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Functional constipation in patients with hemorrhoids: a systematic review and meta-analysis

Jenneke Kalkdijk[a,b,c,d], Paul Broens[a,c], Richard ten Broek[b], Joost van der Heijden[b], Monika Trzpis[a,c], Jean Pierre Pierie[d,e] and Bastiaan Klarenbeek[b]

Hemorrhoids are common anorectal pathology, with high recurrence rates after surgical treatment. It is hypothesized that high straining forces during paradoxical contractions and inadequate relaxation are causally related to hemorrhoids. This review aimed to assess the coprevalence of functional constipation and dyssynergic defecation in a population with hemorrhoids. Moreover, the effects of rubber band ligation (RBL) were analyzed. Sources included *Pubmed*, *Embase* and *CENTRAL*. Randomized trials, cohort and case-control studies that investigated the prevalence of constipation in patients with hemorrhoids or the prevalence of hemorrhoids in patients with constipation compared to healthy subjects were included. Manometric studies were also eligible. Quality assessment was performed by using the Newcastle Ottawa Quality Assessment Scale. The primary outcome was the prevalence of functional constipation or dyssynergic defecation in patients with hemorrhoids. Nineteen studies were included. Prevalence of constipation was significantly higher in patients with hemorrhoids compared to controls [OR (odds ratio), 2.09; 95% CI (confidence interval), 1.27–3.44]. No significant difference in the prevalence of hemorrhoids between patients with constipation compared to controls was found (OR, 2.37; 95% CI, 0.67–8.44). Anal pressures in patients with hemorrhoids were significantly higher compared to healthy controls in all manometric studies. After RBL, these pressures remained significantly higher in patients with hemorrhoids ($P=0.001$). Functional constipation, dyssynergic defecation and higher basal anal pressures are more prevalent in patients with hemorrhoids compared to controls. Improvement of therapy for functional constipation, especially dyssynergic defecation patterns, might lead to better long-term outcomes and reduce recurrence. Eur J Gastroenterol Hepatol 34: 813–822
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Introduction

Hemorrhoidal disease is the most common anorectal disorder in western society with prevalences up to 44% [1–4]. A considerable group of patients remains asymptomatic, but others show signs of rectal bleeding, itching, soiling or pain. Treatment of hemorrhoids can be conservative or surgical by nature. Conservative treatment includes changes in diet and lifestyle and the application of topical ointments. These treatment options might relieve symptoms of discomfort and bleeding but are often not effective for symptoms, such as pain and anal prolapse. Also, these interventions require a long period of time before reduction of symptoms can be expected [4]. Therefore, many patients choose surgical treatment by means of rubber band ligation (RBL). RBL is the preferred surgical treatment for patients that encounter their first episode of hemorrhoids. RBL is associated with recurrence rates of 64–87% [5,6] and continues to rise in the years thereafter [5,6]. Especially grade III-IV hemorrhoids are prone to higher recurrence rates which is why more invasive treatment modalities, such as Doppler-guided hemorrhoidal artery ligation, sutured or stapled hemorrhoidopexy and hemorrhoidectomy are more often used in these patients [5]. Nevertheless, even after these treatments, the long-term recurrence rates remain up to 59.5–64% [1,5]. These poor long-term results might be explained by the hypothesized causal relationship between constipation and hemorrhoids. Hemorrhoids occur from swelling and prolapse of the anal cushions [7,8]. These cushions are part of the physiologic anorectal anatomy and consist of a submucosal arteriovenous plexus which contributes to fecal continence. The exact pathogenesis of hemorrhoids is still unclear, but it is suggested that the supporting connective tissue of the anal cushions disintegrates, causing abnormal distension and downward displacement of the arteriovenous plexus [4,9,10]. A major risk factor in this disintegration might be the presence of dyssynergic defecation which is part of the functional constipation syndrome as defined by the Rome IV criteria [11]. Not only this dyssynergic defecation but also high basal anal pressures can cause this disintegration. These high basal anal pressures are the result of the damage of the mucosal tissue of the anal canal by straining forces and results into activation of the anal continence reflex [12]. This might start a vicious

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circle of dyssynergic defecation all over again. Although functional constipation is a known risk factor for hemorrhoids, the association between hemorrhoids, functional constipation and recurrence rates after treatment has been poorly investigated [5]. Although constipation might also be caused by motility disorders, most of the constipation problems are results of dyssynergic defecation pattern. Two-thirds of the patients with slow transit constipation also have a dyssynergic defecation pattern [13]. When the evidence for this association is provided, adding pelvic floor physiotherapy might be of value to improve long-term control over hemorrhoidal symptoms because it has been demonstrated that dyssynergic defecation can be treated effectively by this therapy [11,14]. Therefore, this systematic review aims to assess the association between functional constipation and hemorrhoids.

Methods

This review was conducted in accordance with PRISMA guidelines [15]. A comprehensive search was undertaken in the *Cochrane Library*, *Medline* and *Embase*. Searches have been carried out using medical subject headings (MeSH): hemorrhoids, constipation, obstructed defecation, dyssynergia defecation, outlet obstruction, anismus, hemorrhoids and pathophysiology, pathogeneses and etiology. The full search strategy is available in Supplementary Appendix I, Supplemental digital content 1, *http://links.lww.com/EJGH/A749*.

