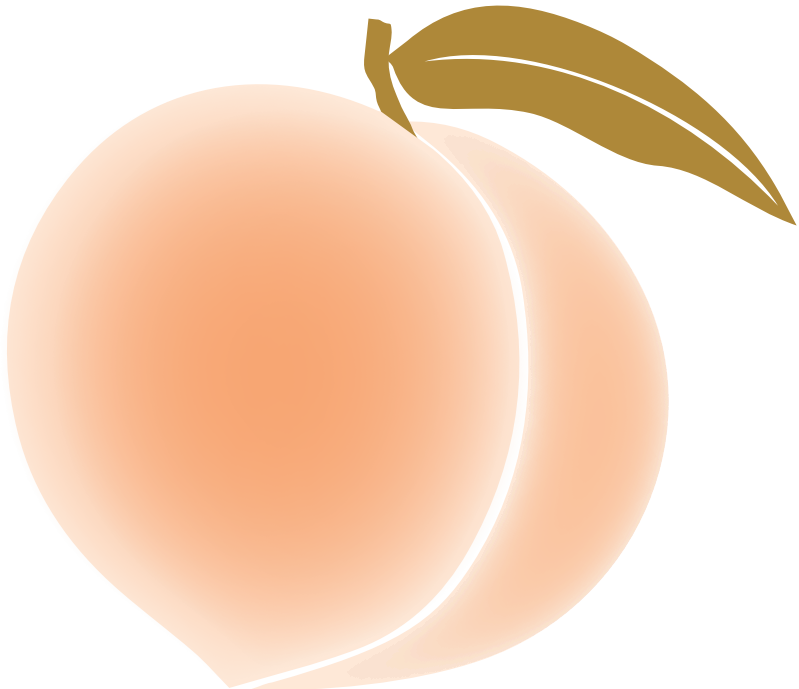
Optimising treatment for

SACROCOCCYGEAL PILONIDAL SINUS DISEASE



Akke Pronk

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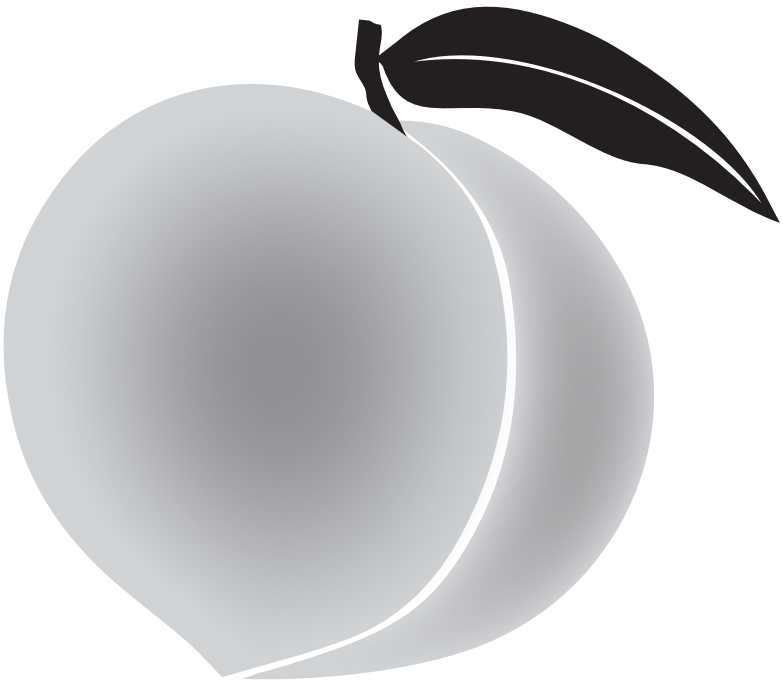

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OPTIMISING TREATMENT FOR SACROCOCCYGEAL PILONIDAL SINUS DISEASE

HET OPTIMALISEREN VAN DE BEHANDELING VAN EEN SINUS PILONIDALIS

(met een samenvatting in het Nederlands)

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de
Universiteit Utrecht
op gezag van de
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ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op

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door

Anne Akke Pronk

geboren op 8 augustus 1991
te Utrecht

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Copromotoren:	Dr. N. Smakman Dr. E.J.B. Furnée

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CHAPTER 1

Introduction and outline of thesis

INTRODUCTION

Sacrococcygeal pilonidal sinus disease (SPSD) is a benign condition affecting the skin and subcutaneous tissue. SPSD was first described in 1833 by Herbert Mayo, British physiologist, anatomist and surgeon, as a sinus containing hair follicles [1]. Hodges assigned the name pilonidal sinus in 1880, combining the Latin words *pilus* (hair) and *nidus* (nest). Hogdes also stated SPSD as a congenital disorder. Embryological knowledge was increasing in the second half of the nineteenth century and SPSD was suspected as a fault of development. Different theories emerged, such as cystic remnants of the medullary canal that persists in the region or a faulty development of the median raphe which becomes a cyst and later a sinus. The theory of Hogdes was accepted until Patey and Scarff in 1946 reported a case of pilonidal sinus in the interdigital space in a barber's hand which undermined the theory of congenital origin. More recent theories suggested that SPSD starts with an infectious skin lesion with secondary entrance of hair and debris or the result of penetration of the skin by a hair which may introduce an infection [2]. In a recent study, Bosche et al. investigated the characteristics of hairs found in the pilonidal cyst [3]. They found multiple short hair fragments with sharp cut ends which might imply that cutting head hair or shaved hair by razor depilation at the back, shoulders and lumbar region contribute to the occurrence of a pilonidal sinus. Additionally, they stated that young men develop more often SPSD as the head hairs in young men is cut more frequently [4)]. However, the etiology is still not fully understood.

SPSD has a high incidence (United States: 26 per 100,0000 population) and young adults and men are affected twice as often as women (ratio 2.2 to 1.0) [5]. It is a common disorder seen by many different specialists, including dermatologists, general practitioners, surgeons, emergency doctors and plastic surgeons. Symptoms related to SPSD range from no complaints to a major impact on daily life. Despite the high incidence and the risk of major impact on quality of life, there is still no consensus on etiology, risk factors and optimal treatment of SPSD. Since SPSD is a common condition, reaching consensus about these aspects have an enduring impact.

CLINICAL PRESENTATION

Patients can present with acute, chronic or recurrent SPSD, although SPSD can also be asymptomatic. In the case of an 'acute SPSD', an abscess develops within a few days in this area and the most important symptom is pain. Chronic or recurrent SPSD can result in fluid discharge, pain, burning sensation and itching which are intermittent most of the time.

Risk factors commonly described to be associated with SPSD include high density of body hair, obesity, sedentary occupations and a poor hygiene [6]. SPSD is also referred to as 'jeep driver disease', because of the high incidence of SPSD found in vehicle drivers [7]. Rigid and hard seats may cause minor traumas in the nates of jeep drivers, resulting in a cyst.

TREATMENT

The choice of treatment is clear in patients with no or minimal symptoms or in patients with an abscess; in patients with minimal or no symptoms related to SPSD, no surgical treatment should be offered to prevent the negative consequences of a treatment, such as infection and delayed or absent wound healing. In case of presentation with an abscess incision and drainage is required which will promptly alleviate the symptoms. In chronic or recurrent SPSD with significant symptoms impairing quality of life, several treatment options have emerged in past years. An overview of these options is shown in table 1. Surgical site infection, reported in up to 24% of patients and recurrence rate, reported in up to 11.1% of patients, are both known problems after treatment of SPSD [10]. Surgical site infection leads to secondary wound healing which may take several months to cure [11]. Radical surgical excision with primary wound closure or secondary wound healing is the most often used technique [8,9] however no consensus on the optimal treatment exists. Although the risk of wound infection is 8-10% after both primary wound closure and secondary wound healing, faster wound healing was reported after the former [10]. However, the risk of recurrence of SPSD has been reported to be higher compared to secondary wound healing (8.9 versus 5.3%). Primary wound closure should always be outside the midline as wound infections were higher after midline closure (relative risk 3.72; 95% confidence interval (CI): 1.86 - 7.42) [10]. Additionally, primary wound closure will result in faster wound healing (mean: 5.4 days, 95% CI: 2.3 - 8.5) and a lower risk of recurrence (1.5 – 2.4% after off-midline closure

versus 9.4% after midline closure) [10]. Nonetheless, wound infections after surgery for SPSD are still a major problem. The use of local antibiotics (gentamicin-absorbed collagen sponge) on the sacrococcygeal fascia was introduced to reduced infection rate. One study reported a reduced infection rate with a gentamicin-absorbed collagen sponge after primary closure from 20% to 5% [12], although another study could not confirm this reduction (26% versus 22%) [13]. Therefore, no consensus with regard to this topic exists in the literature so far. In addition, excision with primary closure, including flap techniques, or secondary wound healing can be mutilating and can result in a long postoperative morbidity, especially in the young patient's population suffering SPSD.

In recent years, several minimally invasive techniques have been developed and are increasingly used as treatment for patients with SPSD. The phenolisation technique has already been described three decades ago [14]. Phenol is a sclerosing agent that destroys the epithelium and debris in the sinus and is thus able to promote healing of the sinus. Previous series have shown a recurrence rate between 8.7 and 33.3% after a follow-up of 22 to 26 months. Mean wound closure varied from 16 to 28 days, surgical site infection from 0 to 8.7% and return to work from 0 to 3 days [15–19]. Although previous series have shown promising results, evidence for the use of this minimal invasive technique from large randomised trials comparing it to the more conventional excision techniques is lacking [20]. The trend towards minimal invasive techniques, also in disorders like SPSD, has resulted in the emergence of endoscopic treatments, including the 'endoscopic pilonidal sinus treatment'(EPSiT) and 'video-assisted ablation of pilonidal sinus'(VAAPS). In the EPSiT and VAAPS techniques a small endoscope is introduced in the sinus and hair and debris is removed where after the walls of the sinus are coagulated. The main difference between these two methods is that a different endoscope is used. Small cohort studies have been published reporting that the technique is safe and patients had no postoperative wound infections. Recurrence rates were varying between 3.7 and 14.8% after 12 – 25 months of follow-up [21–24]. Although cohort studies have shown that these techniques are safe, randomised trials for this minimal invasive technique are lacking as well. The use of a laser diode is another minimal invasive technique. The laser diode is introduced in the sinus after nettoyage of the sinus and the walls of the sinus are treated. Small cohort studies reported it as a safe technique, while 5-7% of the patients developed a wound infection [25–27]. However, randomised controlled trials are lacking. In conclusion, the main advantages of these minimal invasive techniques seems to be smaller wounds, less pain and faster wound healing based on cohort studies. Further research is needed to compare minimal invasive techniques with excision with or without primary wound closure.

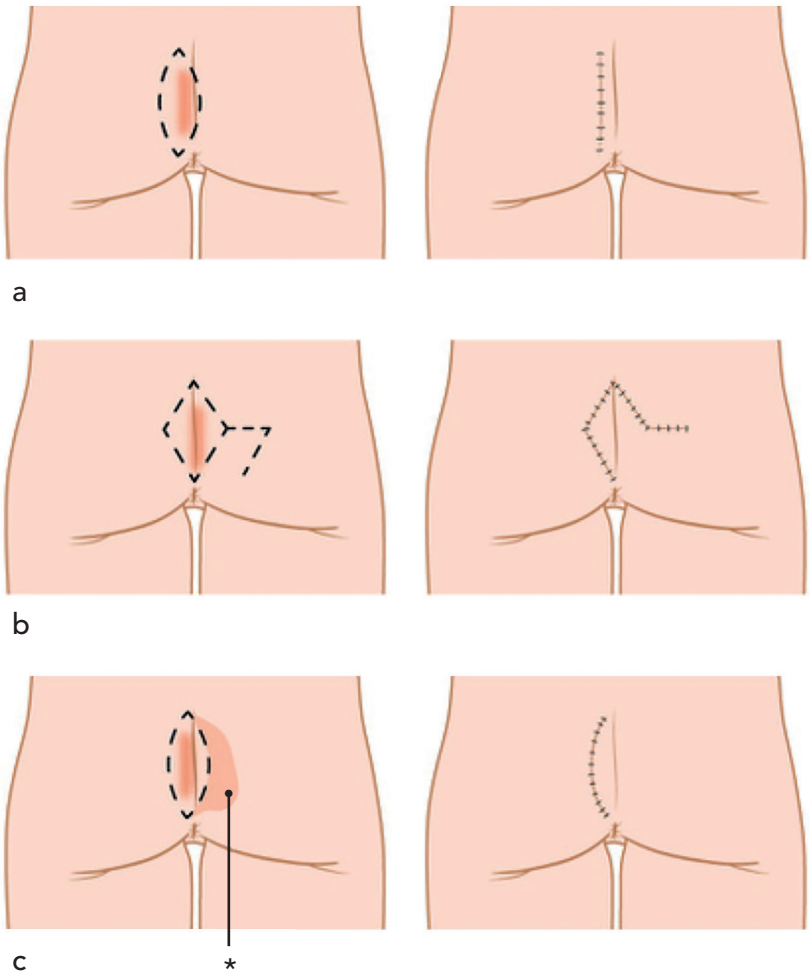

Figure 1. Three most common excision techniques for SPSD [20]

Left side: excision lines, right side: reconstruction after closure.
a: Karydakis plasty
b: Limberg flap
c: Bascom cleft lift. *The skin on the opposite side of the cleft is mobilised to allow primary closure away from the midline without tension and the new natal cleft is less deep.

Permission to use illustration from Maartje Kunen, Medical Visuals

Table 1. Treatment options for chronic SPSD

Surgical excision	Excision with primary midline closure
	Excision with secondary wound healing
	Karydakis plasty
	Limberg flap
	Bascom cleft lift
	Other: Z-plasty, rotational flap
Minimal invasive techniques	Pit excision with phenolisation of the sinus tracts
	Video-assisted ablation of pilonidal sinus (VAAPS)
	Endoscopic pilonidal sinus treatment (EPSiT)
	Laser treatment

RECURRENCE

Recurrence, occurring in up to 43% of patients, is also a major problem after surgical treatment for SPSD [10]. As described above, midline closure should be prevented after primary surgical excision to reduce the risk of recurrence. In addition, patients are advised to keep the natal cleft free of hairs after surgery for SPSD to prevent recurrence. Options to remove hair are laser treatment, shaving or depilation cream. Several studies have investigated the effect of hair removal on the recurrence rate after surgical treatment. However, the sample size of these studies was relatively small and in most studies no control group was included. It is unclear if one option of hair removal is superior and further research is needed.

THESIS OUTLINE

The aim of this thesis was to clarify various aspects in treatment and prevention of SPSD.

As described, wound infections after surgery for SPSD are a major problem, with an infection rate reported in up to 24% of patients [10]. Since several randomised controlled trials have shown that systematic antibiotics do not significantly contribute to the reduction of wound infections, local application of antibiotics by a gentamicin collagen sponge was introduced to attempt to prevent surgical site infection [28–31]. Some small randomised and case-control studies have been published on the outcome of a gentamicin collagen sponge [12,13,32–35]. In **chapter 2** the available data from these trials have been pooled to analyse the effect of intra-operative local administration of gentamicin collagen sponge after excision of SPSD with the aim to provide a recommendation for or against the use of local antibiotics.

It has been suggested that a high density of body hair at or around the natal cleft may present a risk factor for SPSD and that the presence of hair may be a risk factor to develop a recurrence after surgery for SPSD [36,37]. Razor shaving, cream depilation and laser treatment are methods applied for hair removal. In **chapter 3,** the literature on hair depilation after surgical treatment of SPSD is summarised presenting the risk of recurrence after the different methods of hair removal.

