TRABAJO ORIGINAL

3 % polidocanol foam sclerotherapy *versus* hemorrhoidal artery ligation with recto anal repair in hemorrhoidal disease grades II-III: a randomized, pilot trial

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ABSTRACT

Purpose: polidocanol foam sclerotherapy (SP) *versus* doppler-guided hemorrhoidal artery ligation with recto-anal repair (HAL-RAR) in the treatment of hemorrhoidal disease (HD) was analyzed.

Methods: a prospective, randomized study including patients with HD grades II and III was performed. Participants were randomly assigned (1:1) into SP or HAL-RAR, during a recruitment period between September 2019 and February 2020. Therapeutic success (Sodergren's and bleeding scores) was the primary outcome. Other outcomes evaluated included complications and implication in the professional life. Efficacy and safety outcomes were evaluated during the eight weeks after surgery or the final SP session.

Results: forty-six patients were allocated either to SP (n = 22) or HAL-RAR (n = 24). Most patients achieved therapeutic success (SP 100 % *vs* HAL-RAR 90.9 %, p = 0.131). Complete success was higher in the SP group (91.7 % *vs* 68.2 %, p = 0.045) and SP patients had less complications (25 % *vs* 68.2 %, p = 0.003). HAL-RAR had a greater negative impact on work activity of the patient.

Conclusion: SP was more effective and safer than HAL-RAR. SP patients had less impact on their work activity.

Keywords: Hemorrhoidal disease. Polidocanol foam sclerotherapy. Doppler-guided hemorrhoidal artery ligation.

Conflict of interest: the authors declare no conflict of interest.

Author contributions: all authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Sara Neves, Daniela Falcão, Paulo Salgueiro and Ana Povo. The first draft of the manuscript was written by Sara Neves and Daniela Falcão. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval: this study protocol was approved by the institute's committee on human research (2019.292 [235-DEFI/252-CE]). Clinical trials identifier NCT04675177.

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INTRODUCTION

Hemorrhoidal disease (HD) is an extremely frequent anal disorder. Although it is very difficult to accurately assess the exact prevalence, it can be as high as 38.9 % in adult patients undergoing colonoscopy for colorectal cancer screening (1,2). The prevalence is similar in both sexes and peaks between the ages of 45 and 65, with a subsequent decrease after age 65 years (3).

Treatments include medical therapies, office-based procedures and surgery (4,5). Hemorrhoidal sclerotherapy is indicated for grades I-III HD (6). Polidocanol foam has better outcomes than liquid formulation (7). Polidocanol damages the endothelium causing vessel occlusion and local fibrosis (8). Polidocanol foam sclerotherapy (SP) can present complications such as local discomfort, bleeding and less commonly, erectile dysfunction and urinary retention (6). Surgical hemorrhoidectomy is usually reserved for refractory cases or higher HD grades (9,10). However, the less invasive hemorrhoidal artery ligation with/without recto-anal repair (HAL-RAR) is also used in grades II-III HD (6,11).

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Since there is an overlap in the treatment of grade II and III HD (office based *versus* surgical therapy) and there are no comparative studies between SP and HAL-RAR, this study included this subgroup of patients. Therefore, this study aimed to compare SP (3 %) *versus* HAL-RAR in the treatment of grades II-III HD.

METHODS

Patients over 18 years of age with grades II-III HD unresponsive to conservative treatment (diosmin + topical analgesics for four weeks) referred to Centro Hospitalar Universitário do Porto were included. Participants were randomly assigned to either SP or HAL-RAR between September 2019 and February 2020. Randomization was computer-generated (assignments were enclosed in sequentially numbered and sealed envelopes). Since the procedures use different techniques, it was not possible to blind the patient or the clinician to the applied treatment. Therapeutic arms were hidden from the investigators who processed the data. Pregnant/breast-feeding women and patients with cirrhosis, bleeding disorders, immunosuppression, allergy to polidocanol or other perineal diseases were excluded. All the participants signed an informed consent. The trial was approved by the institution's ethics committee and registered at ClinicalTrials.gov (NCT04675177).