In December 2019 two reviewers (J.K. and B.K.) and one independent reviewer (O.D.) performed the study selection. Two reviewers (J.K. and B.K.) analyzed the included studies. Disagreements between the reviewers were resolved by discussion until consensus was reached. Allowed for inclusion were all randomized controlled trials, cohort studies and case-control studies that investigated the prevalence of hemorrhoids in patients with constipation or the prevalence of constipation in patients with symptomatic hemorrhoids and made a comparison with healthy subjects. Those studies that investigated manometric outcomes (resting and maximal contraction pressures) were considered eligible as well. No limitations regarding the size of the study population were set and only English studies were included. Primary outcome was the prevalence of functional constipation or dyssynergic defecation in patients with hemorrhoids. Secondary outcomes were the prevalence of hemorrhoids in patients with functional constipation, and the mean anal basal pressures and straining pressures (based on the criteria of dyssynergic defecation) in patients with symptomatic hemorrhoids compared with healthy age-matched subjects by anal manometry. Quality assessment was performed by using the Newcastle Ottawa Quality Assessment Scale for case-control studies and cohort studies. Each quality domain was scored and greater than or equal to 7 points represented high-quality studies, less than 7 points were categorized as low quality [16].

Analysis

The inverse variance method of pooling prevalences was used within groups for continuous data. The Mantel–Haenszel method was applied for pooling dichotomous data. Prevalence between groups was presented as relative risks (RR) with 95% confidence intervals (CI). A P value of <0.05 was considered to be statistically significant. Heterogeneity was explored using I^2 tests, as recommended by the Cochrane Handbook for Systematic Reviews of Intervention [17]. An I^2 value between 50 and 75% was defined as substantial heterogeneity, and an I^2 value of greater than or equal to 75% was defined as considerable heterogeneity. A fixed-effects model was used for meta-analysis. In the presence of significant statistical heterogeneity, a random-effects model was used. Subgroup analyses were made for the type of diagnostic confirmation [e.g. validated versus nonvalidated questionnaires and epidemiological codes (ICD)] and for comparison of high versus low-quality studies. Data were analyzed using Review Manager 5.0 (RevMan; Version 5.1; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, 2011) and R version 2.12.0.

Results

In *Medline*, *Embase* and *Cochrane library* a total of 622 studies were retrieved. Finally, 19 studies were included in this systematic review (Fig. 1).

Study characteristics and quality control

A total of 17 case-control and two cohort studies were included (Table 1) [18–35]. Studies reporting the prevalence of constipation in patients with hemorrhoids included 98 901 patients with the hemorrhoidal disease and 99 451 healthy subjects [18–22]. The studies reporting the prevalence of hemorrhoids in patients with constipation included 301 310 patients with constipation and 1 505 803 healthy subjects [23,24,26]. Manometric studies included 682 patients with hemorrhoids and 730 healthy subjects [25,27–36] (Fig. 2 general characteristics of the studies). Five studies reported on the prevalence of constipation in patients with hemorrhoids [18–22] and only three on the prevalence of hemorrhoids in constipated patients [23,24,26]. The other 11 studies presented manometric data of patients with hemorrhoids compared with healthy age-matched subjects [25,27–36]. All 19 included studies were of low quality with Newcastle Ottawa Quality scores ranging from 2 to 5 (see Table 1).

The prevalence of constipation in patients with hemorrhoids

For an overview of studies that analyzed the prevalence of constipation in patients with hemorrhoids see Fig. 2. Only three studies were suitable for meta-analysis [18,20,22], since two studies did not present the necessary information for meta-analysis [19,21]. Meta-analysis showed that patients with hemorrhoids had a significantly higher prevalence of constipation compared to controls [OR (odds ratio), 2.09; 95% CI, 1.27–3.44, see Fig. 3] [18,20,22]. The pooled point prevalence of constipation in patients with hemorrhoids was 24% (0.24; 95% CI, 0.04–0.45) with a high heterogeneity (I (2) = 100%, see Fig. 2). The results of two studies that were not suitable for this analysis were in accordance with these findings [19,21]. For the diagnosis of constipation, questionnaires were used.

