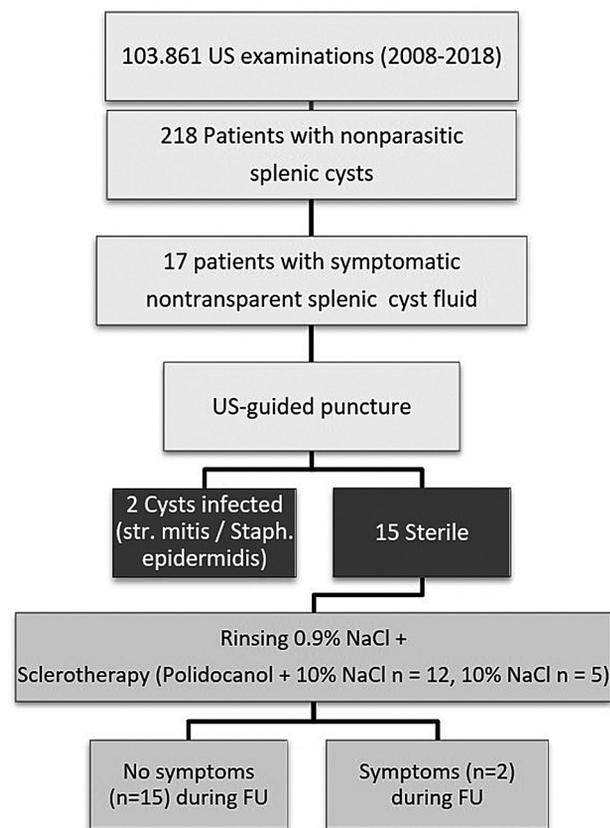


Fig. 1 Screening procedure of patients with turbid nonparasitic splenic cyst fluid. US, ultrasound; str., *Streptococcus*; NaCl, sodium chloride; FU, follow-up.

physicians. Toshiba Aplio XG machine (Toshiba Medical System, Japan) with a special puncture probe (linear 6L3) allowing fine needle biopsy under direct visualization was used. Local anesthesia was injected reaching the peritoneum using a 22-G Chiba needle (Pajunk, Geisingen, Germany). The splenic cyst was subsequently punctured using a 20-G 220-mm Chiba needle (Pajunk; shown in ►Fig. 2a–c). Throughout the procedure, the tip of the needle was monitored to keep it in the middle of the cyst ensuring a safe and efficient position. The cystic fluid was drained as much as possible until the cyst was almost emptied to the point of collapse. The drained fluid was examined cytologically and underwent microbiological incubation. Due to the turbid cyst fluid, all cysts were generally rinsed extensively first with 0.9% saline prior to sclerotherapy. When the drained cyst fluid was almost clear and the cyst was almost totally evacuated, an injection of 10% of the evacuated volume with polidocanol (Aethoxysklerol 1%; Kreussler Pharma, Wiesbaden, Germany) or 10% sodium chloride was made for at least 3 minutes. This leads to an irreversible damage of the cyst epithelium. Afterward, the cyst was emptied as much as possible to minimize the remaining amount of sclerosing agent. Patients were closely monitored after the interventional procedure to detect side effects of the sclerosing agents at an early stage (e.g., allergic reactions). Periodically, patients were examined for free fluid around the spleen and in the deep pelvic region, as cardiotoxicity has been described for polidocanol usage.¹⁴



Fig. 2 Ultrasound-guided puncture and sclerotherapy of a symptomatic nonparasitic splenic cyst (a–c).

Patients were examined on the day after the first interventional therapy to check for local complications and for the size of the splenic cysts. This is necessary because in the early days after sclerotherapy, the cyst may increase its volume due to the reactions of the inflammation. These are caused by the destruction of the epithelial cells of the cyst after instillation of polidocanol.

10% sodium chloride was especially used in patients with a history of surgical cyst de-roofing and in patients with subcapsular cysts without tissue covering to minimize pain after potential peritoneal contact of the sclerotherapy agent.