The advantages of the minimal invasive techniques for SPDS, such as smaller wounds, less pain and faster wound healing, have been proposed to result in faster recovery and return to normal daily activities. Pit excision with phenolisation of the sinus tract is a frequently applied minimal invasive technique for SPSD, but the above mentioned advantages over radical excision have never been proven. Hence, a randomised controlled trial was performed to compare the phenolisation technique with radical excision and primary wound closure in patients with SPSD. In **chapter 4**, the short-term outcomes of this randomised controlled trial are reported.

In addition to the putative short-term advantages of the phenolisation technique, the recurrence rate is another important outcome measure of the surgical treatment of SPSD. In **chapter 5**, the long-term results of a randomised controlled trial comparing the phenolisation technique with surgical excision and primary off-midline closure, focusing on the recurrence rate, are described.

Recurrence could possibly have a large burden upon patients' quality of life. While the phenolisation technique has primarily been investigated in patients with primary SPSD, this technique has not yet been studied in recurrent SPD. In **chapter 6**, the short-term results of a prospective cohort study in patients with recurrent SPSD treated by the phenolisation technique are reported.

Evidence exists that symptoms related to SPSD have a negative impact on quality of life [38]. Sexual function is one of the issues upon which quality of life is based. Due to the location of SPSD and the average (young) age at which SPSD occurs, we hypothesised that sexual function is significantly affected by this disorder. In **chapter 7**, prospective data focusing on the impact of SPSD and its treatment on sexual function in male patients are reported.

Chapter 8 discusses the main results of the studies presented in this thesis with special emphasis on future research.

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CHAPTER 2

Local administration of gentamicin collagen sponge in surgical excision of sacrococcygeal pilonidal sinus disease: *a systematic review and meta-analysis of the literature*

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Tech Coloproctol 2016 Feb;20(2):91-100

ABSTRACT

INTRODUCTION

Surgical site infections occur in up to 24% of patients after surgical excision of sacrococcygeal pilonidal sinus disease with primary wound closure. Local administration of antibiotics by a gentamicin collagen sponge could reduce this infection rate. The objective of this systematic review and meta-analysis was to evaluate the effect of a gentamicin collagen sponge on outcome after surgical excision in patients with sacrococcygeal pilonidal sinus disease.

METHODS

A structured literature search was performed in the PubMed, Embase, The Cochrane Library, and Scopus databases. Studies comparing surgical excision of sacrococcygeal pilonidal sinus disease with versus without a gentamicin collagen sponge were included. Outcome measures were surgical site infection, wound healing and recurrence.

RESULTS

The search strategy yielded six studies with a total of 669 patients. Three randomised controlled trials, comparing excision of pilonidal sinus disease and primary wound closure with versus without gentamicin collagen sponge, were eligible for inclusion in the meta-analysis (319 patients), demonstrating a trend towards reduced surgical site infections after administration of gentamicin collagen sponge (absolute risk reduction 20%, 95% confidence interval (CI) 1–41%, p = 0.06). The wound healing (absolute risk reduction 22%, 95% CI 32–77%, p = 0.42) and recurrence rate (absolute risk reduction 8%, 95% CI 7%–22%, p = 0.30) were not significantly different between both groups.

CONCLUSION

Administration of a gentamicin collagen sponge after surgical excision of sacrococcygeal pilonidal sinus disease showed no significant influence on wound healing and recurrence rate, but a trend towards a reduced incidence of surgical site infections. Therefore, additional larger well-designed randomised controlled trials are required.

INTRODUCTION

Sacrococcygeal pilonidal sinus disease (SPSD) is an acquired disorder of the skin and subcutaneous tissue. It is most common among young adults, affecting men twice more often than women [1-3]. Patients present with recurrent or persistent discharge, discomfort and / or pain in the natal cleft. The treatment of SPSD involves eradication of the sinus tract by surgical excision, deroofing or phenol application. Radical excision of the sinus, however, is the most commonly applied treatment option. Healing of the overlying skin can be achieved by primary wound closure, in-midline, off-midline, i.e. Karydakis flap reconstruction, or rarely, with Limberg flap reconstruction. In recent decades, off-midline closure has become the preferred method due to a lower recurrence rate [4,5] and the Karydakis Flap reconstruction is advised for treatment of uncomplicated SPSD [6]. The disadvantage of primary closure, however, is the high rate of surgical site infection, occurring in up to 24% of patients [1,3,4,7]. Another commonly applied method after radical excision is secondary healing of the wound by open granulation; however, this results in a longer wound healing time [4,5].

Administration of systemic antibiotics after primary wound closure may be an option to reduce the incidence of surgical site infections. However, several randomised controlled trials (RCT's) have not shown any significant benefit [8-11]. Therefore, local application of a gentamicin collagen sponge in the wound cavity after excision of the SPSD has been introduced to reduce the incidence of surgical site infections. Compared to systemic antibiotics, this local administration leads to prolonged and higher local therapeutic concentrations [12,13]. Several RCT's have been performed comparing primary wound closure with the administration of a gentamicin collagen sponge after surgical excision of SPSD versus either primary wound closure [14-16] or secondary wound healing [17,18], both without a gentamicin collagen sponge. The outcome regarding surgical site infection, wound healing, and recurrence rate is quite different in these studies. Therefore, to date, a consensus on the optimal treatment for SPSD with regard to the local administration of antibiotics does not exist.

The objective of this systematic review and meta-analysis was to analyse whether the local intra-operative administration of a gentamicin collagen sponge after excision of SPDS benefits the outcome with regard to surgical site infection, wound healing, and recurrence rate.

MATERIAL AND METHODS

A systematic review and meta-analysis was conducted according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) [19].

SEARCH STRATEGY

A search of the literature was conducted in the databases of PubMed, Embase and the Cochrane Library on October 30th 2014. Different synonyms for "SPSD", "gentamicin", "local antibiotics", "surgical site infection", "wound healing" and "recurrence" were used as search terms (Table 1). For the search in PubMed, additional MeSH terms were used. No search limitations were applied. Additionally, cited references of the included articles were screened using the Scopus database. Finally, reference lists of the included articles were manually searched in order to identify potentially eligible studies.

Table 1. Search terms

Patient population	Pilonidal OR "Pilonidal Sinus"[Mesh] OR 'coccygeal sinus' OR 'sacrococcygeal sinus' OR (jeep AND disease) OR (hair-containing AND abscess) OR (hair-containing AND sinus) OR (tailbone AND cyst) OR (tailbone AND abscess)
Intervention	Gentamicin OR gentamycin OR gentacycol OR genticin OR garamycin OR gentavet OR G-myticin OR 'G Myticin' OR "Gentamicins"[Mesh] OR (collagen AND sponge) OR (local AND antibiotic) OR (local AND antibiotics) OR (local AND anti-bacterial) OR (local AND anti bacterial) OR (local AND antibacterial) OR (local AND antimicrobial) OR (local AND bacteriocidal) OR (local AND bacteriocides)
Outcome parameters	'Surgical wound infection' OR 'surgical wound infections' OR "Surgical wound infection"[Mesh] OR 'postoperative wound infection' OR 'postoperative wound infections' (wound AND healing) OR 'surgical wound dehiscence' OR "Surgical Wound Dehiscence"[Mesh] OR recurrence OR recurrences OR "Recurrence"[Mesh] OR relapse OR recrudescence OR recrudescences

STUDY SELECTION

Studies were screened on title, abstract, and full texts for identifying potentially relevant studies according to predefined inclusion criteria. Studies were included if the patients had SPSD. The intervention consisted of application of a gentamicin collagen sponge versus no gentamicin collagen sponge after surgical excision of the SPSD. The primary outcomes were surgical site infection, wound healing, and/or recurrence. All types of study design were included. Studies describing patients with an abscess and treatment options other than surgical excision were excluded from further analysis.

QUALITY ASSESSMENT

The included studies were methodologically assessed, according to the items described in the Cochrane Handbook for systematic reviews of interventions, version 5.1.0 [20]. Additionally, the level of evidence was assessed according to the Centre for Evidence Based Medicine at the University of Oxford [21].

DATA ACQUISITION

Data of the included studies were acquired by using a standard data extraction form, collecting information on the year of publication, study design, sample size, wound closure technique, size and number of gentamicin collagen sponges, duration of follow-up, surgical site infection rate, wound healing rate, time to wound healing, and recurrence rate.

STATISTICAL ANALYSIS

Data were analysed by using RevMan 5.2 software (Review Manager Version 5.0: The Nordic Cochrane Centre, Copenhagen; The Cochrane Collaboration, 2012). Outcome parameters were summarised per individual study using absolute risks (AR), absolute risk reduction (ARR) and the number needed to treat (NNT) with corresponding 95% confidence intervals (95% CI). Statistical heterogeneity of the pooled data was assessed by using the Chi-square test and I^2 statistic. Heterogeneity was considered statistically significant with $p < 0.1$ and $I^2 > 75\%$. Forest plots were made for the absolute risk differences (RD) using a random effects model, since significant statistical heterogeneity was present.

RESULTS

The original search yielded 40 articles. After removal of duplicates, 22 articles remained which were screened on title and abstract according to predefined inclusion criteria. Subsequently, ten articles remained and were screened on full text. Eventually, five RCT's [14-18] and one retrospective case-control study [22] were eligible for inclusion (Figure 1).

The methodological quality assessment of the five included RCT's is shown in table 2. Andersson et al. had no negative score on any of the assessed items [14]. The method of randomisation was not reported in two studies [16,17]. Studies performed by Vogel et al. [15] and Rao et al. [18] had a loss to follow-up of more than 10%. In four trials, blinding of patients, surgeons, and assessors for the intervention and whether analysis was performed according to the intention to treat principle was not reported [15-18]. Doll et al. executed a retrospective case-control study (excision of SPSD with or without gentamicin collagen sponge) [22]. The study groups and interventions were adequately described, and outcomes were adequately assessed according to predefined criteria.

The level of evidence according to the Oxford Centre for Evidence Based Medicine for the five RCT's [14-18] was 1b and for the individual cohort study [22] was 2b.

PRIMARY CLOSURE WITH VERSUS WITHOUT GENTAMICIN COLLAGEN SPONGE

Three RCT's [14-16] and one retrospective case control study [22] were conducted comparing surgical excision followed by primary closure with or without a gentamicin collagen sponge.

Andersson et al. executed a double-blinded multicenter RCT in Sweden comparing primary closure with (77 patients) versus without a gentamicin collagen sponge (82 patients) after surgical excision of SPSD (Table 3) [14]. This study showed no significant differences in terms of surgical site infection rates at two weeks after surgery (Table 4). The wound healing and recurrence rate at one-year follow-up were also not significantly different between both groups (Table 5 and 6, respectively).
Vogel et al. [15] performed a RCT in Germany with 40 patients in each group comparing application of a gentamicin collagen sponge versus no gentamicin collagen sponge after surgical excision (Table 3). One to four gentamicin collagen sponges were administrated depending on the size of the wound.

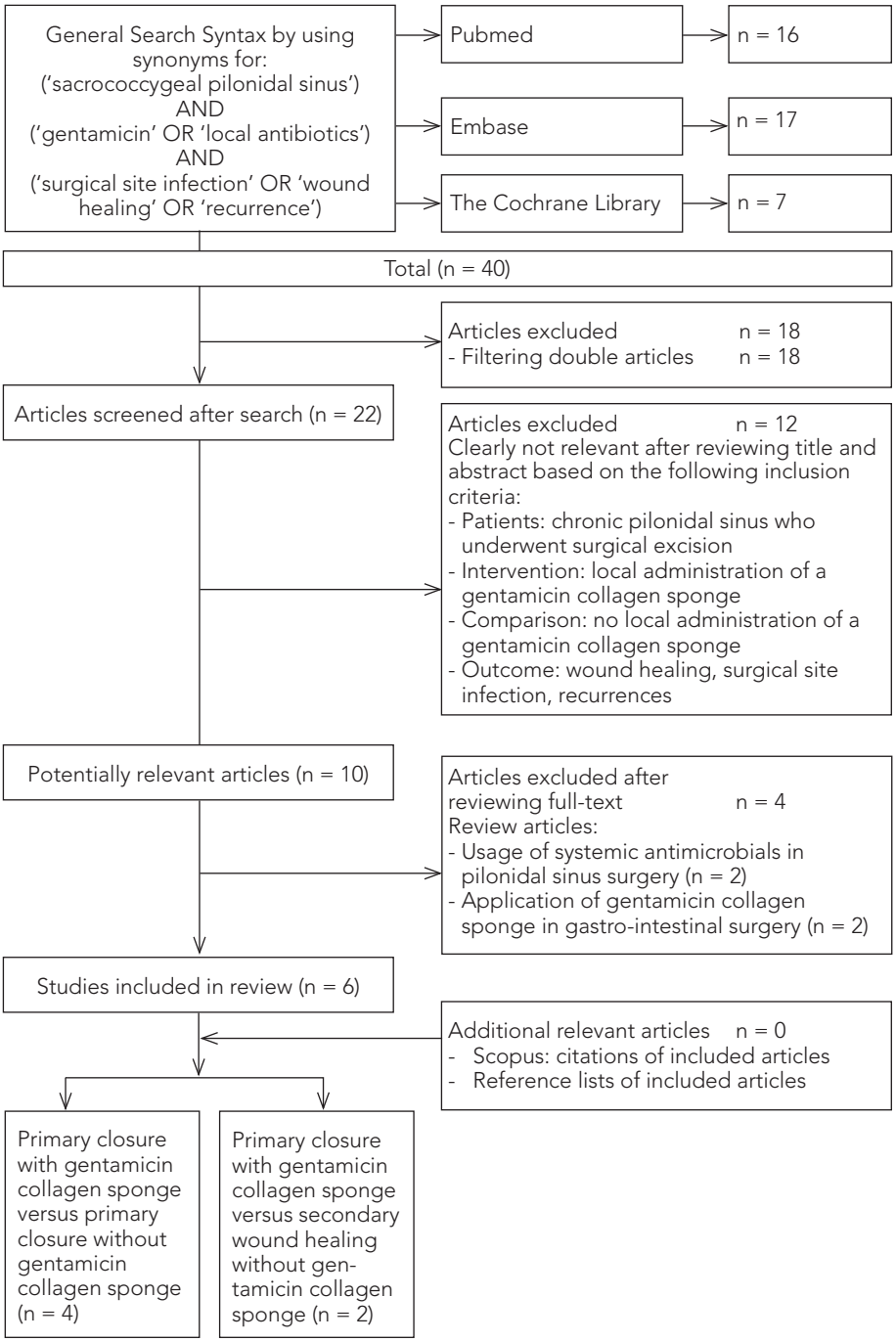


Figure 1. Flow chart of search strategy and study selection

Table 2. Methodological quality assessments of included randomised trials

	Random sequence generation (selection bias)	Concealment of allocation (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Analysis conform intention to treat	Cross-over > 10%
Andersson et al. [14]	+	+	+	+	+	+	+	NA
Vogel et al. [15]	++	NR	NR	NR	-	+	NR	NR
Yetim et al. [16]	+/-	NR	NR	NR	+	+	NR	NR
Holzer et al. [17]	+/-	NR	NR	NR	+	-	NR	NR
Rao et al. [18]	+	NR	NR	NR	+/-	-	NR	NR

Random sequence generation: ++ randomisation by computer system or random table; + randomisation by closed/sealed envelopes; +/- randomisation method not reported; - no randomisation
Concealment of allocation: + yes; - no
Blinding for participants and performance: + yes; - no
Blinding for outcome assessment: + yes; - no. Incomplete outcome data: + < 10%; +/- 10-15%; - > 15%
Selective reporting: + all pre-specified outcomes have been reported; - not all pre specified outcomes have been reported or were reported incompletely
Analysis conform intention to treat: + yes; - no
Cross-over: + < 10%; +/- 10-15%; - > 15%
Abbreviations: NR, not reported; NA, Not applicable

With regard to surgical site infections, the ARR was 42.5% (95% CI: 25.0-60.0, $p < 0.001$) in favor of the gentamicin collagen sponge group with a corresponding number needed to treat (NNT) of 3.0 (95% CI: 1.7-4.0) (Table 4). The absolute risk reduction (ARR) of the rate of non-healed wounds was 50,0% (95% CI: 31.8-68.2, $p < 0.001$) in favor of application of a gentamicin collagen sponge (Table 5). No recurrences occurred at follow-up (Table 6).