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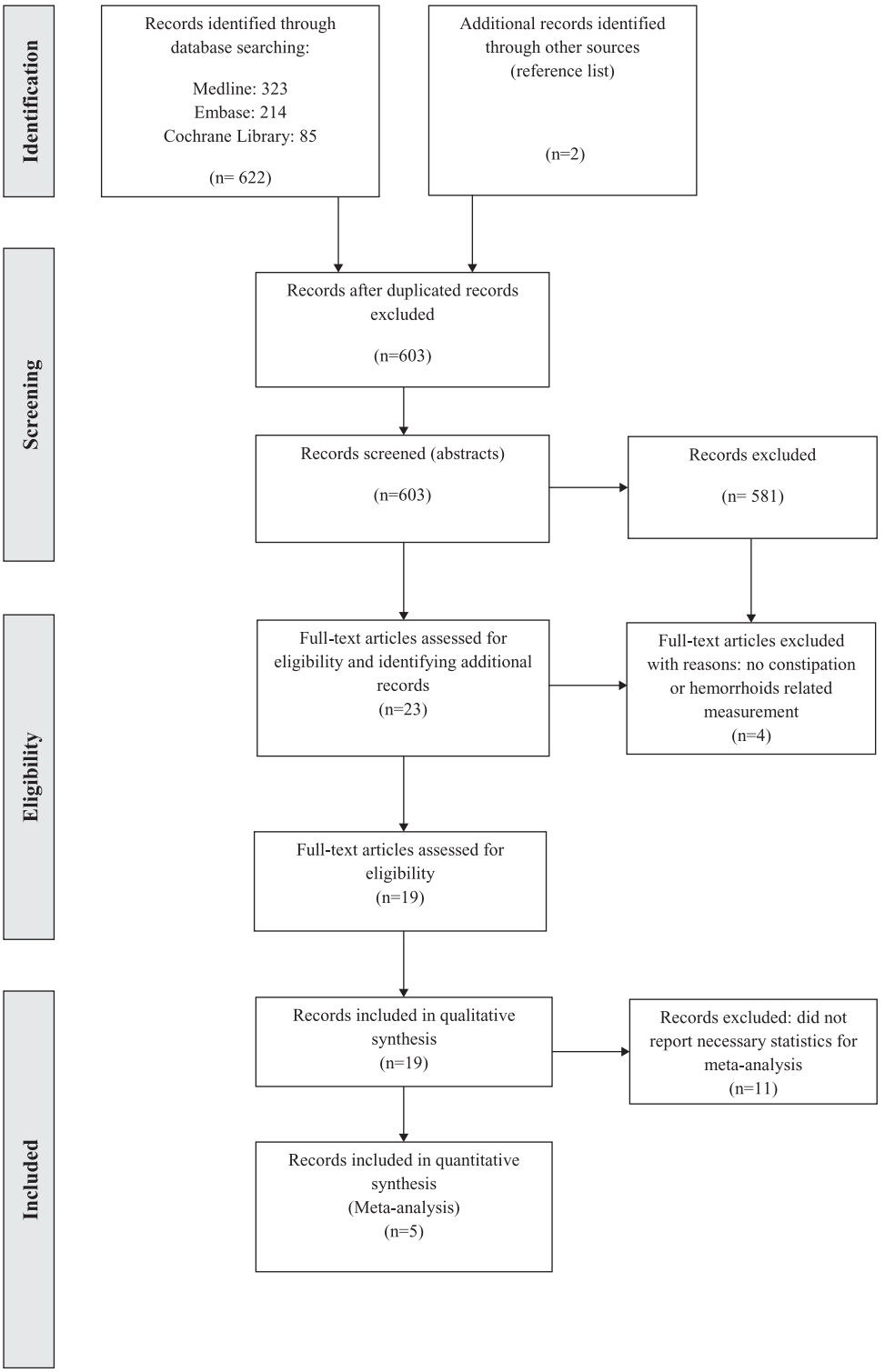


Fig. 1 Prisma flow diagram.

One study used a validated questionnaire based on the Rome I criteria [18], one study used the ICD-9 codes 455.0–455.9 [22] and one used a not specified patient report [20] (Fig. 2). The point estimate and RR of constipation in patients with hemorrhoids were significantly higher in the study that used a nonvalidated questionnaire [20] compared to studies that did use a validated questionnaire based on the Rome 1 criteria or the ICD-9 codes 455.0–455.9 (Table 1) [18,19,21,22].

The prevalence of hemorrhoids in constipated patients

See Table 1 for an overview of studies that analyzed the prevalence of hemorrhoids in patients with constipation. Two out of three studies were suitable for meta-analysis [23,26]. Although not significant, a substantially higher prevalence of hemorrhoids was found in patients with constipation compared to controls (OR, 2.37; 95% CI, 0.67–8.44, see Fig. 4). The pooled point prevalence of constipation in patients with hemorrhoids was 39% (95% CI,

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Table 1 General characteristics of the studies