The following punctures were performed depending on the time course and amount of exudate. Initially, patients were examined weekly for 4 weeks. Subsequently, additional sonographic controls were performed depending on the amount of exudate and patient's symptoms. Anti-infective therapy was injected if a cyst infection was seen as possible. Samples of the cyst fluid were regularly sent for microbiological and cytological examination. Cyst size reduction was first evaluated 3 months after the initial sclerotherapy.

Statistics

Statistical analysis was undertaken using GNU R (version 4.0.3). Unless otherwise stated, mean values and standard deviation are given. The comparison of the groups (polidocanol and 10% sodium chloride) was performed with the two-sided *t*-test. $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics

Seventeen patients who underwent first sclerotherapy showed a median age of 30 years. Twelve (71%) of these

patients were female and 5 (29%) were male. All underwent interventional therapy starting with puncture of the cyst. Most patients suffered from one symptomatic cyst (average number of cysts: 1.35 ± 0.7). The splenic size was also enlarged due to the size of the cyst. The patients showed a splenomegaly of approximately 14.67 ± 3.89 cm. Patient characteristics are given in ►Table 1.

Initial Sclerotherapy and Repuncture

Despite the presence of turbid cyst fluid, a positive culture was detected only in two patients. One culture revealed a streptococcus mitis and the other one revealed a *Staphylococcus epidermidis*. All other 15 microbiological incubations were sterile. After an initial rinsing of the cyst fluid and sclerotherapy intervention, most patients underwent reinterventions (range: 0–15 reinterventions, median: 3) in the form of puncture to evacuate the cyst from the exudative liquid after first sclerotherapy (as shown in ►Table 2). During follow-up, an average of 4.24 ± 3.89 repunctures were needed to get a stable cyst volume without exudative liquid. The entire procedures were well tolerated without any severe complications. The cytological examination revealed a light bleeding only in two patients, which was not significant. The patients reported no pain and needed no transfusion of erythrocyte concentrates. After the first sclerotherapy, the median number of days the patients had to stay in hospital was 6 days (average: 6.47 ± 3.34 days). Furthermore, there was no correlation ($p > 0.05$) between a patient's length of hospital stay and cyst size at initial puncture.

Follow-up Period

The mean follow-up time was 43.65 ± 40.18 months. After follow-up, the cysts reduced to a maximum of $21\% \pm 19\%$

Table 2 Initial sclerotherapy and repuncture ($n = 17$)

Procedure characteristics	
No. of cysts	1.35 ± 0.7
Total puncture volume [mL]	$2,202 \pm 2,905$
Initial puncture volume [mL]	721 ± 725
Repuncture (n)	4.2 ± 4.28
Maximum cyst size [mm × mm]	$13,352 \pm 9,982$
Inpatient time [days]	6.47 ± 3.34

Table 1 Patient characteristics at baseline ($n = 17$)

Clinical features	
Gender (f/m)	71%/29%
Age [years], mean ± SD (range, median)	31.5 ± 13.6 (14–53, 30)
Spleen size [cm], mean ± SD (range, median)	14.7 ± 3.9 (9.6–23–3, 13.5)
Dominant cyst size (mm), mean ± SD (range, median)	117.3 ± 46.33 mm

Abbreviations: f: female; m, male; SD: standard deviation.