Yetim et al. [16] conducted a RCT in Turkey with 80 patients comparing local administration of a gentamicin collagen sponge to postoperative oral antibiotic therapy for seven days after surgical excision with primary midline closure (Table 3). For the outcome surgical site infections, a significant ARR of 15.0% (95% CI 0.9-29.0, $p = 0.04$) was achieved after application of a gentamicin collagen sponge (Table 4). The mean time to wound healing was reported to be shorter after application of a gentamicin collagen sponge (8.9 versus. 15.1 days, $p = 0.001$) [16]. Additionally, a significant ARR of 15.0% (95% CI 4.0-26.1, $p = 0.01$) in favor of the gentamicin collagen sponge group was demonstrated with regard to recurrence at one-year follow-up (Table 6).

Doll et al. [22] retrospectively examined a population of 187 men with SPSD who underwent excision with primary midline closure with or without a gentamicin collagen sponge (Table 3). Application of a gentamicin collagen sponge yielded a significant ARR of 13.6% (95% CI: 0.9-26.2, $p = 0.03$) with regard to surgical site infections (Table 4). All wounds were healed after 12 days. No statistically significant difference in the recurrence rate existed between the groups (Table 6).

PRIMARY CLOSURE WITH GENTAMICIN COLLAGEN SPONGE VERSUS SECONDARY WOUND HEALING WITHOUT GENTAMICIN COLLAGEN SPONGE

Holzer et al. [17] executed a multicenter RCT in Austria that included 103 patients comparing primary closure with a gentamicin collagen sponge versus secondary wound healing without a gentamicin collagen sponge after surgical excision of SPSD (Table 3). In the gentamicin collagen sponge group, 27.5 % (95% CI: 17.0-41.0) of the wounds were not healed at 2 weeks of follow-up. The median time to healing in the primary closure with gentamicin collagen sponge group was 17 days (range 7-39 days) versus 68 days (range 10-161 days) in the secondary wound healing group ($p < 0.001$) [17]. Two patients in the gentamicin collagen sponge group developed a surgical site infection in the first two weeks after surgery, which required conversion to open treatment (Table 4). The surgical site infection and wound healing rates for

the secondary wound healing group were not reported. After a follow-up period of 26 weeks, one recurrence was seen in the primary closure group versus none in the open treatment group (Table 6).

Rao et al. [18] performed a single-center RCT in Northern Ireland that enrolled 60 patients who underwent surgical excision of SPSD. In the primary closure group (30 patients), one or two gentamicin collagen sponges were implanted in the wound depending on the size of the wound. The surgical site infection rate was not reported. The rate of non-healed wounds at 4-week follow-up was significantly higher in the group of patients, who underwent surgical excision followed by secondary wound healing without a gentamicin collagen sponge (Table 5). Furthermore, the median wound healing time (interquartile range) was also significantly shorter in the gentamicin collagen sponge group (10 (10-26) days versus 50 (40-90) days; $p < 0.001$)) [18]. At 5-year follow-up, there was no significant difference in terms of recurrence (Table 6).

POOLING OF DATA

The study data from three RCT's [14-16] comparing surgical excision followed by primary closure with versus without a gentamicin collagen sponge were pooled. The risk difference (RD) for surgical site infections was 20 % (95% CI: 1-41) in favor of the treatment with the gentamicin collagen sponge, although this was not statistically significant ($p = 0.06$) (Figure 2a). Pooled data of two RCT's [14,15] reported no significant difference in rate of non-healed wounds at one-year follow-up after administration of local antibiotics (RD 22 %, 95% CI: range 32-77, $p = 0.42$) (Figure 2b). Additionally, heterogeneity was significantly present for both outcome parameters. There was no significant difference regarding recurrence rate between both treatments at one-year follow-up (Figure 2c).

Table 3. Study characteristics

	Study design	LoE	Closure technique	Study groups	GCS size and number	Outcomes	Follow-up
Andersson et al. [14]	MC RCT	1B	Primary midline closure	GCS (n = 82) versus no GCS (n = 77)	1 GCS	Surgical site infection Delayed wound healing Recurrences	2 weeks 1 year 1 year
Vogel et al. [15]	SC RCT	1B	Primary midline closure	GCS (n = 40) versus no GCS (n = 40)	1-4 GCS	Surgical site infection Delayed wound healing Recurrences	1 year 1 year 1 year
Yetim et al. [16]	SC RCT	1B	Primary midline closure	GCS (n = 40) versus oral antibiotics (n = 40)	Whole 5x5x0.5 cm GCS	Surgical site infection Time to healing Recurrences	1 year NR 1 year
Doll et al. [22]	R	2B	Primary midline closure	GCS (n = 111) versus no GCS (n = 76)	NR	Surgical site infection Delayed wound healing Recurrences	15 years 15 years 15 years
Holzer et al. [17]	MC RCT	1B	Primary midline closure versus secondary wound healing	GCS (n = 51) versus no GCS (n = 52)	Whole 5x8 cm GCS	Delayed wound healing Time to healing Recurrences	2 weeks NR 26 weeks
Rao et al. [18]	SC RCT	1B	Primary midline closure versus secondary wound healing	GCS (n = 30) versus no GCS (n = 30)	Whole 1-2 GCS	Delayed wound healing Time to healing Recurrences	4 weeks NR 5 years

Abbreviations: GCS, Gentamicin collagen sponge; LoE, level of evidence; MC, multicenter; N, number of patients; NR, not reported; SC, single center; R, retrospective cohort study; RCT, randomised controlled trial

Table 4. Surgical site infection rates

	Treatment (GCS) n / N	Control (no GCS) n / N	AR GCS (%) (95% CI)	AR no GCS (%) (95% CI)	ARR (%) (95% CI)	p-value for ARR	NNT (95% CI)	Follow-up
Primary closure with versus without gentamicin collagen sponge								
Andersson et al. [14]	18/82	20/77	22.0 (14.3 – 32.1)	26.0 (17.4 – 36.8)	4.0 (-9.3 – 17.3)	0.55	25.0 (NNTH 10.8 to ∞ to NNTB 5.8)	2 weeks
Vogel et al. [15]	3/40	20/40	7.5 (1.9 – 20.6)	50.0 (35.2 – 64.8)	42.5 (25.0 – 60.0)	<0.001	3.0 (1.7 – 4.0)	1 year
Yetim et al. [16]	2/40	8/40	5.0 (0.5 – 17.4)	20.0 (10.2 – 35.0)	15.0 (0.9 – 29.0)	0.04	7.0 (3.4 – 113.2)	1 year
Doll et al. [22]	20/111	24/76	18.2 (11.9 – 26.3)	31.6 (22.2 – 42.7)	13.6 (0.9 – 26.2)	0.03	8.0 (3.8 – 111.3)	15 years
Primary closure with gentamicin collagen sponge versus secondary wound healing without gentamicin collagen sponge								
Holzer et al. [17]	2/51	NR	53.9 (0.3 – 14.0)	NR	NR	NR	NR	NA
Rao et al. [18]	NR	NR	NR	NR	NR	NR	NR	NA

Abbreviations: AR, absolute risk; ARR, absolute risk reduction; CI, confidence interval; GCS, gentamicin collagen sponge; n, number of patients with positive outcome; N, total number of patients; NA, not applicable; NNT, number needed to treat; NNTB, number needed to benefit; NNTH, number needed to harm; NR, not reported

Table 5. Rates of non-healed wounds

	Treatment (GCS) n / N	Control (no GCS) n / N	AR GCS (%) (95% CI)	AR no GCS (%) (95% CI)	ARR in % (95% CI)	p-value for ARR	NNT (95 % CI)	Follow-up
Primary closure with versus without gentamicin collagen sponge								
Andersson et al. [14]	12/82	8/77	14.6 (8.4 – 24.0)	10.4 (5.1 – 19.4)	-4.2 (-6.0 – 14.5)	0.42	NNTH = 24 (NNH 6.9 to ∞ to NNTB 16.7)	1 year
Vogel et al. [15]	5/40	26/40	12.5 (5.0 – 26.6)	62.5 (47.0 – 75.8)	50.0 (31.8 – 68.2)	<0.001	2.0 (1.5 – 3.1)	1 year
Yetim et al. [16]	NR	NR	NR	NR	NR	NR	NR	NA
Doll et al. [22]	0/111	0/76	0	0	NA	NA	NA	15 years
Primary closure with gentamicin collagen sponge versus secondary wound healing without gentamicin collagen sponge								
Holzer et al. [17]	14/51	NR	27.5 (17.0 – 41.0)	NR	NR	NR	NR	2 weeks
Rao et al. [18]	3/30	26/30	10.0 (2.7 – 26.4)	86.7 (69.7 – 95.3)	76.7 (60.4 – 92.9)	<0.001	2.0 (1.1 – 1.7)	4 weeks

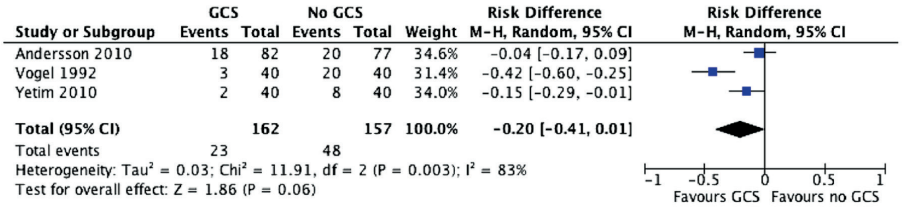
Abbreviations: AR, absolute risk; ARR, absolute risk reduction; CI, confidence interval; GCS, gentamicin collagen sponge; n, number of patients with positive outcome; N , total number of patients; NA, not applicable; NNT, number needed to treat; NNTB, number needed to benefit; NNTH, number needed to harm; NR, not reported

Table 6. Recurrence rates

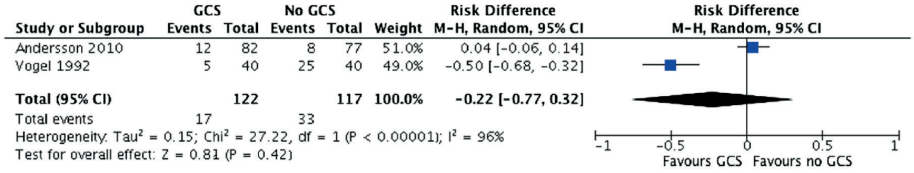
	Treatment (GCS) n / N	Control (no GCS) n / N	AR GCS (%) (95% CI)	AR no-GCS (%) (95% CI)	ARR in % (95% CI)	p-value for ARR	NNT (95 % CI)	Follow-up
Primary closure with versus without gentamicin collagen sponge								
Andersson et al. [14]	9/82	9/77	11.0 (5.7 – 19.8)	11.7 (6.1 – 21.0)	0.7 (-9.2 – 10.6)	0.89	141.0 (NNTH 10.9 to ∞ to NNTB 9.5)	1 year
Vogel et al. [15]	0/NR	0/NR	0	0	NA	NA	NA	1 year
Yetim et al. [16]	0/40	6/40	0 (0 – 10.4)	15.0 (6.7 – 29.5)	15.0 (4.0 – 26.1)	0.01	7.0 (3.8 – 25.4)	1 year
Doll et al. [22]	34/111	20/76	30.6 (22.8 – 39.8)	26.3(17.7 – 37.2)	-4.3 (-8.8 – 17.4)	0.52	NNTH = 24.0 (NNTH 5.7 to ∞ to NNTB 11.4)	15 years
Primary closure with gentamicin collagen sponge versus secondary wound healing without gentamicin collagen sponge								
Holzer et al. [17]	1/51	0/52	2.0 (0 – 11.3)	0 (0 – 8.2)	-2.0 (-1.8 – 5.8)	0.31	NNTH = 51.0 (NNTH 17.3 to ∞ to NNTB 54.2)	26 weeks
Rao et al. [18]	2/25	2/24	8.0 (1.1 – 26.1)	8.3 (1.2 – 27.0)	0.3 (-15.0 – 15.7)	0.97	300.0 (NNTH 6.7 to ∞ to NNTB 6.4)	5 years

Abbreviations: AR, absolute risk; ARR, absolute risk reduction; CI, confidence interval; GCS, Gentamicin collagen sponge; n, number of patients with positive outcome; N, total number of patients; NA, not applicable; NNT, number needed to treat; NNTB, number needed to benefit; NNTH, number needed to harm

a Surgical site infection



b Delayed wound healing



c Recurrences

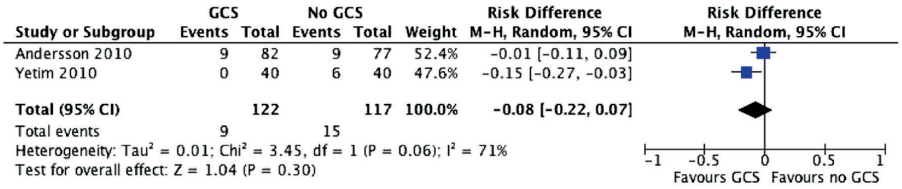


Figure 2. Forest plots for surgical site infection (a), delayed wound healing (b) and recurrence rate (c)
Abbreviations: CI, confidence interval; GCS Gentamicin collagen sponge

DISCUSSION

This systematic review summarises the available literature with regard to the effect of intraoperative local administration of a gentamicin collagen sponge after surgical excision of SPSD. Meta-analysis of three RCT's that investigated surgical excision of SPSD followed by primary closure with versus without a gentamicin collagen sponge, demonstrated a trend towards less surgical site infections with the application of a gentamicin collagen sponge. However, the wound healing and recurrence rate were not significantly influenced [14-16]. Additionally, a retrospective cohort study showed a significant reduction in surgical site infection with the administration of a gentamicin collagen sponge, but there was no statistically significant difference in the wound healing and recurrence rates [22].

In this meta-analysis, the results did not reach a statistical significant difference in terms of surgical site infection, probably due to the relatively small sized and therefore underpowered RCT's. Heterogeneity of the included studies was present as well. However, the results showed a trend towards a reduction in the rate of surgical site infections ($p = 0.06$). These results are supported by a systematic review and meta-analysis performed by Chang et al. [23], consisting of fifteen RCT's, which confirmed that gentamicin collagen sponges significantly reduce the incidence of surgical site infections after different types of surgery (odds ratio (OR) = 0.51; 95% CI: 0.33-0.77; $p = 0.01$). Although current evidence is not yet overly convincing, the advantage of applying a gentamicin collagen sponge is that the antibiotics remain localised and do not enter the systemic circulation. Moreover, no adverse events due to the application of a gentamicin collagen sponge were reported in the included trials.