Studies on hemorrhoids and constipation: prevalence of constipation in patients with hemorrhoids						
Study: Authors	Methods sample size	Median, range age	Sex	Outcome measurement	Results	New Castle -Ottawa Scale Study quality
Peery *et al.*, (2015) [18]	2813 participants who underwent coloscopy in Colorectal Adenoma Prevention trial and had detailed assessment by questionnaires SG 1074 CG 1739	SG: 58.7 (± 7.2) CG: 56.6 (±6.7)	SG: 60% male 40% female CG: 63% male 37% female	Presence of hemorrhoids evaluated by coloscopy. Questionnaires based on Rome I criteria	Constipation is associated with increased prevalence of hemorrhoids OR (95% CI):1.43 (1.11–1.86). 13% of SG reported straining during bowel movements, CG: 8%, $P<0.0001$; OR (95% CI):1.58 (1.23–2.03). 13% of SG reported incomplete emptying during defecation, CG:10%, $P=0.04$; OR (95% CI):1.27 (1.00–1.61) 16% of SG group reported hard stools, CG: 13%, $P=0.03$; OR (95% CI):1.28 (1.03–1.58).	*****
Riss *et al.*, (2011) [19]	976 participants of Austrian Nationwide Healthcare Program for Colorectal Cancer enrolled prospectively between 2008 and 2009 SG: 380 CG: 596	(SG): 61.98 (±8.82) (CG) 61.49 (±9.46)	SG: 199 (40.78%) female 181 (37.09%) male CG: 289 (59.22%) female 307 (62.91%) male	Constipation recorded by Constipation scoring system (Agachan 1996), Coloscopy and anorectal examination	Median Constipation Score (MCS) significantly higher in SG compared with CG ($P=0.01$). MSC significantly higher in patients with symptomatic hemorrhoids compared to asymptomatic hemorrhoids ($P=0.03$). Association constipation score and degree hemorrhoids (Spearman CC Rs = 0.084). Patients with hemorrhoids ($n=177$; 46.8%) had more painful evacuation than healthy controls ($n=235$; 40.1%), $P=0.0394$. Patients with hemorrhoids (2.9%) used digital assistance for evacuation more than healthy individuals (0.9%), $P=0.01$.	*****
Pigot *et al.*, (2005) [20]	SG: 1033 CG: 1028	SG: 47 (±14.5) CG: 52 (±16.5)	SG: 542 male (52.5%), 491 female (47.5%) CG: 504 male 524 female.	Patient report	Recent, acute episodes of constipation during 15 days preceding consultation was a risk factor for hemorrhoidal crises OR (95% CI):3.93 (3.09–5.00).	**
Johannsson *et al.*, (2005) [21]	SG: 100 before hemorrhoidectomy CG1: 200 CG2: 100 (before an orthopedic procedure)	SG: 55 (33–84) CG1: 55 (33–84) CG2: 53 (30–79)	SG: 51 male 49 female CG1: 51 male 49 female CG2: 51 male 49 female.	Questionnaire with five domains of bowel symptoms	37% of SG described bowel movements as normal, CG1: 55%, CG2:67% ($P<0.001$) 36% of SG had to strain hard to defecate, CG1: 11%, CG2: 10% ($P<0.001$) 53% of SG had to spend a long time at the toilet to empty (>10–>20 min), CG1:8%, CG2: 14 ($P<0.001$) 55% of SG had a feeling of incomplete evacuation, CG1: 10%, CG2: 15% ($P<0.001$) 47% of SG needed repeated toilet visits to feel satisfied, CG1:11.5%, CG2:19% ($P<0.001$) 37% of SG reported bloating, CG1:18%, CG2: 26% (P<0.001) 34% of SG reported abdominal pain associated with bowel evacuation, CG1: 3%, CG2: 5%, ($P<0.001$)	***
Delco *et al.*, (1998) [22]	Military veterans SG: 96.314 CG: 96.314	SG: 59.6 (±13.9) CG: 60.1 (±14.8)	SG: 94.458 male 1.856 female CG: 93.764 male 2.550 female	ICD codes 455.0–455.9	Association between hemorrhoids and constipation: OR (95% CI): 1.54 (1.48–1.61). Association between hemorrhoids and anal spasm: OR (95% CI): 4.26 (1.879.70).	**

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Table 1 (Continued)

Study: Authors	Methods sample size	Median, range age	Sex	Outcome measurement	Results	New Castle -Ottawa Scale Study quality
Studies of constipation and hemorrhoids: prevalence of hemorrhoids in patients with constipation.						
Arora *et al*., (2012) [23]	SG:147.595 CG: 142.086 with GERD (unrelated illness-gastro-esophageal reflux disease) (Medicaid database of California) Index date: the date 3 months before first physician visit for CC. Preindex:12 months before index date. Postindex: 12 months after index date.	SG: 54.2 CG: 56.3	SG: 69.7% female CG: 65.3% female	ICD-9 codes 564.0x	The most prevalent concurrent condition with CC is hemorrhoids: preindex 2.80% versus postindex 7.63 %: OR (95% CI): 2.86 (276–2.97). Comparison odds ratios CC to GERD : adjusted OR (95% CI): 1.24 (1.20–1.30).	*****
Mitra *et al*., (2007) [24]	SG: 48.585 CG: 97.170 By analyzing the i3 Innovus Lab Rx database. Index date 3 months prior to the first observed constipation diagnosis Preindex and postindex date 12 months prior to and following index date.	Not specified	Not specified	ICD-9 codes 564.0x	SG had a substantially and significantly greater likelihood of hemorrhoids (OR = 4.2, $P < 0.01$) during the postindex period compared to preindex.	***
Singh *et al*., (2005) [26]	SG: 105 130 (488 921 patient-years of observation) enrolled in California Medicaid Program with at least 1 physician visit for constipation CG: 1 266 547 (3242 925 patient-years of observation).	Age >18 years	Not specified	ICD-9 codes 564.0x	SG: Cases hemorrhoids: 3136.9 (±26.80) rate per 100 000 patient-years of observation. CG: Cases hemorrhoids: 718.8 (±4.76) rate per 100 000 patient-years of observation. RR: 4.10; 95% CI: 4.01–4.18; $P < 0.0001$.	***
Studies of hemorrhoids and anal pressures						
Jain *et al*., (2019) [36]	SG: 57 (hemorrhoids, anal fissure, SRUS) CG: 369	SG: 44.2 (18–82) CG: 46 (18–78)	SG: 50 male 7 female CG: 268 male 101 female	CC scored by Rome IV criteria. Functional evacuation disorders were scored by ARM, balloon expulsion test and digital examination. Hemorrhoids, anal fissure and SRUS were evaluated by sigmoidoscopy, colonoscopy.	In SG the resting anal pressure was higher compared to CG [$P < 0.03$, 80 (56–144) versus 69 (45–120)]. In SG functional evacuation disorder was higher compared to CG ($P < 0.0001$, 66.7% versus 20.3%). In SG dyssynergic defecation was higher compared to CG ($P < 0.0001$, 77.2% versus 46.8%). In SG abnormal balloon expulsion was higher compared to CG ($P < 0.0001$, 66.7% versus 20.3%). Subgroup analysis showed no significant difference in resting and squeeze pressures among patients with hemorrhoids, anal fissure and SRUS ($P < 0.16$). Dyssynergic defecation and abnormal balloon expulsion were more common in anal fissure and SRUS compared to hemorrhoids ($P < 0.028$).	****