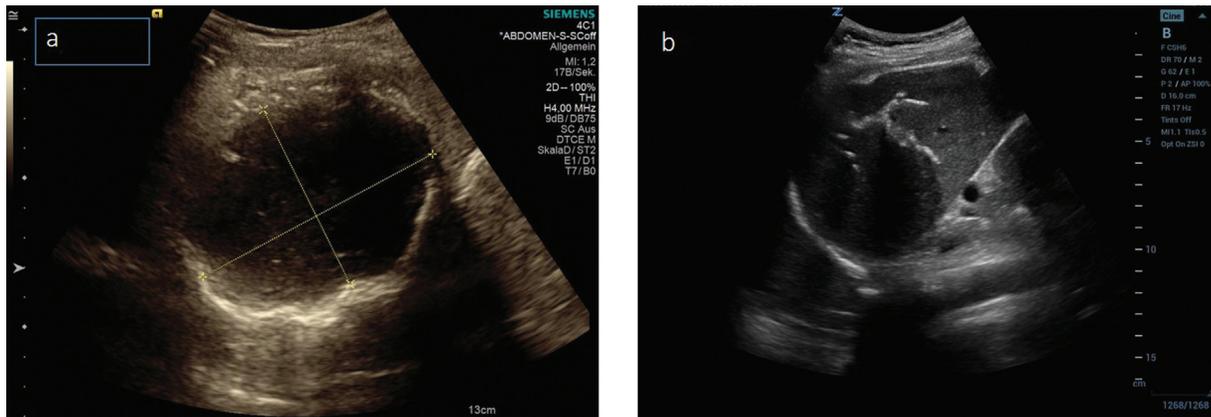


Fig. 3 Sonographic images of a splenic cyst (a) prior to sclerotherapy and (b) 1 year after sclerotherapy. The cyst is completely collapsed and shows regressive changes.

the initial volume (79% reduction in size). At the end of follow-up, 15 out of the 17 patients did not have any continuous symptoms. In ►Fig. 3, a typical sonographic image of a splenic cyst prior to sclerotherapy and after a 1-year follow-up is shown. In ►Fig. 4, the relative cyst size compared with a baseline for all 17 patients during the course of the first year after puncture (►Fig. 4a) and over a maximum period of 12 years (144 months) is shown (►Fig. 4b).

Only two patients reported mild symptoms (*patient 2 and patient 3*). Both showed smaller cysts before first intervention (8-cm-long diameter), and both were female and younger than 30 years; both cysts underwent sclerotherapy with polidocanol. In addition, both cysts were sterile in microbiological examination and despite the fact that both patients reported of mild ongoing symptoms, the size of their cysts decreased significantly by 67% in one patient and the other one by 99%.

Comparison of Sclerotherapy—Polidocanol (\pm 10% Sodium Chloride) versus 10% Sodium Chloride

Out of all 17 patients, 12 underwent sclerotherapy with polidocanol (during follow-up reintervention was done by using 10% sodium chloride) and five cysts were treated only with 10% sodium chloride. ►Table 3 shows the characteristics of the two subgroups. The median age in both groups was 32 years ($p > 0.05$) and showed no significant difference. 71% of all patients were female (83% in the polidocanol group and 40% in the 10% sodium chloride group) without any statistical difference. There was also no difference in the number of cysts or the splenic size. During the splenic cyst therapy, the mean aspiration volume was $2,365 \pm 3,257$ mL in the polidocanol group and $1,810 \pm 2,079$ mL in the sodium chloride group ($p > 0.05$). The patients had to stay in hospital for 6 ± 2.6 days in the polidocanol group and 7.2 ± 5.1 days in the sodium chloride group ($p > 0.05$). 4.4 ± 4 repunctures were needed after initial polidocanol therapy to get a stable cyst volume, whereas 3.8 ± 5.3 repunctures were done in the sodium chloride group ($p > 0.05$). The maximum size reduction in the polidocanol group was $76 \pm 18\%$ and $84 \pm 21\%$ in the sodium chloride group ($p > 0.05$). Compared with the size

and the average aspiration volume, the maximum cyst size was reduced in both groups ($14,062 \pm 10,582$ mm \times mm in the patients who were treated first with polidocanol and $11,649 \pm 9,249$ mm \times mm in patients who were treated only with 10% sodium chloride; $p > 0.05$).

Discussion

Splenic nonparasitic cysts are rare findings, even in a tertiary-care ultrasound center. From more than 100,000 reports, only 218 patients were identified with splenic cysts (0.22%), which is in line with previous reports from autopsies.^{15–18} In a 2013 publication of the Ultrasound Center of the Hannover Medical School, it was shown that percutaneous ultrasound-guided sclerotherapy is a useful new approach for the treatment of symptomatic splenic cysts, as most patients' cyst size and symptoms could be significantly reduced during one hospital stay with this therapy.¹⁰ In this retrospective analysis, focused was placed on symptomatic patients who showed turbid cyst fluid. Consequently, the purpose of this study was to investigate whether the response to ultrasound-guided sclerotherapy with polidocanol or 10% sodium chloride in patients with symptomatic splenic cysts is influenced by a turbid cyst aspirate.