The results of this systematic review showed no significant difference with regard to wound healing with the use of gentamicin collagen sponges, therefore this still remains a problem in a substantial proportion of patients. It should be noted that primary midline closure was applied in the included studies, whereas several meta-analyses have shown that off-midline closure should be the treatment of choice considering the lower rate of surgical site infections, faster healing rates and lower recurrence rates associated with this type of closure [4,5]. Additionally, wound healing could be impeded when the gentamicin collagen sponge is inserted between both edged of the wound, as this may become a barrier to adequate wound healing. Some included studies reported details regarding the size [16,17] and number [14,15,18] of inserted sponges in the wound cavity. However, they did not report whether the gentamicin

sponge was inserted in the wound as a whole, although some images included in the articles demonstrate that the gentamicin collagen sponge was in situ in the wound after surgical excision as a whole [16-18]. In order to promote wound healing, however, the gentamicin collagen sponge can be cut into small pieces before insertion in the wound cavity. Whether cutting the sponge into small pieces will improve wound healing needs further investigation.

There also were two RCT's [17,18] included in this systematic review that compared primary wound closure with a gentamicin collagen sponge versus secondary wound healing (without a gentamicin collagen sponge) after excision of SPSD. The surgical site infection rate was not adequately reported in both studies and, there was no statistically significant difference in recurrence rate between both groups [17,18]. Both studies reported that in terms of wound healing, primary closure with a gentamicin collagen sponge was superior to secondary wound healing. However, it is commonly known that primary closure accelerates wound healing. Therefore, the additional effect of a gentamicin collagen sponge on wound healing cannot be determined from these studies.

There are a few limitations to this systematic review, which are mainly due to the quality, heterogeneity, and size of the included studies. First, four RCT's [15-18] did not state details about concealment of allocation, and whether blinding for participants, personnel and patients was performed. Therefore, these studies are at risk for selection bias, performance bias, and detection bias, respectively. Second, two studies [15,16] reported a remarkable recurrence rate of 0 %, which leads us to questions the validity of these studies as this seems, in our opinion, unlikely in this patient population. Third, most RCT's [15-18] did not record whether their studies were appropriately powered. Fourth, it is remarkable that the relatively smaller RCT's showed statistically significant differences with regard to surgical site infections [15,16], wound healing rate [15] and recurrences [16] by adding a gentamicin collagen sponge to the surgical treatment, whilst the largest RCT [14] does not support these findings. This may be due to publication bias, where statistically significant results may be more likely to be published than non-significant results regardless of the size, design, and methodology of the study. This could lead to overestimation of the effect of the gentamicin collagen sponge. Finally, to the best of our knowledge, the cost-effectiveness of the application of a gentamicin collagen sponge in patients with SPSD has not yet been evaluated. The cost-effectiveness of local application of a gentamicin collagen sponge has been confirmed in the prevention of sternal wound infections following cardiac surgery [24].

However, future research has to be performed to determine whether the application of gentamicin implants in patients with SPSD will also be cost-effective.

CONCLUSION

This systematic review and meta-analysis has demonstrated that the administration of a gentamicin collagen sponge after surgical excision of SPSD does not accelerate wound healing or reduce recurrence rate, but there is a trend towards less surgical site infections. Therefore, larger well-designed RCT's are needed in order to demonstrate a more reliable and accurate effect of the application of a gentamicin collagen sponge on the outcome after surgical excision of SPSD.

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CHAPTER 3

The effect of hair removal after surgery for sacrococcygeal pilonidal sinus disease: *a systematic review of the literature*

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Tech Coloproctol 2018 Jan;22(1):7-14

ABSTRACT

INTRODUCTION

It has been suggested that removal of body hair in the sacrococcygeal area prevents recurrence after surgery for sacrococcygeal pilonidal sinus disease (SPSD). The aim of this study was to review the literature regarding the effect of hair depilation on the recurrence rate in patients surgically treated for SPSD.

METHODS

A systematic search was performed in PubMed, EMBASE and The Cochrane Library by using synonyms for SPSD. Title, abstract and full text were screened by two independent reviewers. Data were systematically collected from all included studies by using a standardised data extraction form.

RESULTS

The search and selection yielded 14 studies, involving 963 patients. The study design of the included studies was: retrospective cohort (n = 7), prospective cohort (n = 3), randomised controlled trial (n = 2) and case-control (n = 2). The mean length of follow-up was 37.0 (standard error of the mean: 35.0) months. The recurrence rate was 9.3% (34 out of 366 patients) in patients who had laser hair removal, 23.4% (36 out of 154 patients) in those who had razor shaving/cream depilation and 19.7% (85 out of 431 patients) in those who had no hair removal after surgery for SPSD.

CONCLUSIONS

This systematic review showed a lower recurrence rate after laser hair removal compared to no hair removal and razor/cream depilation. Due to the small sample size and limited methodological quality of included studies, a high quality randomised controlled trial is required.

INTRODUCTION

Sacrococcygeal pilonidal sinus disease (SPSD) is a common disorder [1]. Risk factors include male sex, family history, obesity and hirsutism [2]. The most common symptoms of SPSD are discomfort or pain and fluid discharge from the natal cleft. Therefore, SPSD can severely interfere with daily activities and have a huge impact upon quality of life. Various surgical treatments are used to treat symptomatic patients, comprising radical excision, unroofing and debridement of the sinus tract followed by phenolisation and less invasive treatments such as with fibrin glue [3,4]. Surgical site infection occurs very often after surgical treatment leading to delayed wound healing [5]. In addition, recurrence is a major problem, occurring in up to 43% of patients, according to a Cochrane review [5].

Although the etiology of SPSD is not fully understood it had been suggested that a high density of body hair, at or around the natal cleft, may be a risk factor for SPSD and the presence of body hair, even after surgical treatment, may contribute to recurrence [6,7]. Different methods of hair removal exist, including razor shaving, crème depilation and laser treatment. Several studies investigated the effect of hair removal on the recurrence rate of SPSD after surgical treatment [3,8-20]. However, the sample size of these studies was relatively small and in most studies no control group was included. Therefore, combining the results of these individual studies could provide more accurate results of the effect of hair removal on the recurrence rate after surgical treatment of SPSD.

The aim of this study was to review and summarise the literatus on the effect of hair depilation on the recurrence rate in patients surgically treated for SPSD.

MATERIAL AND METHODS

A systematic review of the literature was conducted according to a review protocol based on the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) [21].

SEARCH STRATEGY

A literature search was performed in PubMed, EMBASE and Cochrane Central Register of Controlled Trials from dates of inception until April 15, 2017, to identify all relevant

studies. Several synonyms for SPSD were used in the search. The complete search strategy is shown in table 1.

STUDY SELECTION

Articles identified by the search strategy were independently selected by two authors (A.P. and L.E.). In the case of disagreement, the opinion of a third reviewer was asked (E.F.). First, both authors screened all articles yielded by the search strategy on title and abstract. The inclusion and exclusion criteria were used for study selection were as follows. All studies describing patients with primary or recurrent SPSD who had hair removal after surgery were included. All types of study design were accepted, except studies including less than ten patients. Studies were excluded if the pilonidal sinus disease was outside the sacrococcygeal area or patients did not have hair removal. Studies remaining after screening of the title and abstract were subsequently screened on full text using the same criteria. Thereafter, all citing papers already identified and articles in references were screened to identify additional relevant studies.

DATA ACQUISITION

The following data from the included studies were collected by using a standard data extraction form; study design, patient characteristics (i.e., age and sex), primary or recurrent SPSD, type of previous (if applicable) and current surgery, details on depilation (in the case of laser depilation, the number of sessions, time interval, wavelength and area of depilation), duration of follow-up, definition of recurrence, recurrence rate and number and type of complications.

Table 1. Search strategy

Database	Search terms
PubMed	Free text words: pilonidal*[tw] OR "coccygeal cyst"[tw] OR "sacrococcygeal cyst"[tw] OR "sacrococcygeal sinus"[tw] OR "coccygeal sinus"[tw]
Embase	Free text words: pilonidal*:ti:ab OR "coccygeal cyst":ti:ab OR "sacrococcygeal cyst":ti:ab OR "sacrococcygeal sinus":ti:ab OR "coccygeal sinus":ti:ab AND [embase]/lim NOT [medline]/lim
The Cochrane library	Free text words: "pilonidal*" OR "sacrococcygeal sinus"

Abbreviations: tw, text word; ti, title; ab, abstract; lim, limits

CRITICAL APPRAISAL

All included studies were methodologically assessed. The Jadad score was used to assess the methodological quality of randomised controlled trials (RCT) (score form 0 to 5: 0 = poor, 5 = excellent) [22]. The methodological quality of cohort and case-control studies was assessed on the Newcastle-Ottawa Scale (NOS) which assesses the quality of non-randomised studies in meta-analysis (score from 0 to 9: 0 = poor, 9 = excellent) [23].

According to the methodological quality assessment, a level of evidence was assigned to the studies according to the Oxford Centre of Evidence Based Medicine Levels of Evidence [24]. Level of Evidence (LoE) 2B was assigned to RCTs with a Jadad score <4 and LoE 1B to RCTs with a Jadad score of 4-5. LoE 4 was assigned to cohort studies with a NOS score < 6 LoE 4 and LoE 2B to those with a NOS of 6 or 7. LoE 3B was assigned to all case-controle studies 3B.

DATA ANALYSIS

Data were analysed using SPSS version 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Values with a normal distribution were expressed as mean (standard error of the mean (SEM)) and values with non-normal distribution as median (range). Statistical pooling was not performed due to unacceptable clinical heterogeneity between the included studies.

RESULTS

The search strategy in PubMed, Embase and Cochrane yielded a total of 2481 hits after removal of all duplications (Figure 1). By applying the inclusion and exclusion criteria, 14 articles remained after screening title and abstract. None of these articles were excluded after further screening of the full text. The citing articles and screening of the articles in the references of the included studies yielded no additional studies. Therefore, a total of 14 studies were available for inclusion in this systematic review.

The included studies comprised seven retrospective and three prospective cohort studies, two RCTs and two case-control studies of which one prospective and one retrospective. In the ten cohort studies, patients with SPSD treated by laser depilation to prevent recurrence after surgical treatment were included [3,9,11–16,18,20]. The prospective case-control study compared a group of patients with laser hair removal

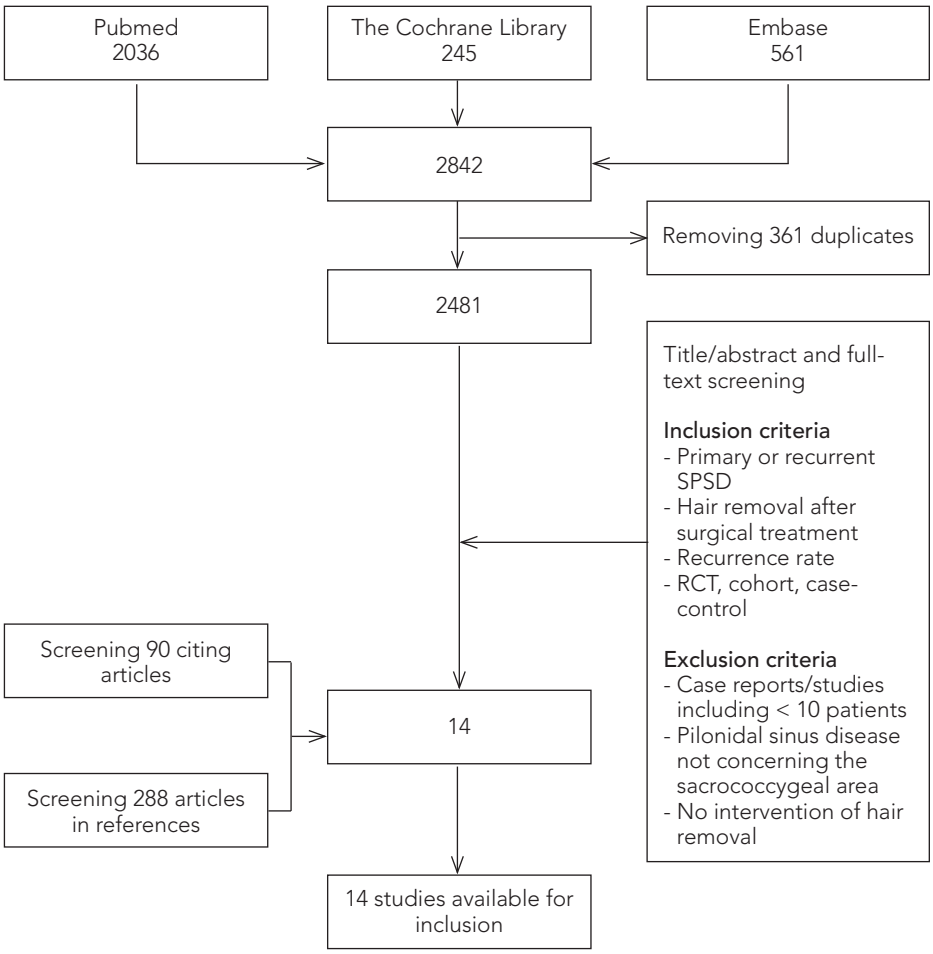

Figure 1. Flow diagram of search and study selection process

versus no hair removal [8,9]. One RCT compared laser treatment to razor shaving/cream depilation and the other RCT laser hair removal to no hair removal[11,19]. They had a Jadad score of 1 and 2, respectively. The mean NOS for the cohort studies was 3.9 (SEM 1.0), and 4.5 (SEM 1.5) for the case-control studies. According to the Oxford Centre for Evidence Based Medicine, two studies had LoE 2B, two studies LoE 3B and the remaining 9 studies had LoE 4. The data of the individual studies are shown in table 2.

PATIENT POPULATION

Of the 14 included studies, two studies reported a patient population with recurrent SPSD only, seven studies reported patients with both primary and recurrent SPSD and the remaining five studies did not adequately report whether SPSD was primary or recurrent. The studies included a total of 963 patients. The baseline characteristics of these patients are shown in table 3. Of the patients treated with hair removal, 378 patients (39.3%) underwent hair removal by laser treatment and 154 patients (16.0%) by razor shaving and cream depilation. 431 patients (44.8%) had no hair removal. Of all included patients, 150 patients (15.6%) had previous surgery for SPSD; 19 (12.7%) had abscess drainage, two (1.3%) excision of SPSD with secondary wound healing, one (0.7%) had a Karydakis procedure and the type of previous surgery was not reported in the other 128 patients (85.3%). Different types of current surgical treatment modalities were used, including excision with secondary wound healing, primary wound closure and flap reconstruction in 311 (32.3%), 192 (20.0%) and 102 patients (10.6%), respectively. Phenol treatment was used in 42 patients (4.4%), marsupialisation in 31 (3.2%), surgical excision without specification of type of closure in 26 patients (2.7%) and abscess drainage in 21 patients (2.2%). The type of surgery was not reported in 238 patients (24.7%).

HAIR REMOVAL BY LASER TREATMENT

Of all included patients, 378 patients (39.3%) had hair removal by laser treatment. The number of laser sessions ranged from 1 to 8 with a mean of 4.2 (SEM 1.9) sessions (Table 4). In one study, hair was completely removed by laser treatment before surgery. In nine studies, hair removal was started postoperatively; in five studies in the completely healed wound phase, in three in the non-healed wound phase. The phase of the wound healing was not reported in one study. In two studies, hair removal was started in the preoperative phase and this was continued postoperatively. In the remaining study, it was not reported whether laser treatment was performed in the pre- or postoperative phase. The time interval of laser treatment ranged from one treatment every two to one treatment every eight weeks. The reason/decision to end laser hair removal treatment in the different studies is given in table 4.