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Table 1 (Continued)

Study: Authors	Methods sample size	Median, range age	Sex	Outcome measurement	Results	New Castle -Ottawa Scale Study quality
Chauhan *et al*., (2007) [25]	SG: 32, randomized into two groups: SG1: 16 (selected for RBL) SG2: 16 (treated by injection sclerotherapy) CG: 20	SG1: 35.9 (18–55) SG2: 35.7 (18–55)	SG1: 10 male 6 female SG2: 11 male 5 female	Anal manometry before treatment and 8 weeks after completion of treatment. Treatment success was evaluated by symptom relief scores and proctoscopy.	Pretreatment anal pressures were similar in both groups: 69.38 cm H_2O (95% CI 58.67–80.08) vs. 67.75 cm H_2O (95% CI 56.86–78.64) and significantly higher than in controls: 45.25 cmH_2O (95% CI 38.36–52.14) ($P=0.0001$ in both groups). After treatment a significant drop in the anal pressures in both groups was seen ($P=0.0001$ SG1; $P=0.001$ SG2) matching the normal values of CG: 46.75 (39.28–54.22) vs. 47.75 (40.03–55.47).	****
Lin *et al*., (1989) [27]	SG1: 50 SG2: 29 patients with anal fissure CG: 36	SG1: 50.9 (±14.3) SG2: 44.3 (±17.2) CG: 47.9 (±14.4).	SG1: 31 male 19 female SG2: 19 male 10 female CG: 19 male 17 female	Anal manometry	Maximal basal pressure in SG1 and in SG2 were significantly higher than in CG (SG1: 85.3 ± 27.7, SG2: 87.4 ± 38.8 versus CG: 71.2 ± 24.9) ($P<0.05$). Maximal contraction pressure in SG1 (158.8 ± 58.0) and in SG2 (162.1 ± 64.5) were significantly higher ($P<0.05$) than in CG (132.9 ± 44.9).	***
Gibbons *et al*., (1988) [29]	SG1: 23 SG2: 12 (women with severe constipation) CG: 25	SG1:male 47.6 (±12.6) female 58.1(± 12.1) SG2: 37.8 (±10.8) CG: male 41.2 (±13.4) female 44.7 (±13.4)	SG1: 13 male 10 female SG2: 12 female CG: 14 male 11 female	Anal manometry and anal compliance measurement	SG1 had significant higher maximum resting pressures at all levels ($P<0.01$). Maximum resting pressure increased in SG1 for both sexes but only reached statistical significance in men ($P<0.001$). Defecation was less frequent in women than in men ($P<0.01$), independent of present of hemorrhoids.	****
Deutsch *et al*., (1987) [28]	SG: 38 CG: 29	SG: male: 54.40 (±15.52) female 40.61(±10.73) CG: male: 49.86 (±18.62) female: 43.84 (±15.72)	SG:male: 25female: 13CG:-male:16female: 13	Anal manometry: measurement before treatment by RBL and 3–4 months after treatment	Anal pressures significantly higher in SG before treatment (102 ± 26.33 mmHg) compared to CG (76.75 ± 19.56 mmHg, $P<0.001$). Three months after RBL: a small drop in anal pressures was measured (100 ± 26.84 mmHg) but remained significantly higher than CG. A significant correlation between symptoms and level of anal pressures was found ($P<0.01$), and a significantly higher pressure in males of SG <42 years compared with male of SG >42 years ($P<0.01$).	***
Schouten *et al*., (1986) [30]	SG: 119 75 patients with first or second degree hemorrhoids 44 patients with third or fourth degree hemorrhoids. CG: 31	SG: 44.8 (19–82) CG: 37.5 (14096)	Not specified	Anal manometry before treatment and 2 weeks after treatment (lateral internal sphincterotomy)	In SG the mean maximal anal pressure (152 ± 29 cm H_2O) was higher compared to CG (109 ± 27 cm H_2O) throughout the entire length of the anal canal ($P<0.001$). 96/119 patients had high anal pressures (>125 cm H_2O). Two weeks after treatment: 27% reduction in maximal anal pressure and the same as CG.	***