In this study, it was shown that ultrasound-guided sclerotherapy using polidocanol is a sufficient and safe alternative that leads to asymptomatic patients in most cases. It should be highlighted that also for macroscopically nontransparent cyst fluid, it is possible to reach significant reduction of the cyst size by sclerotherapy (an average of 80% reduction was shown in all cases). Furthermore, no patient needed analgesics after intervention, no transfusion was needed, and nothing serious was observed to occur. Only in two cases did cytological analysis show some fresh erythrocyte effusion, which did not lead to any medical consequence. All patients showed a significant reduction in the cyst size, with only two patients reporting mild symptoms at the end of follow-up. This observation suggests that symptoms may not be associated with cyst size reduction or superinfection. Both patients who reported mild symptoms at the end of follow-up showed negative microbiological reports.

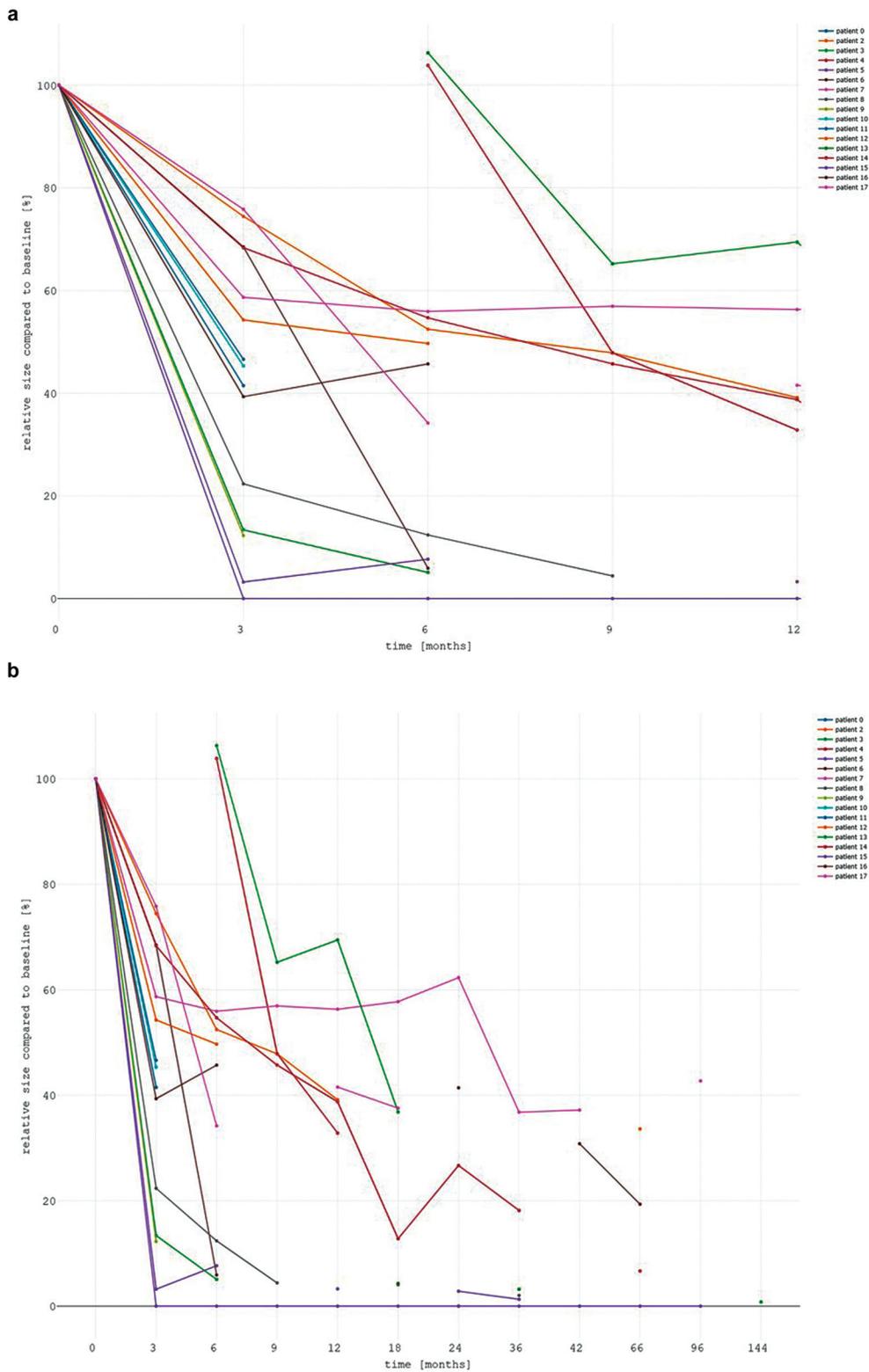


Fig. 4 Relative cyst size (%) during follow-up in comparison to baseline. (a) One-year follow-up after sclerotherapy; (b) most recent follow-up after sclerotherapy (maximum: 144 months).

Our observation also shows the low rate of superinfection in patients with splenic cysts and turbid cyst fluid. Only two patients with symptomatic splenic cysts showed microbiological detection of bacteria (*Streptococcus mitis* and *Staphylococcus epidermidis*).

Compared with liver and renal cysts, the follow-up of splenic cysts (short-term and long-term) is definitely more important because of the more intense exudative reaction of splenic cysts. Consequently, more repunctures are needed, especially in the first weeks after initial sclerotherapy. Thus,

Table 3 Comparison of sclerotherapy with polidocanol (+10% sodium chloride) versus 10% sodium chloride

	Polidocanol + 10% sodium chloride	10% sodium chloride	p-Value
No. of patients	12	5	
Age at first sclerotherapy [years]	32 ± 13	32 ± 15	> 0.05
Female [%]	83	40	> 0.05
No. of cysts	1.5 ± 0.8	1	> 0.05
Spleen size at baseline [cm]	14.55 ± 4.19	14.0 ± 3.62	> 0.05
Inpatient time [days]	6 ± 2.6	7.2 ± 5.1	> 0.05
Total puncture volume [mL]	2,365 ± 3,257	1,810 ± 2,079	> 0.05
Initial puncture volume [mL]	827 ± 832	468 ± 295	> 0.05
Repuncture	4.4 ± 4	3.8 ± 5.3	> 0.05
Maximum cyst size [mm × mm]	14,062 ± 10,582	11,649 ± 9,249	> 0.05