In six studies the laser device deployed short wavelengths (≤755 nm), in four studies long wavelengths (>755 nm) and in two studies a wide wavelength range. One study did not report the used wavelengths.

Table 2. Baseline characteristics of the individual studies

First Author	Study design	Jadad / Newcastle ottawa score* – level of evidence	No. of patients hair removal versus control group	Treatment type	Duration of follow-up (months)	No. of patients available for follow-up	Recurrence		
							Subjective	Objective	Method of follow-up not reported
Badawy and Kanawati [8]	Prospective case control	3/9 – 3B	15	Laser hair removal	12 – 23	13 (86.7%)	N/A	0 (0%)	N/A
			10	No hair removal	12 – 23	10 (100%)	N/A	7 (70.0%)	N/A
Conroy et al. [9]	Retrospective cohort	3/7 – 4	14	Laser hair removal	12	12 (85.7%)	NR	NR	0 (0%)
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Demircan et al. [19]	RCT	2/5 – 2B	30	Laser hair removal	12	30 (100%)	6 (20%)	N/A	N/A
			30	No hair removal	12	30 (100%)	1 (3.3%)	N/A	N/A
Ghnnam and Hafez [10]	RCT	1/5 – 2B	45	Laser hair removal	24	45 (100%)	N/A	0 (0%)	N/A
			41	Razor shaving and cream depilation	24	41 (100%)	N/A	2 (4.9%)	N/A
Girgin et al. [11]	Retrospective cohort	2/7 – 4	42	Laser hair removal	24	42 (100%)	N/A	0 (0%)	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lindholt – Jensen et al. [12]	Retrospective cohort	4/7 – 4	41	Laser hair removal	15.2	37 (90.2%)	7 (18.9%)	N/A	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lukish [20]	Retrospective cohort	5/7 – 4	28	Laser hair removal	24.2	28 (100%)	N/A	1 (3.6%)	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Khan et al. [13]	Retrospective cohort	4/7 – 4	19	Laser hair removal	NR	19 (100%)	NR	NR	3 (15.8%)
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Kok et al. [14]	Retrospective cohort	3/7 – 4	17	Laser hair removal	23.6	15 (88.2%)	1 (6.7%)	N/A	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Odili and David [15]	Prospective cohort	4/7 – 4	14	Laser hair removal	60	14 (100%)	N/A	4 (28.6%)	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Oram et al. [16]	Retrospective cohort	5/7 – 4	60	Laser hair removal	57.6	60 (100%)	8 (13.3%)	N/A	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A

Petersen et al. [17]	Retrospective case control	6/9 – 3B	113	Razor shaving and cream depilation	122.4	113 (100%)	34 (30.1%)	N/A	N/A
			391	No hair removal	140.4	391 (100%)	77 (19.7%)	N/A	N/A
Schulze [18]	Prospective cohort	5/7 – 4	23	Laser hair removal	NR	19 (82.6%)	NR	NR	0 (0%)
			N/A	N/A	N/A	N/A	N/A	N/A	N/A
Shafigh et al [3]	Prospective cohort	4/7 – 4	30	Laser hair removal	31	30 (100%)	N/A	4 (13.3%)	N/A
			N/A	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: NR, not reported; N/A, not applicable; RCT, randomised controlled trial
*The Jadad score was used to assess the methodological quality of randomised controlled trials with a minimum score of zero (poor randomised trial) and a maximum score of 5 (excellent randomised trial); the methodological quality of cohort and case-control studies was assessed by the Newcastle-Ottawa Assessment of the quality of nonrandomised studies in meta-analysis with a minimum of zero (poor methodological study) and a maximum of 7 for cohort studies and a maximum of 9 for case-control studies (excellent methodological quality)

Table 3. Baseline characteristics of included patients

Total number of patients	963	(%)
Sex		
Male	864	(89.7)
Female	97	(10.1)
Not reported	2	(0.2)
Age (years)*	24.3 (3.7)	
Patient population		
Primary sacrococcygeal pilonidal sinus disease	209	(21.7)
Recurrent sacrococcygeal pilonidal sinus disease	79	(8.2)
Not reported	675	(70.1)

*Values are given as mean (standard error of the mean, SEM).

Table 4. Characterisitcs of laser treatment by individual study

Studies applying laser treatment	13	Number of studies (%)
Number of laser sessions		
1 – 3	6	(46.2)
3 – 6	5	(38.5)
6 – 9	2	(15.4)
Laser interval		
2-4 weeks	3	(23.1)
4-6 weeks	5	(38.5)
6-8 weeks	3	(23.1)
Not reported	2	(15.4)
End of laser treatment		
After two sessions	1	(7.7)
After four sessions	1	(7.7)
Most/all of the body hairs removed	3	(23.1)
After sinus healing and no signs of inflammation	1	(7.7)
Indicated by the patient	1	(7.7)
Not reported	6	(46.2)
Wavelength		
<755 nanometer	1	(7.7)
755 nanometer	5	(38.5)
>755 nanometer	4	(30.8)
Wide range (500-1200 nanometer)	2	(15.4)
Not reported	1	(7.7)

In five studies, hair removal was performed in the affected area including an additional 8 cm (one study), 5cm (two studies) or 2 cm (two studies). In two studies the intergluteal sulcus was treated. In one study, the natal cleft and sinus openings were treated with laser hair removal in two parallel rows on both sides of the natal cleft with maximum overlap of one-third. In another study, hair was removed from the buttocks, anal region and lower back. In four studies, the area of hair removal was not reported.

Complications due to laser hair removal occurred in 106 of the 378 patients (28.0%); 45 patients (11.9%) reported discomfort, 39 (10.3%) had temporary pain in the treated area, 13 (3.4%) had superficial wound dehiscence, eight (2.1%) wound infection, one (0.3%) developed an abscess and another patient (0.3%) reported folliculitis. In 58 patients (15.3%), it was not reported whether any complication occurred or not.

OUTCOME

Objective outcome was reported in six studies and subjective outcome in five. In the remaining three studies the outcome was reported, although it was unclear whether this was objective or subjective. Method of follow-up was by phone interview in all five studies with subjective follow-up. Recurrence was defined as 'ongoing symptoms' in one study, whereas a definition was not reported in the other four studies with subjective outcome. Objective outcome was assessed by inspection of the treated area at the natal cleft and recurrence was defined as 'ongoing disease during wound inspection' in one study, 'recurrent abscess, sinus or cellulitis after completion of therapy' and 'the presence of debris/blood in operated area' in three studies. A definition of objective recurrence was lacking in the remaining study. Mean duration of follow-up was 37.0 (SEM 35.0) months in three studies. Length of follow-up was not reported in two studies.

In the group of patients treated with laser hair removal, 366 of 378 patients (96.8%) were available for follow-up and 34 of these available patients (9.3%) had a recurrence. In patients treated with razor shaving and cream depilation, all 154 patients (100%) were available for follow up and 36 of these available patients (23.4%) had a recurrence. In the no hair-removal group, all 431 patients (100%) were available for follow-up and 85 of these available patients (19.7%) had a recurrence (Table 5).

Table 5. Outcome

	N	%
Patients available at follow-up		
Laser	366/378	(96.8)
objective	160/366	(43.7)
subjective	156/366	(42.6)
method of follow-up not reported	50/366	(13.7)
Razor shaving and cream depilation	154/154	(100)
objective	41/154	(26.6)
subjective	113/154	(73.4)
No hair removal	431/431	(100)
objective	10/431	(2.3)
subjective	421/431	(97.7)
Recurrence		
Laser	34/366	(9.3)
objective	5/160	(3.1)
subjective	26/156	(16.7)
method of follow-up not reported	3/50	(6.0)
Razor shaving and cream depilation	36/154	(23.4)
objective	2/41	(4.9)
subjective	34/113	(30.1)
No hair removal	85/431	(19.7)
objective	7/10	(70.0)
subjective	78/421	(18.5)

Abbreviation: N, number of patients.

DISCUSSION

In this systematic review, all available literature regarding the effect of hair removal on the recurrence rate of SPSD after surgical treatment was summarised. Combining the data of the included studies showed a recurrence rate of 9.3% in patients treated with laser hair removal compared to a recurrence rate of 19.7% in the group of patients with no hair removal. The recurrence rate in the group of patients using razor shaving and cream depilation was 23.4%.

Hair removal before or after the surgical treatment of SPSD to prevent recurrence has been recommended because of the suggested physiopathology of SPSD. All existing theories are based on the common idea that SPSD is an acquired condition caused by hair insertion [6,25]. Guidelines on SPSD have recommended razor depilation as a routine part of treatment after surgery [26]. This review showed that laser hair removal seemed more effective than no hair removal in preventing recurrence, but that razor and cream depilation increased the chances of recurrence compared to no hair removal. This finding was mainly influenced by the inclusion of the largest prospective case control study by Petersen et al., showing a significant difference in recurrence rate after a follow-up of 11 years in favor of the no hair removal group compared to the group of patients who removed hair by razor depilation after surgical resection of SPSD (19.7% versus 30.1%, respectively, $p = 0.01$) [17]. The reason for the difference in recurrence rate between laser and razor depilation is unclear. However, a plausible explanation for this would be that laser depilation may permanently remove hair, whereas razor or cream depilation is dependent on patient compliance which may decrease over time. Additionally, loose hairs, mainly produced by depilation techniques, might fall into the non-healed wound causing a recurrence in the short or long term. However, recent studies have suggested that hair found in pilonidal sinus tracts often originates in the occiput and is rootless, suggesting implantation after the cutting of hair on the head, in which case hair removal from the buttocks may show little benefit [27,28]. The results of this systematic review support the view that laser hair removal should be the preferred method if buttock hair removal is considered. This and other findings do need to be interpreted with caution because of the methodological problems inherent in these studies.

In the included studies, hair removal was carried out preoperatively in one study and in two studies hair was removed preoperatively, and hair removal was continued after surgery. In the remaining studies, hair removal was performed after the procedure

only. In the postoperative phase, hair removal in some studies started in before complete healing of the wound, but after complete wound healing in the other studies. Additionally, in some studies hair removal was stopped when 'most hairs were removed'. In our opinion, hair removal should be started preoperatively and continued until all visible hairs have been removed. Surgical treatment of symptomatic SPSD should only be undertaken if the natal cleft is completely freed from body hair.

With regard to the outcome, it was not reported whether the outcome was objective or subjective in three studies and the definition of recurrence was not reported in eight studies. Also, the definition of recurrence varied in the remaining studies. An obvious difference was seen between the objective and subjective recurrence rates and subjective recurrence was higher in both the laser hair removal and razor shaving/ cream depilation groups. In the group of patients with no hair removal an objective recurrence rate of 70% was seen, but this was only in one study involving ten patients and should therefore be interpreted with caution. Subjective patient opinion may be the best indicator of good surgical outcome as symptoms compromise quality of life.

A total of 14 studies were included in this systematic review. In all of them, patients were treated with some form of hair removal after surgical treatment for symptomatic SPSD. However, comparing these studies is complicated as there were obvious differences between studies with regard to the type of SPSD, i.e. primary or recurrent, kind of surgery, method and type of laser treatment, and definition of recurrence. Because of this heterogeneity among the included studies, a meta-analysis was not performed. In addition, the methodological quality of the included studies was limited as more than half of all studies had a retrospective study design and only two studies reached level of evidence 2B. However, most studies had a relatively long-term follow-up and the number of patients lost to follow-up was surprisingly small: none were lost to follow-up in most studies included. Long term follow-up is essential in patients with SPSD, as recurrences may occur up to five years after surgery [29].

CONCLUSION

This systematic review of the literature showed a reduced recurrence rate after laser hair removal (9.3%) performed to prevent recurrence after surgical treatment of SPSD, compared to no hair removal (19.7%) and razor and cream depilation (23.4%). However, the methodological quality of the included studies was limited and heterogeneity among the studies, mainly with regard to study population, type of surgical treatment and definition of outcome, was obviously present. Therefore, a high quality RCT is required to be able to make an evidence-based decision about whether or not laser hair removal reduces the recurrence rate after surgical treatment for SPSD.

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CHAPTER 4

Short-term outcomes of radical excision versus phenolisation of the sinus tract in primary sacrococcygeal pilonidal sinus disease: *a randomised controlled trial*

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ABSTRACT

INTRODUCTION

Phenolisation of sacrococcygeal pilonidal sinus disease (SPSD) seems to have advantages over radical excision; however, a randomised controlled trial (RCT) comparing both techniques is lacking. The aim of our study was to compare sinus pit excision and phenolisation of the sinus tract with radical excision in SPSD in terms of return to normal daily activities.

METHOD

This study was a single-center RCT. 50 patients who presented with primary SPSD were randomised to phenolisation and 50 patients to excision. The primary endpoint was time to return to normal daily activities. Secondary endpoints were quality of life, complaints related to SPSD, surgical site infection and wound epithelisation. Patients were treated in a one-day surgery setting. Complaints related to SPSD were evaluated and symptoms were scored by the participants on a six-point scale before surgery and patients kept a diary for two weeks on complaints related to the surgical treatment (the same scoring system as preoperatively) and pain, evaluated with a VAS. Quality of life (QoL) was measured preoperatively with a VAS and the Short Form-36 Health Survey (SF-36). At two, six and 12 weeks after surgery, patients were evaluated using a questionnaire containing the following items: patients' satisfaction (disease, compared with preoperatively, scored as cured, improved, unchanged or worsened), five complaints related to the surgical treatment (the same scoring system as preoperatively and in the diary), QoL (VAS and SF-36), and return to normal daily activities. The wound was assessed 2, 6, and 12 weeks postoperatively by one of the investigators (EF or NS), using an assessment form

RESULTS

The mean time to return to normal daily activities was significantly shorter after phenolisation (5.2 ± SD 6.6 days versus 14.5 ± 25.0 days, $p = 0.023$). two weeks after surgery, all patients in the phenolisation group and 85.4% of patients in the excision group returned to normal daily activities ($p = 0.026$). Pain was significantly lower after phenolisation at two weeks postoperatively (0.8 ± 1.0 versus 1.6 ± 1.3, $p = 0.003$). Surgical site infection occurred significantly more often after radical excision ($n = 10$, 21.7% versus $n = 2$, 4.0%, $p = 0.020$). At six and 12 weeks, complete wound epithelialisation was more frequently achieved after phenolisation (69.0% versus 37.0%, $p = 0.003$ and 81.0% versus 60.9%, $p = 0.039$, respectively).

CONCLUSION

Pit excision with phenolisation of SPSD resulted in la quicker return to normal daily activities, less pain and quicker wound epithelialisation compared to radical excision. Surgeons should consider phenolisation in patients with primary SPSD.

INTRODUCTION

Sacrococcygeal pilonidal sinus disease (SPSD) is an acquired disorder at the natal cleft with a prevalence of 8.3% [1]. SPSD is most common in men between 20 and 30 years old [2]. For patients with symptoms of chronic SPDS (pain, itching and discharge with soiling of the underwear) that interfere with their normal daily life, several treatment options have emerged. Radical surgical excision of the sinus with primary wound closure or secondary wound healing is the most often used. However, a high rate of wound complications after surgical excision often results in a long healing time and consequently a long time to return to normal daily activities [2]. Since SPSD is mainly seen in the young healthy working population, this leads to a high socio-economic burden.