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Table 1 (Continued)

Study: Authors	Methods sample size	Median, range age	Sex	Outcome measurement	Results	New Castle -Ottawa Scale Study quality
Hiltunen *et al*., (1985) [31]	SG: 50 CG: 50	SG: 47 (±13)CG: age-matched patients	SG:male: 23female: 27CG: sex-matched patients	Anal manometry	SG had higher basal pressures compared to CG ($P \leq 0.02$, 106 ± 21 cm H_2O versus 96 ± 27 cm H_2O). SG had higher maximal voluntary contraction pressure compared to CG ($P < 0.05$, 88 ± 43 cm H_2O versus74 ± 33 cm H_2O). With advancing age the basal pressure was lower in SG (r:−0.386, $P < 0.01$) and in CG (r:−0.264, $P < 0.05$).	****
El Gendi *et al*.,(1985) [32]	SG: 30 CG: 20	SG:29.7 (20–58) CG:32.1 (20–50)	No difference in sex distribution was found between SG and CG	Anal manometry on 5 levels (1,2,3,4,5 cm from anal verge). Measurement before treatment by hemorrhoidectomy and 1 week after treatment.	In SG the mean resting pressure was higher compared to CG at all levels of the anal canal, but was statistically significant only at 3.2 cm and 1 cm from the anal verge (no *P* value was mentioned). One week after hemorrhoidectomy all patients of SG had significant reductions in mean resting anal pressures (42.37 ± 13.0 cm H_2O) compared with the preoperative levels (24.32 = −9.33 cm H_2O) (no *P* value was mentioned).	***
Shafik *et al*., (1984) [33]	SG: 76 CG: 32	SG:41.3 (±11.6) CG: 42.6 (±14.3)	SG:male: 46female: 30 CG: similar in age to SG	Anal manometry on 5levels (1,2,3,4,5 cm from rectal neck outlet). measurement before and after treatment by internal sphincterotomy.	Long before hemorrhoid symptoms started, straining at stool was present in all hemorrhoid patients. This was reported in only one control subject In SG the mean maximal neck pressure at rest was significantly higher compared CG (118 ± 24 cm H_2O versus 76 ± 18 cm H_2O) (no *P* value was mentioned). Postoperative pressure measurements in 67 patients of SG revealed a normalized pressure (64 ± 14 cm H_2O).	***
Arabi *et al*., (1977) [37]	SG1: 145 SG2: 48 (patients with anal fissure) CG: 78	SG1: 46 (±12.8) SG2: 36.6 (±11.5) CG: 49 (±11.0)	SG1:male: 101female: 44SG2: male: 29female: 19CG: male: 45female: 33	Anal manometry Digital examination (assessment sphincter tone: tight, normal or lax) Abdominal examination Anal inspection Protoscopy, Sigmoidoscopy	In SG1 the mean maximal anal pressures were higher compared to CG ($P < 0.001$, 106 ± 40 cm H_2O versus 88 ± 34 cm H_2O). In SG2 the mean basal sphincter pressures were higher compared to CG ($P < 0.001$, 130 ± 43 cm H_2O versus 88 ± 34 cm H_2O). The anal pressures in patients with pain, bleeding or irritation were significantly higher than those with prolapse ($P < 0.001$). No significant difference between anal pressures in patients with prolapse and control subjects. Men <46 years had higher maximal anal pressures than the age- and sex-matched controls ($P < 0.001$).	***
Hancock *et al*., (1976) [35]	SG: 84 CG: 40	SG: 47.4 (±13.1) CG: 47.9 (±15.2)	Not specified	Anal manometry Before and after dilatation	In SG the mean anal pressure was higher compared to CG ($P < 0.001$, 107 ± 23.0 cm H_2O versus 85.0 ± 20.5 cm H_2O). In SG straining at stool was more common compared to CG ($P < 0.001$, 57% versus 20%). In SG 41% had a history of straining before symptoms started. After dilatation there was a significant reduction in pressure in 46 patients (from 113.9 ± 19.1 cm H_2O to 69.8 ± 15.8 cm H_2O). No *P* value was mentioned.	***

CC, chronic constipation, CG, control group, CI, confidence interval, MCS, Median Constipation Score; RR, relative risk; GERD, gastroesophageal reflux disease; OR, odds ratio; SG, study group; SRUS, solitary rectal ulcer syndrome.

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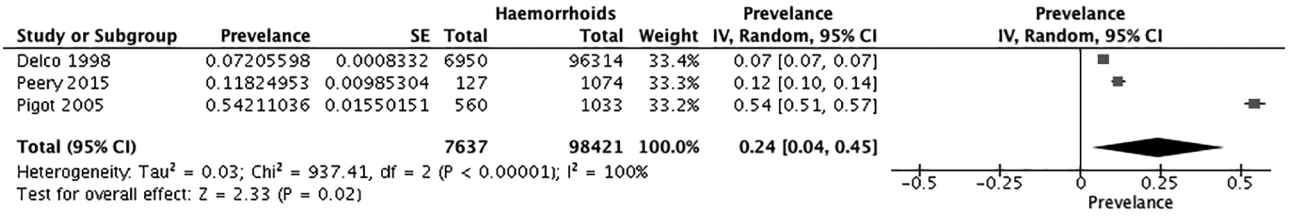


Fig. 2 Prevalence of constipation in patients with hemorrhoids.