Efficacy and safety outcomes

Sodergren hemorrhoidal severity score (SHSS) (12) and HD bleeding grade (HDBG) (13) were used to assess HD severity (Tables 1 and 2). Primary efficacy outcome was therapeutic success (evaluated eight weeks after the final procedure), classified as complete (SHSS = 0 and HDBG ≤ 1), partial (SHSS and HDBG improvement over baseline) or therapeutic failure (worsening/maintenance of SHSS and HDBG). Primary safety outcome evaluated complications categorized as mild (pain/discomfort, minor bleeding), moderate (external hemorrhoidal thrombosis, bleeding without hemodynamic instability) and severe (sepsis, perineal abscess, bleeding with hemodynamic instability). Implications on the professional life of the patients (number of work-loss days) was a secondary outcome.

Table 1. *Sodergren hemorrhoid symptom severity scoring system*

Have you considered or excluded another pathology? Yes □ No □ Does the patient suffer from rectal bleeding? Yes □ No □		
How severe are your symptoms of itching or irritation?	0: No symptoms	0
	1: Mild/do not really bother me	0
	2:	0
	3: Moderately bothersome	0
	4:	4
	5: Severe	4
How severe are your symptoms of pain or discomfort at rest?	0: No symptoms	0
	1: Mild/do not really bother me	0
	2:	0
	3: Moderately bothersome	3
	4:	3
	5: Severe	3
How severe are your symptoms of pain or discomfort on opening your bowels?	0: No symptoms	0
	1: Mild/do not really bother me	0
	2:	0
	3: Moderately bothersome	0
	4:	3
	5: Severe	3
How often do you feel that you might have a lump at your anus (prolapse)?	0: Never	0
	1: Less than once a month	0
	2: More than once a month	0
	3: More than once a week	0
	4: Every day	4

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Table 2. *Bleeding grade in hemorrhoidal disease*

Type of bleeding	Grade
No rectal bleeding	0
Bleeding when passing stool less than once a week	1
Bleeding when passing stool 1-6 days per week	2
Bleeding when passing stool every day or hemodynamic and/or laboratorial changes (anemia, with or without transfusion, signs of hypovolemia)	3

Intervention: technical aspects (Fig. 1)

SP group

1. Polidocanol (aethoxysklerol 3 %) foam was prepared using Tessari's technique (14).
2. An intravenous needle was used for intra-hemorrhoidal injection (through an anoscope).
3. The number of sessions (maximum of three sessions at three-week intervals) depended on the clinical response (if three weeks after the treatment the participant scored SHSS = 0 and HDBG ≤ 1, there would be no additional therapy).
4. Maximum dose per session of 20 ml (4 ml of polidocanol with 16 ml of air).

HAL-RAR group

1. HAL-RAR was performed in the operating-room, under local anesthesia. A doppler-transducer (A.M.I.® HAL/RAR System) was used to identify the superior rectal artery branches, which were ligated above the dentate line.
2. The procedure was repeated 1-1.5 cm below the first series of sutures.
3. RAR procedure (continuous suture applied longitudinally over the hemorrhoid starting 2-3 cm above the dentate line) was performed in HD grade III.
4. Surgical treatment was performed only once.

Statistical analysis

The SPSS® v.26 software was used. Significance was preset at $p \leq 0.05$. Pearson's Chi-squared test was used for categorical data. Normality of continuous variables was evaluated using the Kolmogorov-Smirnov test. Wilcoxon-signed-rank and Kruskal-Wallis tests were used for continuous data. Univariate and multivariate binary logis-