Maximum size reduction [%]	24 ± 18	16 ± 21	> 0.05

the sclerotherapy of splenic cysts and the follow-up need to be individualized in accordance with the patient's symptoms and the individual exudative reaction of the cyst. Two patients did not follow the instructions given in the beginning and they showed up at 9 months after initial sclerotherapy with even larger cysts than before the initial treatment. Despite this, we were able to show a significant size reduction in these patients with closer monitoring and repunctures if needed.

These data show that the size reduction of splenic cysts does not depend on the sclerotherapy agent. Nevertheless, one should consider possible toxicity and side effects of, in particular, polidocanol (cardio depressive effect and local tissue toxicity) and also of 10% sodium chloride. For further investigation of potential side effects, a prospective study is suggested.

Conclusion

With this small case series, it was possible to show that ultrasound-guided sclerotherapy of symptomatic nonparasitic splenic cysts is an effective treatment method that leads to a significant reduction in cyst size and improvement of symptoms over the long term in almost all patients treated. The treatment response of polidocanol with or without 10% NaCl showed no difference compared with 10% NaCl alone. Furthermore, it was shown that a turbid cyst fluid is no general contraindication for sclerotherapy of symptomatic nonparasitic splenic cysts and this therapy is associated with an excellent treatment response if appropriate safety precautions are maintained.

Authors' Contribution

M.D.: Acquisition of data, or analysis and interpretation of data; drafting the article.

H.W.: Critical revision for important intellectual content; final approval of the version to be published.

M.G.: Critical revision for important intellectual content; final approval of the version to be published.

A.P.: Conception and design, interpretation of data; critical revision for important intellectual content; final approval of the version to be published.

S.Z.: Conception and design, interpretation of data, drafting and critical revision of the article for important intellectual content; final approval of the version to be published.

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Conflict of Interest

None declared.

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