A minimal invasive treatment modality for SPSD is excision of the sinus pit(s) followed application of phenol to the sinus tract. Phenol is a sclerosant agent that destroys the epithelium and debris in the sinus and is thus able to promote healing of the sinus [3]. Expected advantages of this treatment modality over radical surgical excision of SPSD are smaller surgical wounds, less pain and faster wound healing, and therefore faster recovery and return to normal activities. The previous series have shown a mean wound closure time ranging from16 to 28 days, a surgical site infection (SSI) rate of 0-8.7% and a time until return of zero to three days [3-6]. However, comparison of phenolisation with excision and primary wound closure of SPSD focusing on the difference in time until return to normal daily activities has never been investigated in a randomised controlled trial (RCT).

The aim of this RCT was to compare phenolisation of the sinus tract to radical excision of SPSD in terms of return to normal daily activities.

MATERIAL AND METHODS

STUDY DESIGN

The design of this randomised non-blinded, single-center controlled trial has been described previously [7]. Patients who presented with SPSD at the Department of surgery of the Diakonessenhuis Utrecht (the Netherlands) were considered for participation in this trial. Patient with symptoms due to chronic SPSD, age ≥ 18 years and written informed consent were eligible for inclusion in this trial. Exclusion criteria were no or

minimal symptoms related to SPSD, suspicion of an extensive subcutaneous network of sinus tracts (as these sinuses are not eligible for phenolisation), presence of pilonidal abscess and previous surgery for SPSD, i.e. recurrent SPSD.

RANDOMISATION

Patients were randomly assigned to either pit excision and phenolisation or primary surgical excision with a 1:1 allocation. Surgeons performed randomisation in the out-patient setting using sequentially numbered, sealed and opaque envelopes (contained a folded paper with "phenolisation" or "excision") which were opened one at a time.

SURGICAL INTERVENTIONS

Patients were treated in a day surgery setting under spinal or general anesthesia, depending on the preference of the patient and/or anesthesiologist. The patient was positioned in the prone position. The buttocks were separated with plasters optimising the view. The operative area was shaved. No antibiotics were administrated. The skin was cleaned with antiseptic solution (Betadin 100mg/mL). Probing via the pit(s) of the sinus was performed to determine the direction of the sinus. In the case of pit excision and phenolisation, a limited excision of the midline pit(s) was made. In addition, all off-midline openings were also excised, and the openings were used perform curettage of the tract to remove hairs, debris and granulation tissue. Hemostasis was obtained using electrocautery and external compression. The surrounding skin was protected by a coating of Vaseline (Pharmachemie BV, Haarlem, The Netherlands). Liquid phenol 85% (Meander Medical Centre, Amersfoort, The Netherlands) was injected with one or more one mL syringes, depending on the volume of the sinus tract. Phenol was left in place for one minute and aspirated afterwards. This was repeated once. The sinus was then washed out with ethanol 70% (Fresenius, Schelle, Belgium) to neutralise the remnants of phenol.

In patients who had radical surgical excision of SPSD, a limited asymmetrical incision of the skin around the sinus was made using cautery to ensure off-midline closure of the wound afterwards. All midline and off-midline orifices were included. Subsequently, the sinus was radically excised after the tract was explored with a fistula probe. The subcutaneous tissue was mobilised to be able to close the wound off-midline. After complete hemostasis, the plasters were loosened, a gentamicin-absorbed collagen sponge (Garacol 130mg sponge, EUSA Pharma (Europe) Ltd., Oxford Science Park, Oxford, United Kingdom) was positioned in small pieces on the sacrococcygeal fascia and the subcutaneous tissue was approximated off-midline with several absorbable sutures. The skin was closed with separate non-absorbable vertical mattress sutures.

Postoperatively, patients were advised to keep the area free of hairs by shaving/epilation which was also done during every postoperative outpatient clinical visit.

DATA COLLECTION AND FOLLOW-UP

Preoperatively, baseline characteristics were collected. In addition, complaints related to SPSD were evaluated and symptoms were scored by the participants on a six-point scale from 0 (no complaints) to 5 (daily complaints). Quality of life (QoL) was also measured preoperatively, both with a visual analogue scale (VAS, scored from 0, worst, to 100, best) and the Short Form-36 Health Survey (SF-36) [8]. The SF-36 is a questionnaire designed to measure health-related QoL, consisting of 36 questions comprising nine different domains of QoL. For every domain, a score between 0 and 100 can be obtained; the higher the score, the better quality of life.

During both surgical procedures, the number of midline and off-midline pits, presence of hairs in the sinus, operating time and intraoperative complications were recorded. In the case of phenolisation, the volume of the sinus was measured by the amount of phenol injected. During excision, the weight of the excised tissue and the size of the wound in three dimensions was measured.

After surgery, patients kept a diary for the first two weeks to record complaints related to the surgical treatment (the same scoring system as preoperative). In addition, pain was evaluated with a VAS, scored from 0 (no pain) to 100 (extremely painful). Use of pain medication and whether the patient was able to perform normal daily activities, such as working or doing housekeeping work, was also recorded.

At two, six and twelve weeks after surgery, a questionnaire was used to evaluate the following items: patient's satisfaction (disease, compared with preoperatively, scored as cured, improved, unchanged or worsened), five complaints related to the surgical treatment (the same scoring system as preoperative and in the diary), QoL (visual analogue scale and SF-36), pain and return to normal daily activities [9].

The wound was assessed two, six and twelve weeks postoperatively by one of the investigators (EF or NS) using an assessment form. This form included wound closure (defined as complete epithelisation of the skin), size of the wound in three dimensions in the case of no complete epithelisation and SSI [10].

ENDPOINTS

The primary endpoint was time to return to normal daily activities, measured from the day of operation. Secondary endpoints included symptoms related to, use of pain medication, QoL, time to wound closure and SSI.

STUDY OVERSIGHT

The study protocol was approved by the local Medical Ethics Committee (United Committees of Human Research, Nieuwegein, the Netherlands; reference number: NL43192.100.13) and written informed consent was obtained from all participants [7]. The study was conducted according to the Consolidated Standards for Reporting of Trials (CONSORT) guidelines and in accordance with the principles of the Declaration of Helsinki [11]. This trial was registered at the Dutch trial register (trialregister.nl, NTR4043).

STATISTICAL ANALYSIS

The sample size of this study was based on a reduction of mean time until return to normal activities from 7.5 days in the excision group to four days in the phenolisation group. A more conservative estimation had been considered for both groups as the results from the literature show a relatively broad standard deviation (SD). The sample size calculation was based on two-sided alpha level of 0.05 and a power of 80%. This leaded to a required total sample size of 100 patients (50 per group).

Data were analysed using SPSS for Windows version 23.0 (SPSS Inc., Chicago, Illinois, USA) and analysis was performed according to the intention-to-treat principle. Primary and secondary endpoints were compared between both treatment groups. Continuous values were reported as mean (± SD) or as median (range), depending on whether the data were normally distributed or not. Categorical values were reported as frequencies and percentage of the total number of patients. Statistical analysis of categorical values between both treatment groups was performed by using the Pearson Chi-square test or Fisher's exact test, where appropriate. Continuous values between both groups were statistically analysed by the independent samples *t*-test. Differences were considered statistically significant when the p value was < 0.050.

RESULTS

Between September 2013 and September 2017, a total of 565 patients with SPSD presented at the Diakonessenhuis and 100 patients were randomised for phenolisation or radical excision. Reasons for exclusion of the other patients are shown in figure 1. Phenolisation was performed in 50 and surgical excision in 46 patients as one patient in the excision group withdrew after randomisation, another did not show up for surgery, one patient was suffering from mental illness (presenting after randomisation) and the fourth patient unexpectedly moved abroad. Baseline characteristics of the included patients and intraoperative data are shown in table 1. Most patients were male and approximately two-thirds of the patients had jobs that involved working in a sitting position. No intraoperative complications occurred in either group and hairs were found in the sinus in more than eighty percent of patients. Mean operation time was significant longer in the excision group, 25.5 ± 7.6 minutes versus 18.6 ± 6.8 minutes ($p < 0.001$) (table 1).

All patients in both groups could be discharged on the same day as surgery. SSI occurred significantly more often after excision (n = 10, 21.7% versus n = 2, 4.0%, $p = 0.020$). One patient allocated to excision was readmitted four days after surgery for one day because of pain due to an infected hematoma. Removal of the stiches was required. No other postoperative complications occurred.

The postoperative diary was completed by 40 patients (79.0%) in the excision group and by 45 patients (90.0%) in de phenolisation group. Pain was scored significantly higher on days five, six and eight to fourteen in the excision group (figure 2). In addition, significantly more patients used pain killers in the excision group on days six to thirteen. Fluid discharge was reported significantly more on days often reported on day one to four after phenolisation and on days thirteen and fourteen after excision (figure 3). In both groups, the scores for itching, irritation and a burning sensation during the first two weeks were all scored below one with no significant differences between groups.

FOLLOW-UP DATA

In the excision group, a total of 41, 37 and 35 patients were available for subjective and 40, 38 and 32 patients for objective follow-up two, six and twelve weeks after surgery, respectively, in the excision group. In the phenolisation group, 40, 37 and 33 were available for subjective and 45, 40 and 27 patients for objective follow-up, respectively (figure 1).

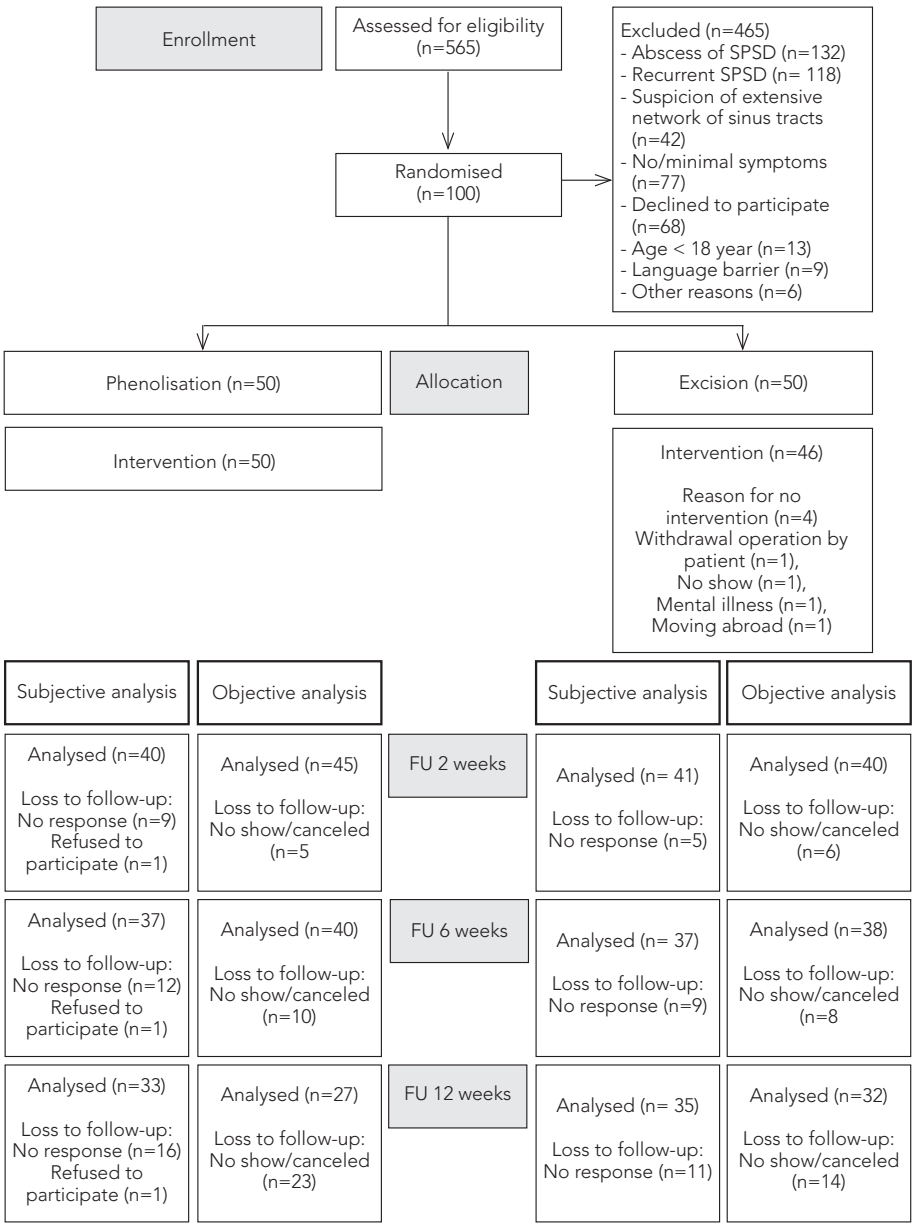

Figure 1. Flow Chart Consort
Abbreviations: SPSD, sacrococcygeal pilonidal sinus disease; FU, follow-up.

Table 1. Baseline characteristics and intra-operative data of excision and phenolisation

	Excision (n = 50)	Phenolisation (n = 50)	p-value
Male sex (%)	43 (86.0)	45 (90.0)	0.538
Age (years)	29.4 (10.1)	27.1 (7.8)	0.207
Body mass index (kg/m^2)	23.9 (2.2)	25.1 (4.7)	0.120
Smoking (%)	16 (32.0)	19 (38.0)	0.689
Family history of SPSD (%)	17 (34.0)	7 (14.0)	0.012
Working in sitting position (%)	33 (66.0)	35 (70.0)	0.505
Duration of preoperative symptoms (months)	16.4 (25.3)	13.1 (34.3)	0.599
Number of sinus pits in midline	2.6 (1.7)	3.0 (1.9)	0.205
Number of patients with off-midline sinus pit(s)			
Right side of midline (%)	6 (12.0)	10 (20.0)	0.318
Left side of midline (%)	13 (26.0)	21(42.0)	0.166
Data on surgical procedures	**n = 46**	**n = 50**	
Length of wound (mm)	56.0 (23.6)	N/A	N/A
Width of wound (mm)	27.7 (8.8)	N/A	N/A
Depth of wound (mm)	21.7 (8.1)	N/A	N/A
Weight of excised specimen (grams)	9.5 (8.9)	N/A	N/A
Volume of sinus (ml phenol)	N/A	1.2 (1.4)	N/A
Hair present in sinus (%)	38 (82.6)	43 (86.0)	0.642
Duration of operation (minutes)	25.5 (7.6)	18.6 (6.8)	0.000

Values are reported as mean ± SD, unless otherwise stated.
Abbreviations: SPSD, sacrococcygeal pilonidal sinus disease, N/A, not applicable

SUBJECTIVE RESULTS

The primary endpoint, time to return to normal daily activities, measured from the day of surgery, was 5.2 (6.6) days after phenolisation compared to 14.5 (25.0) days after excision (p = 0.023). Two weeks after surgery, all patients in the phenolisation group returned to normal daily activities, whilst this was the case in 85.4% of patients in the excision group (p =0.026 table 2).