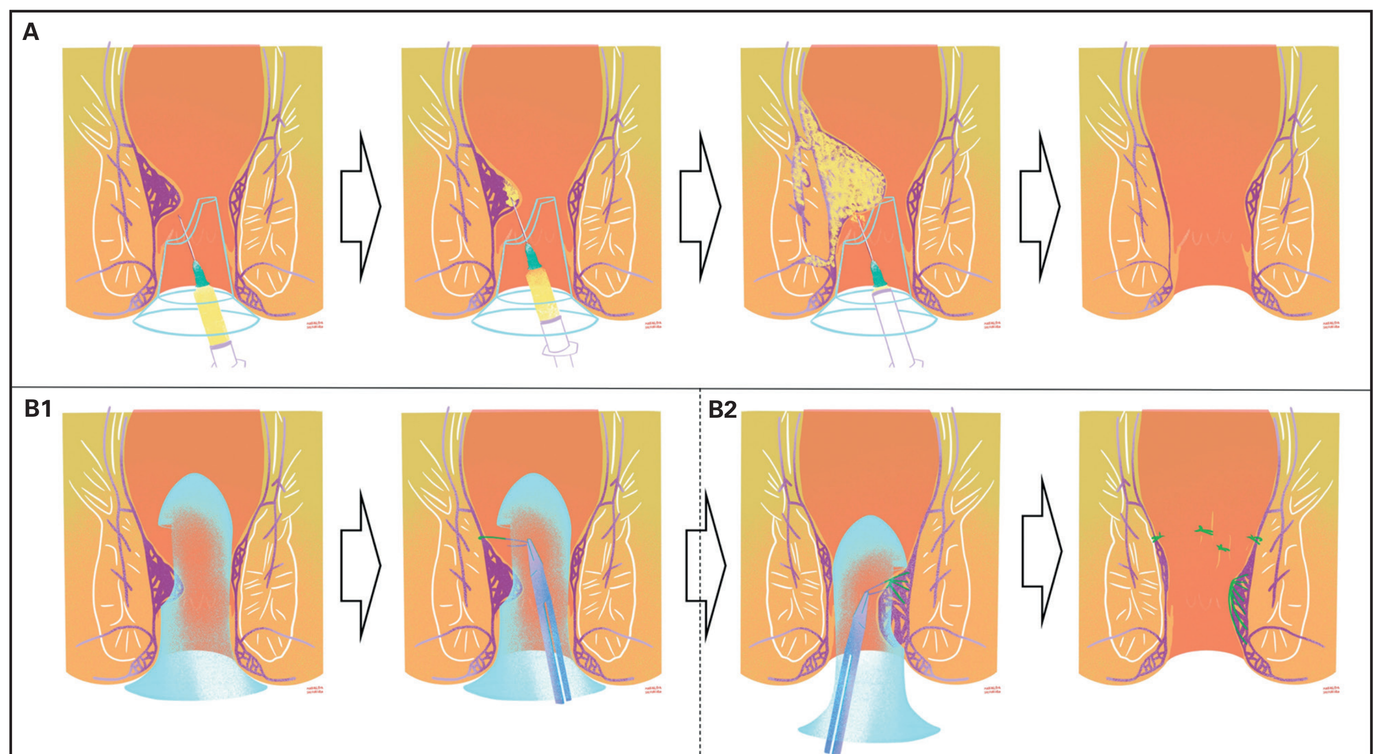

Fig. 1. *A. Schematic representation of polidocanol foam sclerotherapy. B1. Hemorrhoid artery ligation. B2. Recto-anal repair.*

tic regression were used to identify predictors of treatment's complications.

RESULTS

Forty-six patients were included (SP = 24; HAL-RAR = 22). The flowchart of the patient selection process is shown in figure 2. Preoperative characteristics were comparable between groups (Table 3). Overall therapeutic success was similar between the two groups. However, complete success was higher for SP (91.7 % *vs* 68.2 %, p = 0.045) (Table 4). The HAL-RAR group had a higher incidence of minor complications (Table 4). In the HAL-RAR group, pain was significantly higher when RAR was performed (71.4 % *vs* 25 %, p = 0.035). In multivariate analysis, only the type of treatment was a significant predictor of complications (Table 1). HAL-RAR was approximately six-times more likely to develop complications (OR = 6.05, 95 % CI: 1.07-34.33, p = 0.042). Patients undergoing HAL-RAR had more prolonged absences from work (9.5 ± 10.1 days *vs* 0.6 ± 0.2 days, p ≤ 0.001) (Table 4). The study flowchart is represented in figure 2.