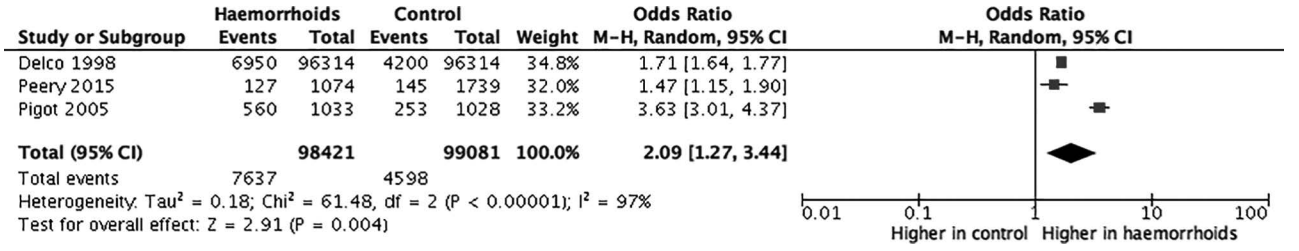


Fig. 3 Prevalence of constipation in patients with hemorrhoids compared to healthy subjects: odds ratios and 95% confidence interval.

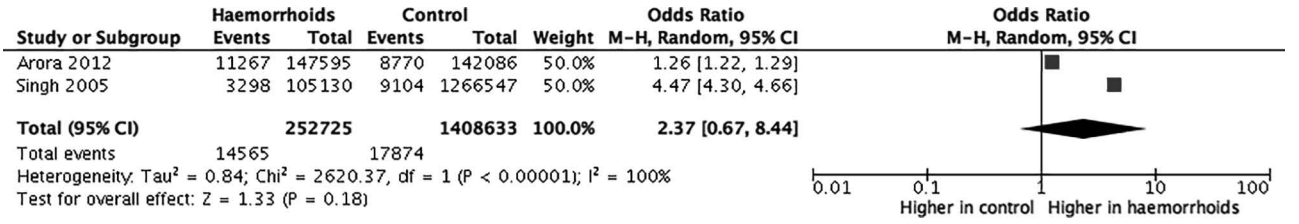


Fig. 4 Prevalence of hemorrhoids in patients with constipation compared to healthy subjects: odds ratios and 95% confidence interval.

Table 2. Prevalence of constipation in patients with hemorrhoids compared to healthy subjects: Odds ratios and 95% CI

	Hemorrhoids		Control		OddsRatio	
Study or subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Delco 1998	6950	96314	4200	96314	43.8%	1.71 [1.64, 1.77]
Peery 2015	127	1074	145	1739	32.0%	1.47 [1.15, 1.90]
Pigot 2005	560	1033	253	1028	33.2%	3.63 [3.01, 4.37]
Total (95% CI)		98421		99081	100%	2.09 [1.27, 3.44]
Total events	7637		4598			

Heterogenity Tau2 = 0.18, Chi2 = 61.48, df = 2 (P, 0.00001); I2 = 97%
Test for overall effect: Z = 2.91 (P = 0.004)

–0.32 to 1.10) with high heterogeneity (I(2)=100%). Both studies used ICD-9 codes 564.0x for defining constipation. The third study also used ICD-9 codes 564.0x for defining constipation, but was not suitable for meta-analysis due to inadequate necessary information [24]. This study showed that the most prevalent concurrent condition associated with constipation was hemorrhoids (OR, 4.2) [24].

Anorectal manometry in patients with hemorrhoids

For an overview of studies that analyzed anal pressures in patients with hemorrhoids compared with healthy subjects see Table 1. Anal pressures in patients with hemorrhoids were significantly higher than that in healthy controls [25,27–36]. Straining during defecation was reported by all patients with hemorrhoids prior to the start of symptoms of hemorrhoidal disease [33]. In patients with hemorrhoids functional evacuation disorder, dyssynergic defecation and abnormal balloon expulsion were more frequent compared to healthy subjects ($P < 0.0001$) [36]. Four studies measured the anal pressures before and after surgery or RBL [25,28,32,35]. Treatment by injection sclerotherapy, hemorrhoidectomy or anal dilatation resulted in a diminution of anal pressures to values that are in line with age-matched controls. After RBL, anal pressures remained significantly higher in patients with hemorrhoids compared to healthy controls (see Table 1) [28]. No meta-analysis was possible due to nonreporting of means and SD of the incidence of basal pressures in patients with hemorrhoids and controls.

Discussion

This systematic review showed that patients with hemorrhoids had a significantly higher prevalence of functional constipation compared to controls (OR, 2.09; 95% CI, 1.27–3.44). Also, a substantially higher prevalence of hemorrhoids was found in patients with constipation compared to controls (OR, 2.37; 95% CI, 0.67–8.44). In patients with hemorrhoids significantly higher resting pressures were reported compared to controls. Straining

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Table 3. Prevalence of constipation in patients with hemorrhoids.