QoL in both treatment groups, measured by VAS, was not significantly different post-operative (table 2). Compared to excision, a significantly lower pain score was reported

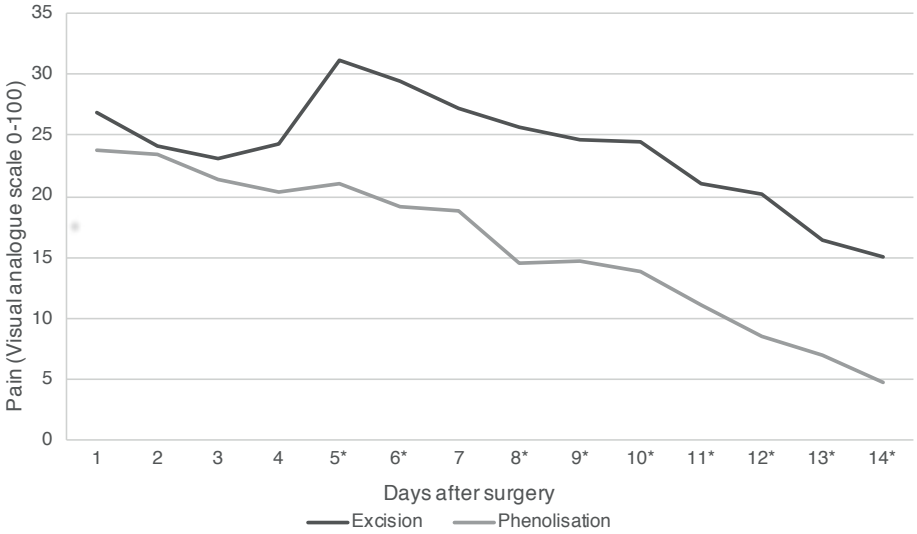

Figure 2. Pain at natal cleft after surgery

*Days showing a statistically significant difference between both groups ($p < 0.05$).

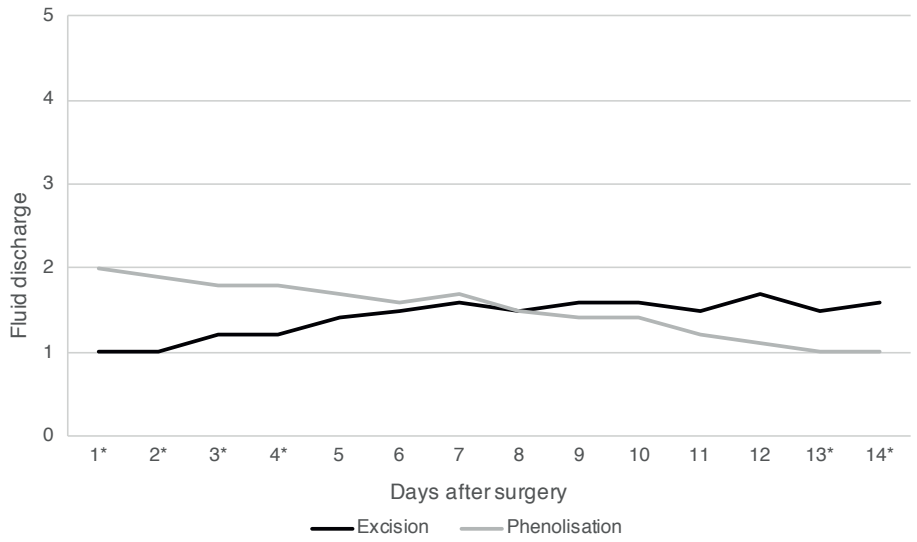

Figure 3. Fluid discharge at natal cleft after surgery

Items scored on a six-point scale from 0 (no discharge) to 5 (daily discharge).

*Days showing a statistically significant difference between both groups ($p < 0.05$).

two weeks after phenolisation. This difference disappeared after six and twelve weeks. No significant differences were seen with regard to postoperative fluid discharge, itching, irritation and burning sensation.

SF-36 scores showed a significant higher score on the domains physical, physical role and social functioning two weeks after phenolisation compared to excision (Figure 4). This difference disappeared after six weeks for physical functioning and after twelve weeks for both other domains. In accordance with pain scored by VAS, pain measured by SF-36 was significantly less two weeks after phenolisation. The other domains of the SF-36 showed no statistically significant differences.

Compared to preoperatively, 33 patients (94.3%) in the phenolisation group and 31 patients (94.9%) in the excision group reported SPSD as cured or improved twelve weeks postoperative.

OBJECTIVE RESULTS

Postoperative assessments showed a significantly higher rate of wound epithelisation after phenolisation than after excision at six and twelve weeks (Table 3). The length of the wound was significantly smaller two and six weeks after surgery in the phenolisation group, while the width and depth of the wound was only significantly smaller six weeks after phenolisation. Twelve weeks after surgery, there was no statistically significant difference in any dimension of the wound between the groups

Table 2. Pre- and postoperative patient-reported outcomes

	Excision	Phenolisation	p-value
Loss of days of normal daily activities	14.5 (25.0)	5.2 (6.6)	0.023
Return to normal daily activities			
2 weeks postoperative (%)	35 (85.4)	39* (100.0)	0.026
6 weeks postoperative (%)	35 (94.6)	37 (100.0)	0.493
12 weeks postoperative (%)	34 (97.1)	32* (100.0)	1.000
Quality of life (visual analogue scale, 0-100)			
Preoperative	67.9 (19.6)	71.1 (16.6)	0.399
2 weeks postoperative	61.5 (17.6)	64.8 (25.3)	0.505
6 weeks postoperative	73.0 (13.2)	76.2 (17.0)	0.391
12 weeks postoperative	71.1 (22.8)	75.8 (19.4)	0.361
Pain**			
Preoperative	1.5 (1.1)	1.8 (1.2)	0.279
2 weeks postoperative	1.6 (1.3)	0.8 (1.0)	0.003
6 weeks postoperative	0.6 (0.8)	0.3 (0.8)	0.136
12 weeks postoperative	0.5 (0.8)	0.5 (1.0)	0.794
Fluid discharge**			
Preoperative	1.6 (1.2)	1.8 (1.2)	0.673
2 weeks postoperative	1.6 (1.3)	1.1 (1.2)	0.069
6 weeks postoperative	0.8 (1.0)	0.4 (0.9)	0.117
12 weeks postoperative	0.5 (1.0)	0.5 (1.1)	0.916
Itching**			
Preoperative	1.3 (1.1)	1.6 (1.3)	0.271
2 weeks postoperative	0.8 (1.0)	0.8 (0.9)	0.700
6 weeks postoperative	0.5 (0.8)	0.4 (0.8)	0.664
12 weeks postoperative	0.3 (0.7)	0.6 (1.1)	0.196
Irritation**			
2 weeks postoperative	0.7 (0.8)	0.4 (0.7)	0.056
6 weeks postoperative	0.3 (0.5)	0.2 (0.6)	0.294
12 weeks postoperative	0.2 (0.7)	0.6 (1.1)	0.125
Burning sensation**			
2 weeks postoperative	0.3 (0.6)	0.2 (0.5)	0.477
6 weeks postoperative	0.1 (0.2)	0.1 (0.3)	1.000
12 weeks postoperative	0.1 (0.5)	0.3 (0.8)	0.178

Values are reported as mean and ± SD, unless otherwise stated.
* One patient did not respond to this question
** Items were scored on a six-point scale from 0 (no complaints) to 5 (daily complaints).

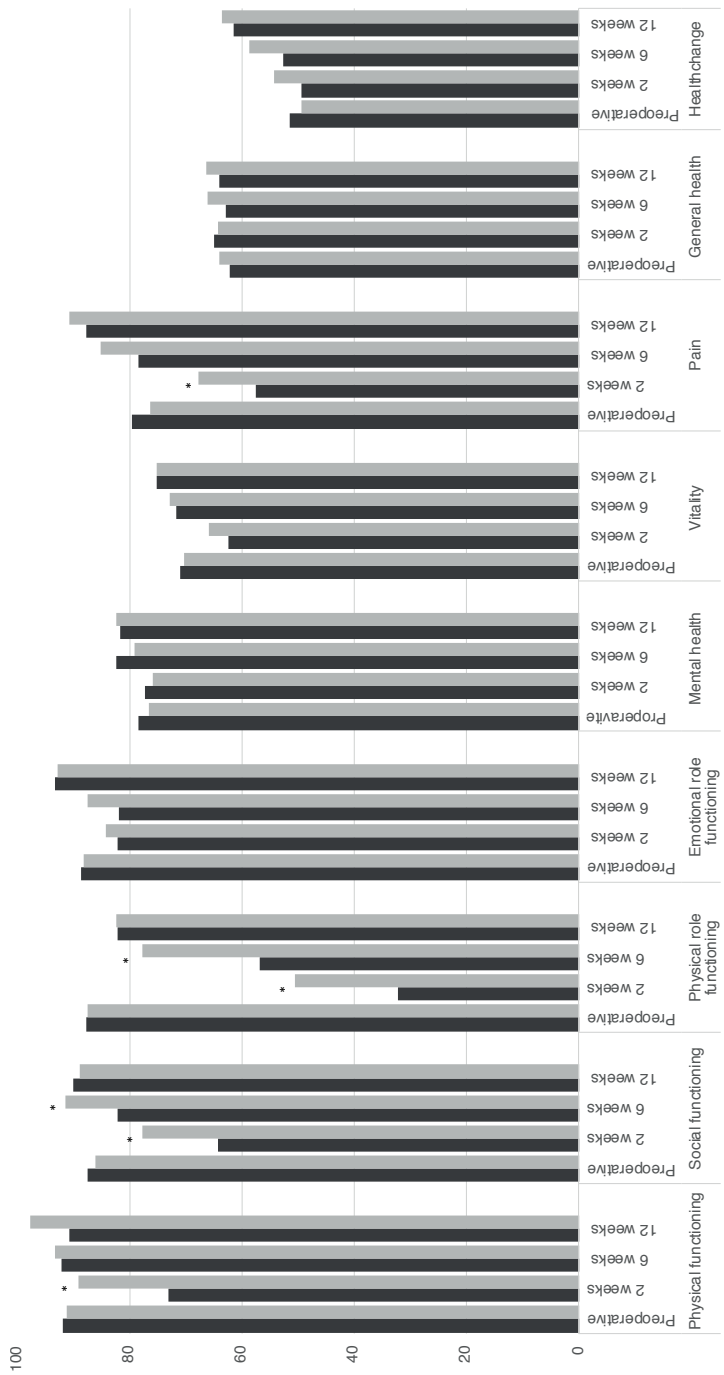

Figure 4. 36-Item Short Form Survey (SF-36), 2, 6 and 12 weeks after surgery
*Items showing a statistically significant difference between both groups ($p < 0.05$).

Table 3. Objective postoperative data

	Excision	Phenolisation	p-value
Number of patients with wound epithelization			
2 weeks postoperative (%)	6/43 (14.0)	6/45 (13.3)	0.932
6 weeks postoperative (%)	17/46 (37.0)	29/42 (69.0)	0.003
12 weeks postoperative (%)	28/46 (60.9)	34/42 (81.0)	0.039
Length of wound (mm)			
2 weeks postoperative	61.1 (31.6)	14.6 (13.2)	< 0.001
6 weeks postoperative	32.1 (26.3)	8.2 (12.4)	0.001
12 weeks postoperative	28.3 (23.0)	10.1 (10.0)	0.064
Width of the wound (mm)			
2 weeks postoperative	6.7 (5.4)	4.7 (3.4)	0.069
6 weeks postoperative	6.8 (4.2)	3.9 (3.8)	0.019
12 weeks postoperative	6.6 (4.4)	5.4 (4.9)	0.586
Depth of the wound (mm)			
2 weeks postoperative	9.1 (8.5)	8.7 (11.2)	0.894
6 weeks postoperative	8.0 (7.4)	3.6 (3.2)	0.048
12 weeks postoperative	4.8 (3.3)	4.4 (3.2)	0.837

Data are shown as mean ± SD, unless otherwise stated.

DISCUSSION

This RCT comparing phenolisation with radical excision in SPSD showed a significantly reduction of time until return normal daily activities in favor of phenolisation. In addition, the operation time in the phenolisation group was significantly shorter, patients had significantly less pain (first two weeks postoperative) and wound epithelisation was significantly quicker.

The minimal invasive character of phenolisation resulted in an earlier return to normal daily activities. The wound was smaller which led to less postoperative pain, especially during the first two weeks. Another advantage was the quicker epithelisation at the natal cleft because of the small size of the wounds. Excision of SPSD is associated with lengthy wound healing due to the location close to the anus, an area with a lot of tension on the skin and a difficult location for wound care and hygiene. Complications such as wound infection and wound dehiscence might result in long-lasting symptoms, like fluid discharge and pain. In addition, this trial showed that phenolisation is safe as no major complications occurred. Minor complications after phenolisation, such as abscesses,

occurred in 4% of the patients in the current study and have been described in the literature with a prevalence of 9% [12].

Despite the high prevalence of SPSD, there is no consensus about which treatment modality is the best. Although radical excision with primary wound closure with or without flap, including Bascom's, Limberg or V/Y-flap, are the most commonly used procedures, there are increasing. Reports of the use of minimally invasive procedures. In addition to phenolisation, another minimal invasive treatment modality for SPSD is 'endoscopic pilonidal sinus treatment' (EPSiT). In this procedure, a fistuloscope is introduced through an external opening and the sinus cavity is ablated under direct vision. Meinero et al. reported, in a prospective cohort study, that the mean time to complete wound healing was 26.7 days, mean time to return to work two days, the recurrence rate 5% and a return of QoL to preoperative level [13]. In the study by Giarratano et al., mean time to return to work after EPSiT was six days, mean wound-healing time was 26 days and the recurrence rate 4% [14]. Laser ablation treatment of the pilonidal sinus is another recently developed minimal invasive technique. In this procedure, the sinus tracts are completely cleaned as in the phenolisation technique and subsequently the fistula tract(s) are destroyed by a laser probe. Only some small cohort studies on this technique have been published so far [15-17]. The laser technique seems to be safe. Wound infections were reported in 5-7% of patients. The recurrence rate was 3-10% after a follow-up of 15 months. Randomised trials on the laser technique have not yet been published. Another minimal invasive technique was described by Salih et al. who compared surgical excision and primary wound closure versus injection a mixture of petroleum jelly (Vaseline), henna powder (*Lawsonia inermis*) and tetracycline in the sinus cavity [18]. This mixture has been suggested to have sclerosing, antimicrobial, and enhanced wound-healing properties. After six weeks of follow-up, complete wound healing was achieved in 94% of patients after one injection as opposed to 89% of patients who had excision. Patients immediately returned to work after injection, used analgesic for one day and in 0.5% of cases they developed a wound infection. Fibrin glue also shows promise as a minimally invasive procedure. In a recent report, patients with primary or recurrent SPSD were treated in a median of nine minutes with healing in 126/130 (96.9%) of patients after two rounds of treatment [19].

Two other randomised trials comparing phenolisation and radical excision have been published, but with different end points to this study [20]. In the study by Calikoglu et al., excision of SPSD was followed by secondary wound healing and the primary endpoint was time to complete wound healing. The pain-free mobilisation was 0.8 hours after phenolisation and 9.3 hours after excision ($p < 0.001$). No data on returning

to daily activities have been reported. Pain was significantly lower after phenolisation, corresponding with our findings. Topuz et al. compared crystallised phenol treatment with surgical excision and primary wound closure in a randomised trial including 40 patients [21]. The mean number of days off work was 0.15 days after phenolisation and 16.2 days after excision. After 23.7 and 32.1 days after phenolisation and excision respectively, a significant difference in QoL in favor of phenolisation was reported.