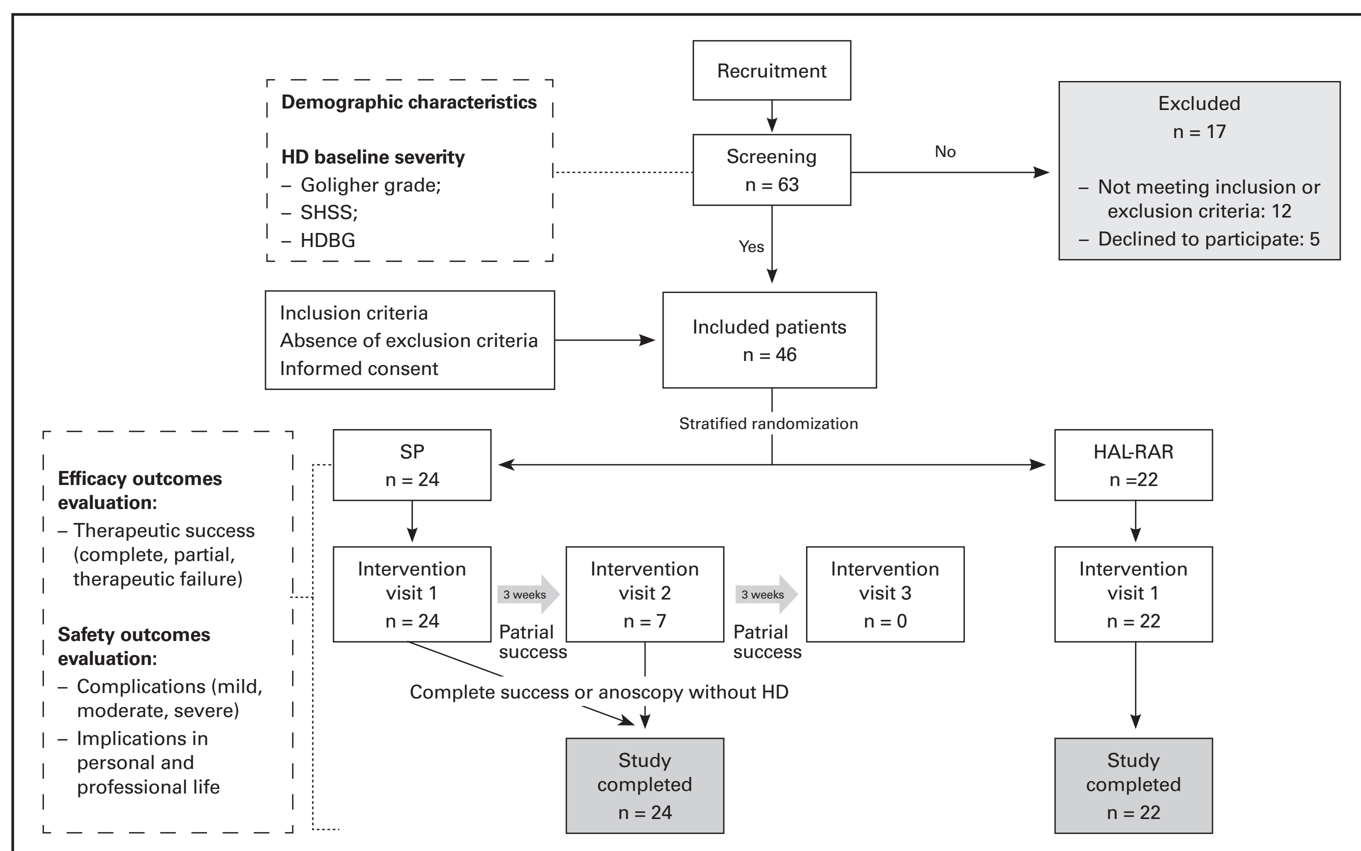

Fig. 2. *Study-design flow chart. HD: hemorrhoidal disease; SHSS: Sodergren hemorrhoidal severity score; HAL-RAR: hemorrhoidal artery ligation with recto-anal repair.*

Table 3. *Baseline characteristics*

	All patients (n = 46)		Polidocanol foam sclerotherapy (n = 24)		Hemorrhoidal artery ligation ± recto anal repair (n = 22)		*p* value
	n | Mean	% | SD	n | Mean	% | SD	n | Mean	% | SD	
Age, years-old	49.6	± 14.6	50.8	± 17.6	48.3	± 10.8	0.077
Sex (male/female)	16/30	34.8/65.2	10/14	41.7/58.3	6/16	27.3/72.7	0.306
Professional status							
Employee/student	32	69.6	16	66.7	16	72.7	0.092
Unemployed/retired	14	30.4	8	33.3	6	27.2	
Goligher's classification							
II	19	41.3	12	50.0	7	31.8	0.211
III	27	58.7	12	50.0	15	68.2	

(Continues on next page)