	Hemorrhoids				Prevalence	
Study or subgroup	Prevalence	Total	Total	Weight	IV, Random, 95% CI	
Delco 1998	0.7205598	0.0008332	6950	96314	33.4%	0.07 [0.07, 0.07]
Peery 2015	011824953	0.00985304	127	1074	33.3%	0.12 [0.10, 0.14]
Pigot 2005	0.54211036	0.01550151	560	1033	33.2%	0.54 [0.51, 0.57]
Total (95% CI)			7637	98421	100%	0.24 [0.04, 0.45]

Heterogenity Tau2 = 0.03, Chi2 = 937.41, df = 2 (P < 0.00001); I2 =100%
Test for overall effect: Z = 2.33 (P = 0.02)

Table 4. Prevalence of hemorrhoids in patients with constipation compared to healthy subjects: Odds ratios and 95% CI

	Hemorrhoids		Control		OddsRatio	
Study or subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Arora 2012	11267	147595	8770	142086	50%	1.26 [1.22, 1.29]
Singh 2005	3298	105130	9104	1266547	50%	4.47 [4.30, 4.66]
Total (95% CI)		252725		1408633	100%	2.37 [0.67, 8.44]
Total events	14565		17874			

Heterogenity Tau2 = 0.84, Chi2 = 2620.37, df = 1 (P <, 0.00001); I2 = 100%
Test for overall effect: Z = 1.33 (P = 018)

during defecation was reported prior to the start of symptoms of hemorrhoidal disease in all patients with hemorrhoids. Also, functional evacuation disorder, dyssynergic defecation and abnormal balloon expulsion were more frequent in patients with hemorrhoids compared to healthy subjects ($P < 0.0001$). After RBL higher maximum resting pressures remained present which suggests that an intervention to lower these (pretreatment increased) pressures, such as pelvic floor physiotherapy is important to improve long-term results of treatment for hemorrhoids. This study distinguishes itself by being the first systematic review with meta-analysis to evaluate the relationship between the prevalence of hemorrhoids and constipation and to evaluate the anal pressures after certain treatment modules such as RBL. Previous reviews of literature in the 20th century were focused on vascular and histological changes in hemorrhoidal tissue as etiological factors [2,37–39] or concluded that straining, excessive amount of standing or the aging process were causative [2,37,40,41]. The reviews of the 21st century presumed that changes in connective tissue in the anal canal results in deterioration of the anal cushions (related to the aging process) are causative in the formation of hemorrhoids [4,42,43]. One review concluded an increased prevalence of hemorrhoids in patients with constipation [44]. Two reviews reported that the recurrence rates of hemorrhoids in patients with constipation were significantly higher compared to the recurrence rate in healthy subjects [44,45]. All previous reviews were descriptive reviews [2,4,9,37–39,41–47]. None of the reviews include studies in quantitative synthesis (meta-analysis). High recurrence rates have always been a problem in the hemorrhoids treatment. With recurrence rates up to 87%, it is evident that improvements are necessary. To improve outcomes, it seems plausible that treatment of the underlying functional constipation caused by dyssynergic defecation is the first step to make and we suggest that this is more effective than repeating RBL procedures only. Moreover, repeated RBL can even be harmful because it can result in soiling problems and pain by damaging the mucosal tissue which can result in activation of the unconscious anal continence reflex [48]. Treatment of the functional constipation first will result in less straining during defecation and more complete emptying. It will therefore have a positive effect on the recurrence rates of symptomatic hemorrhoids and the quality of life.

Some limitation also needs to be discussed. The pooled point prevalence of constipation in patients with hemorrhoids showed very high heterogeneity. This heterogeneity was caused by the higher relative risk of constipation in patients with hemorrhoids in the study which used a non-validated questionnaire (patient report) for the diagnosis of constipation. Quantitative synthesis of the anorectal manometry studies was not performed because of the lack of the necessary data and the high risk of bias in outcomes due to heterogeneity within anorectal measurement equipment all over the world.

The presence of information bias by different assignments of the performer of the anal manometry measurement can also result in different measurement results. Regarding implications for future research, there is an urgent need for studies researching the effect of pelvic floor physiotherapy focused on the relaxation of the high basal anal pressures and the treatment of the dyssynergic defecation pattern in patients with hemorrhoids and the effect on the recurrence rate of hemorrhoids. The distinction between the anal sphincter and puborectal muscle should be measured because both can cause independently dyssynergic defecation. This research will result in detailed information about the relation between the function of the pelvic floor and the development of hemorrhoids. We believe that pelvic floor re-education or biofeedback are the first options for patients with functional constipation due to dyssynergic defecation suffering from hemorrhoids and suggest an evaluation of this hypothesis in a clinical setting to improve long-term treatment results.

Conclusion

Constipation, dyssynergic defecation and higher basal anal pressures are more prevalent in patients with hemorrhoids compared to controls. Treatment of this constipation and dyssynergic defecation and the relaxation of the

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high basal anal pressures will result in less straining during defecation and more complete emptying. Because the results of current treatment strategies for hemorrhoids are poor, aiming for the improvement of functional constipation, especially dyssynergic defecation patterns, might lead to better long-term outcomes and reduce recurrence.

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Conflicts of interest

There are no conflicts of interest.

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