Table 3. (Cont.). *Baseline characteristics*

	All patients (n = 46)		Polidocanol foam sclerotherapy (n = 24)		Hemorrhoidal artery ligation ± recto anal repair (n = 22)		*p* value
	n | Mean	% | SD	n | Mean	% | SD	n | Mean	% | SD	
Sodergren score	8.5	± 3.7	7.6	± 3.4	9.5	± 3.8	0.096
Bleeding grade							
1	11	23.9	6	25.0	5	22.7	0.857
2	35	76.1	18	75.0	17	77.3	

Table 4. *Efficacy and safety outcomes*

	All patients (n = 46)		Sclerotherapy with polidocanol (n = 24)		Hemorrhoidal artery ligation ± recto anal repair (n = 22)		p value
	n | Mean	% | SD	n | Mean	% | SD	n | Mean	% | SD	
Treatments' efficacy							
Therapeutic success							0.131
Complete	37	80.4	22	91.7	15	68.2	0.045
Partial	7	15.2	2	8.3	5	22.7	0.175
Therapeutic failure	2	4.3	0	0.0	2	9.1	0.284
Treatments' complications							
Complications (overall)	21	45.6	6	25.0	15	68.2	*0.003*
Mild complications	18	39.1	5	20.8	13	59.1	
Mild pain/discomfort	15	32.6	4	16.7	10	45.5	*0.003*
Bleeding (minor)	3	6.5	1	4.1	3	13.6	
Moderate complications	3	6.5	1	4.2	2	9.1	
Thrombosed hemorrhoid	1	2.2	1	4.2	0	0.0	0.950
Bleeding	2	4.3	0	0.0	2	9.1	
Professional implications							
No. days off-work	4.9	± 8.2	0.6	± 0.2	9.5	± 10.1	*≤ 0.001*

DISCUSSION

This is the first randomized study comparing SP with HAL-RAR. Overall therapeutic success showed no significant differences between the groups. However, SP had a higher complete success rate, as observed in previous studies, where SP was successful in > 90 % (14-17). However, sclerotherapy with liquid sclerosants in previous studies has shown little efficacy in grade III hemorrhoids (5), whereas the more recent literature shows high and consistent success rates of the polidocanol foam formulation in the treatment of grade III HD (16-18).

The HAL-RAR group had a higher rate of complications, especially pain. Our results are in accordance with previous studies. In a study including 2,000 patients treated with SP, only 2 % reported mild pain (15), whereas in another study of patients with HD grades II and III submitted to SP, 14 % experienced post-procedure pain (18). Regarding HAL-RAR, the post-operative pain rate can reach 30 % (19). When RAR is performed, ours and other studies report a significant increase in postoperative pain (20).

Interventions for HD should also have minimal negative effects on the patients' day-to-day activities. In our study, HAL-RAR had a greater impact on the absence from work. This might reflect not only its more invasive nature, but also the need for anesthesia.

Although an evaluation of the cost-effectiveness of the procedure was not an objective, it should be noted that

HAL-RAR is more expensive since it requires more equipment/professional staff (13). The advantages of SP in terms of logistics and human resources proved to be particularly valuable during all the COVID-19 pandemic contingencies (21).

Limitations include the small sample study size and the short follow-up period, as long-term recurrence would be an important outcome to assess.

To conclude, we have shown that SP could be superior to HAL-RAR in terms of safety, complete therapeutic success and the return to normal day-to-day activity. A large, randomized controlled trial using this pilot study protocol is feasible and necessary to ascertain our results. Future research should also focus on long-term results of both techniques.

REFERENCES

1. Pata F, Sgró A, Ferrara F, et al. Anatomy, physiology and pathophysiology of haemorrhoids. Rev Recent Clin Trials 2021;16(1):75-80. DOI: 10.2174/1574887115666200406115150
2. Riss S, Weiser FA, Schwameis K, et al. The prevalence of hemorrhoids in adults. Int J Colorectal Dis 2012;27(2):215-20. DOI: 10.1007/s00384-011-1316-3
3. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. Gastroenterology 1990;98(2):380-6.
4. Wald A, Bharucha AE, Limketkai B, et al. ACG Clinical Guidelines: Management of Benign Anorectal Disorders. Am J Gastroenterol 2021;116(10):1987-2008. DOI: 10.14309/ajg.0000000000001507
5. Salgueiro P, Caetano AC, Oliveira AM, et al. Portuguese Society of Gastroenterology Consensus on the Diagnosis and Management of Hemorrhoidal Disease. GE Port J Gastroenterol 2020;27(2):90-102. DOI: 10.1159/000502260
6. Sun Z, Migaly J. Review of hemorrhoid disease: presentation and management. Clin Colon Rectal Surg 2016;29(1):22-9. DOI: 10.1055/s-0035-1568144
7. Moser KH, Mosch C, Walgenbach M, et al. Efficacy and safety of sclerotherapy with polidocanol foam in comparison with fluid sclerosant in the treatment of first-grade haemorrhoidal disease: a randomised, controlled, single-blind, multicentre trial. Int J Colorectal Dis 2013;28(10):1439-47. DOI: 10.1007/s00384-013-1729-2
8. Hussar DA, Stevenson T. New drugs: denosumab, dienogest/estradiol valerate, and polidocanol. J Am Pharm Assoc 2010;50(5):658-62. DOI: 10.1331/JAPhA.2010.10536
9. Ganz RA. The evaluation and treatment of hemorrhoids: a guide for the gastroenterologist. Clin Gastroenterol Hepatol 2013;11(6):593-603. DOI: 10.1016/j.cgh.2012.12.020
10. Clinical Practice Committee AGA. American Gastroenterological Association medical position statement: diagnosis and treatment of hemorrhoids. Gastroenterology 2004;126(5):1461-2.
11. Brown SR, Tiernan JP, Watson AJM, et al. Haemorrhoidal artery ligation versus rubber band ligation for the management of symptomatic second-degree and third-degree haemorrhoids (HubBLe): a multicentre, open-label, randomised controlled trial. Lancet 2016;388(10042):356-64. DOI: 10.1016/S0140-6736(16)30584-0
12. Pucher PH, Qurashi M, Howell AM, et al. Development and validation of a symptom-based severity score for haemorrhoidal disease: the Sodergren score. Colorectal Dis 2015;17(7):612-8. DOI: 10.1111/codi.12903
13. Gerjy R L-LA, Nyström PO. Grade of prolapse and symptoms of haemorrhoids are poorly correlated: result of a classification algorithm in 270 patients. Colorectal Dis 2008;10(7):694-700. DOI: 10.1111/j.1463-1318.2008.01498.x
14. Tessari L, Cavezzi A, Frullini A. Preliminary experience with a new sclerosing foam in the treatment of varicose veins. Dermatol Surg 2001;27(1):58-60.
15. Fernandes V, Fonseca J. Polidocanol foam injected at high doses with intravenous needle: the (almost) perfect treatment of symptomatic internal hemorrhoids. GE Port J Gastroenterol 2019;26(3):169-75. DOI: 10.1159/000492202
16. Salgueiro P, Garrido M, Gaio R, et al. Polidocanol foam sclerotherapy versus rubber band ligation in hemorrhoidal disease grades I/II/III: randomized trial. Dis Colon Rectum 2022;65(7):e718-e727. DOI: 10.1097/DCR.0000000000002117
17. Figueiredo LM, Bordalo Ferreira F, Rafael MA, et al. Sclerotherapy using 2% polidocanol foam in the treatment of hemorrhoidal disease - A single-center experience. Rev Esp Enferm Dig 2022;114(3):185-6. DOI: 10.17235/reed.2021.8334/2021
18. Lobascio P, Laforgia R, Novelli E, et al. Short-term results of sclerotherapy with 3% polidocanol foam for symptomatic second- and third-degree hemorrhoidal disease. J Invest Surg 2021;34(10):1059-65.
19. Pol RA, van der Zwet WC, Hoornenborg D, et al. Results of 244 consecutive patients with hemorrhoids treated with Doppler-guided hemorrhoidal artery ligation. Dig Surg 2010;27(4):279-84. DOI: 10.1159/000280020
20. Elmér SE, Nygren JO, Lenander CE. A randomized trial of transanal hemorrhoidal dearterialization with anopexy compared with open hemorrhoidectomy in the treatment of hemorrhoids. Dis Colon Rectum 2013;56(4):484-90. DOI: 10.1097/DCR.0b013e31827a8567
21. Lisi G, Campanelli M, Grande S, et al. Sclerotherapy with 3% polidocanol foam for third- and fourth-degree hemorrhoids as "bridge treatment" during the COVID-19 pandemic in Italy. Int J Colorectal Dis 2021;36(6):1321-2. DOI: 10.1007/s00384-021-03848-3