There are some limitations of this study that should be considered. First, patients and physicians were not blinded for the type of treatment. However, due to the nature of the procedure with a visible difference at the natal cleft, blinding was not possible. Second, the loss to follow-up was relatively large. After twelve weeks, 76% of patients were available for subjective and 70% for objective follow-up in the excision group. In the phenolisation group, 66% and 54% were available for follow-up twelve weeks after surgery, respectively. In our opinion, this could be explained by the type of population, including young healthy working people focusing on daily and social activities and paying less attention for their health. Missing data during follow-up has possibly resulted in worse outcomes, in both groups, as it is probable that patients without complaints are more likely to cancel their visit. Third, the recurrence rate was not reported. In addition to short-term results, recurrence rate is an important outcome in the treatment of SPSD. Since our follow-up was twelve weeks, we were not able to reliably report recurrence rate as this requires a follow-up of at least twelve months. The primary endpoint in this study was the time to return to normal daily activities. As mentioned above, this primary endpoint was chosen as all advantages of phenolisation techniques, i.e., less pain, small wounds, and fast wound healing, contribute to it. We did not choose recurrence rate between surgical excision and phenolisation is very small [22,23] and, therefore, would need a very large study to be adequately powered for recurrence as an endpoint [7]. We did not classify pilonidal sinus disease in our patient group [24]. Finally, only patients with primary SPSD were included and patients with suspicion of an extensive subcutaneous network of sinus tracts. Patients with a pilonidal sinus abscess or recurrent SPSD were not included in this trial, and therefore, the results of this trial are not transferable to those patient groups.

CONCLUSION

Phenolisation is a safe and effective treatment modality associated with less post-operative pain and faster wound epithelisation.

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CHAPTER 5

Long-term outcome of radical excision vs. phenolisation of the sinus tract in primary sacrococcygeal pilonidal sinus disease: a randomised controlled trial

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Submitted

ABSTRACT

INTRODUCTION

The aim of this randomised trial was to compare the long-term outcome between pit excision and phenolisation of the sinus tracts versus radical excision with primary wound closure as treatment for sacrococcygeal pilonidal sinus disease (SPSD).

METHODS

Phenolisation of SPSD has shown to have advantages over radical excision with regard to short-term outcome, however, long-term outcomes are essentially lacking. A total of 96 patients with primary SPSD were randomised; 50 patients underwent phenolisation and 46 radical excision. Long-term outcome was obtained by an online questionnaire, including quality of life (Short-Form-36), recurrence of SPSD and SPSD-related complaints.

RESULTS

A total of 74 patients (77.1%) completed the questionnaire; 36 patients after phenolisation and 38 after excision. Mean (±standard deviation) time to follow-up was 48.4 (±12.8) and 47.8 (±13.5) months, respectively. There was no significant difference between both groups with regard to quality of life and SPSD-related symptoms. In the phenolisation group, two patients (5.6%) developed a recurrence and one patient (2.6%) in the excision group ($p = 0.604$). Five patients (13.9%) in the phenolisation group required a second phenolisation treatment in order for the wound to completely heal. The impact of treatment was significantly less after phenolisation ($p = 0.010$).

CONCLUSIONS

Recurrence rate and quality of life were not significantly different after a four-year period comparing phenolisation and radical excision with primary wound closure for primary SPSD. The impact of the whole treatment was significantly less after phenolisation, however, 14% of patients required a second phenolisation treatment to reach complete wound healing.

INTRODUCTION

The optimal treatment for sacrococcygeal pilonidal sinus disease (SPSD) is still a widely discussed topic with many different surgical treatment options available [1]. Since complications like wound infections and delayed wound healing are still a major problem after surgery, a golden standard to treat patients with SPSD does not currently exist [2]. However, a trend toward minimally invasive techniques, such as phenolisation, laser and endoscopic treatment is seen more and more [3-7]. The aim of these minimally invasive treatments is to reduce the risk of wound infections and delayed wound healing, and thereby the disease burden and subsequent socio-economic damage [1].

Pit excision followed by phenolisation of the sinus tract(s) is a minimally invasive technique to treat patients with SPSD. Phenol is a liquid with sclerosing properties and can therefore be used to destroy remaining debris and epithelisation in the sinus tract(s) [8,9]. Recently, we reported the short-term results of a randomised controlled trial comparing local excision with primary off-midline wound closure versus the phenolisation technique for SPSD. The results showed that the phenolisation technique resulted in smaller surgical wound(s), less pain and discomfort, shorter wound healing times and less loss of days to do normal daily activities when compared to the excision method [10]. Another randomised trial comparing phenolisation versus radical published in 2017 reported comparable short-term outcomes [11]. Additionally, there was no significant difference in the recurrence rate between both treatments after more than three years of follow-up reported in this trial. However, in this study by Calikoglu et al., excision was followed by secondary wound healing and no long-term data are available from randomised trials comparing the phenolisation technique with radical excision with primary wound closure for SPSD, especially with regard to recurrence rate.

The aim of this randomised controlled trial was to compare the long-term outcome of radical excision and primary wound closure and phenolisation of the sinus tract for primary SPSD, focusing on recurrence rate.

MATERIAL AND METHODS

The design of this randomised non-blinded, single center controlled trial has been described previously. The trial was approved by the local Medical Ethics Committee, conducted in accordance with the principles of the declaration of Helsinki and registered

in the Dutch Trial Register (NTR4043). Patients were considered for inclusion if they presented with primary SPSD at the Department of Surgery in the Diakonessenhuis Utrecht, the Netherlands. Inclusion criteria were chronic symptomatic SPSD, age of at least 18 years old and written informed consent. Patients were excluded if they had no or minimal symptoms of SPSD, an acute abscess, recurrent SPSD/previous surgery for SPSD or a suspected extensive subcutaneous network of sinus tracts, as these latter patients would not be eligible for phenolisation as a treatment. As calculated based on the primary short-term end-point "loss of days of normal daily activities", as described in the protocol of this randomised trial [12], 50 patients were randomly assigned to radical excision and 50 patients to phenolisation (1:1 allocation) between 2013 and 2017. Eventually, a total of four patients in the excision group did not receive excision; one patient withdrew from the study after randomisation, another patient was diagnosed with severe mental illness after randomisation, one patient moved abroad and the last patient did not show up for the operation. All patients in the phenolisation group were accordingly treated and there was no cross-over in either of the groups.

SURGICAL INTERVENTIONS

Pit excision with phenolisation of the sinus tract was performed under spinal or general anesthesia with the patient in prone position. No prophylactic antibiotics were used. The sinus pit(s) were probed to determine the course of the sinus tract(s), followed by limited excision of the sinus pit(s) in the midline. Drainage openings, if present outside the midline, were also excised with a limited margin. A curette was used to completely clean the sinus tract(s) and to remove granulation tissue, debris and hair. Subsequently, the skin around the sinus pit(s) was protected by applying Vaseline (Pharmachemie BV, Haarlem, The Netherlands) and liquid phenol 85% (Meander Medical Centre, Amersfoort, The Netherlands) was injected into the sinus with 1mL syringes until the sinus was completely filled. Phenol was removed after one minute and fresh phenol was injected for another minute. Phenol was removed again and neutralised and washed out using ethanol 70% (Fresenius, Schelle, Belgium). The surrounding skin was cleaned and the wound(s) were covered with absorbing bandage. Patients were discharged the same day.

Radical excision was performed in the same setting and position as the phenolisation technique. Also, no oral or intravenous antibiotics were used. The sinus pit(s) were probed to determine the course of the sinus. Radical excision of the sinus was performed including all midline sinus pits and off-midline drainage openings, if present. Excision was performed asymmetrically to the left or right side of the midline

to allow off-midline wound closure. After mobilisation of the subcutaneous tissue, a gentamicin-absorbed collagen sponge (garacol 130mg sponge, EUSA Pharma (Europa) LTD., Oxford Science Park, Oxford, United Kingdom) was placed on the sacrococcygeal fascia in small pieces. Subsequently, the wound was closed off-midline with absorbable sutures in different layers and the skin was also closed off-midline with non-absorbable sutures.

All surgical procedures were performed by two surgeons (NS and EF). Several surgical procedures were performed jointly by both surgeons prior to the start of this trial to ensure that both the phenolisation technique and radical excision were identically performed in the patients included in this trial.

LONG-TERM DATA COLLECTION

After a follow-up of at least two years after the surgical treatment for SPSD, all patients who were included in this study were contacted by phone call or email. After consent was obtained, an online questionnaire was emailed, including questions about SPSD-related complaints, quality of life and patient satisfaction. SPSD-related complaints included current physical symptoms at the natal cleft, such as pain, itching and fluid discharge, and all three were separately scored on a six-point scale from 0 (no complaints) to 5 (daily complaints). The Short Form 36 (SF-36) was used to evaluate quality of life. The SF-36 is specifically designed to measure Quality of Life (QoL) in patient related healthcare, containing 36 questions about nine different domains of QoL [13]. Patient satisfaction was assessed with questions about the whole personal impact of the treatment, scored on a visual analogue scale (0-100, a lower score indicates less impact), and whether they would undergo the same treatment again.

DEFINITION OF RECURRENCE

SPSD was defined as recurrence when objectified by a physician after previous complete wound healing after the index operation. All patient's notes were reviewed to identify an objectified recurrence or an additional surgical procedure for recurrence after the index operation in our hospital. In addition, patients were asked in the questionnaire whether they underwent surgery for recurrent SPSD in another hospital after the index operation. Since a second phenolisation procedure in case of non-complete wound healing was part of the treatment protocol in the phenolisation group, as previously described in the study protocol, a second phenolisation treatment in the phenolisation group was not considered recurrence [12]. Also, patients were asked in the questionnaire whether they had the impression of recurrent SPSD if this was never

objectified by a physician. Patients who indicated in the questionnaire that they had the impression of a recurrent SPSD that was never objectified by a physician received an invitation for an out-patient clinical visit to objectify whether there was actually a recurrence. Patients were scored as no recurrence if they denied the impression of recurrent SPSD in the questionnaire and never had an objectified recurrence or second procedure for recurrent SPSD (with the exception of a second phenolisation treatment in the phenolisation group).

STATISTICAL ANALYSIS

SPSS for Windows Version 23.0 (SPSS Inc., Chicago, Illinois, USA) was used to analyse the data. Depending on whether continuous data were normally distributed or not, data were reported as mean (standard deviation, SD) or median (range), respectively. Categorical data were reported as frequencies with percentages. Outcome parameters were compared between the surgical excision group and phenolisation group. Patients were analysed in the excision or phenolisation group, according to intention to treat principle. Pearson X^2 test or Fischer's exact test were used for statistical analysis of categorical values, and continuous data between both groups were statistically analysed by using the independent samples t-test. A p-value <0.05 was considered statistically significant.

RESULTS

After a follow-up of at least two years after surgical treatment for SPSD, all 96 patients who underwent either surgical excision or phenolisation for primary SPSD after randomisation were contacted by phone call or email; three patients could not be reached and one patient refused participation. A total of 92 patients were sent an online composite survey after consent was obtained. The survey was completed by 74 patients (77.1%); 36 patients in the phenolisation group and 38 patients in the excision group. The remaining 18 patients did not complete the questionnaire after repeated contact (Figure 1). Baseline characteristics of the patients who were available for long-term follow-up are reported in table 1. The mean time to follow-up was 48.4 (±12.8) months in the phenolisation group and 47.8 (±13.5) months in the excision group.

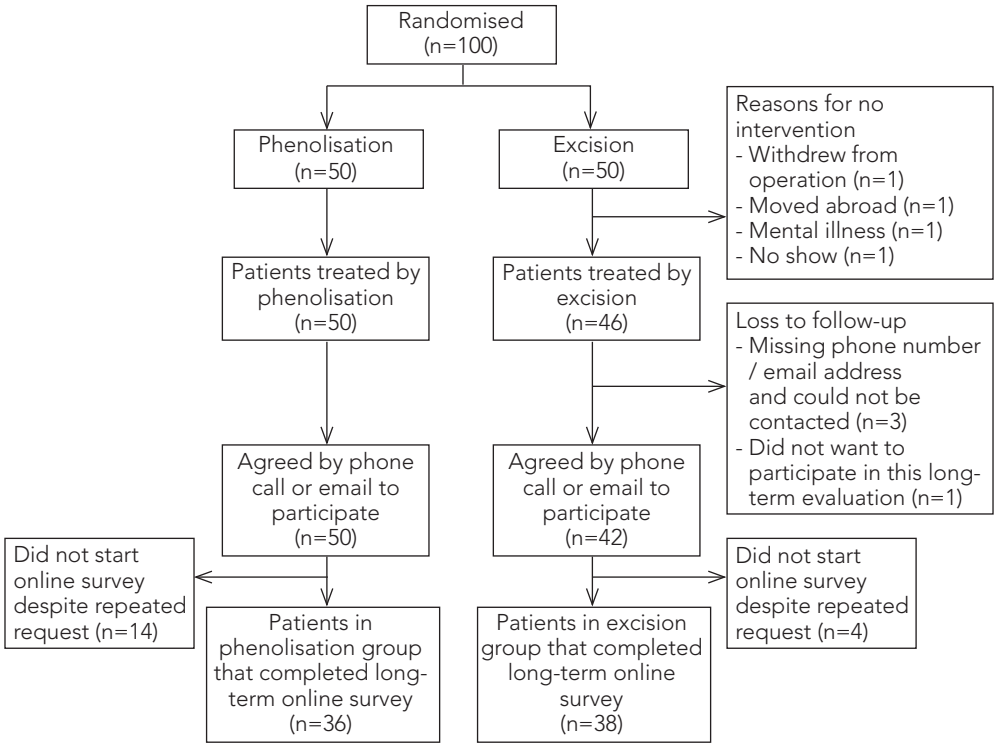

Figure 1. Flowchart of patients included in long-term follow-up

Table 1. Baseline characteristics

	Phenolisation group (n = 36)	Excision group (n = 38)
Male sex (%)	31 (86.1)	32 (84.4)
Age (years)	33.1 (±8.3)	34.3 (±11.0)
Body mass index (kg/m^2)	26.1 (±4.8)	24.7 (±2.1)
Smoking (%)	6 (16.7)	9 (23.7)
Family history of SPSD (%)	6 (16.7)	14 (36.8)
Working in sitting position (%)	29 (80.6)	26 (68.4)
Duration of preoperative symptoms (months)	16.0 (±40.5)	16.2 (±21.9)
Duration of follow-up (months)	48.4 (±12.8)	47.8 (±13.5)

Values are reported as mean (± standard deviation), unless otherwise stated.
Abbreviation: SPSD, sacrococcygeal pilonidal sinus disease

RECURRENCE

In the phenolisation group, two patients underwent reoperation for a recurrence (5.6%); one patient underwent surgical excision for recurrent SPSD with off-midline closure 24 months after the index operation and the other patient had recurrence after two subsequent phenolisation treatments and radical excision with rhomboid flap reconstruction was performed 27 months after the index operation. Wounds in both patients were completely healed at follow-up. In addition, another five patients (13.9%) in the phenolisation group underwent a second phenolisation treatment as the wounds and sinus did not heal after the first treatment. Complete wound healing was reached after the second phenolisation treatment in all five patients and no recurrence of SPSD occurred during follow-up. Since a second phenolisation procedure was part of the treatment protocol in the phenolisation group, those five patients who did not have a recurrence after the second phenolisation treatment were not considered to have experienced recurrence, as defined in our study protocol.

In the excision group, one patient (2.6%) had additional surgery for a recurrence 9 months after the index operation. The recurrence was treated by the phenolisation technique. The wound was completely healed after phenolisation and no recurrence occurred during follow-up.

No other patients developed an objectified recurrence during follow-up after the index operation in the excision or phenolisation group. In addition, none of the patients in either group indicated in the questionnaire the impression of recurrent SPSD. So, according to the definition, there was a recurrence in two patients (5.6%) in the phenolisation group and in one patient in the excision group (2.6%) ($p = 0.604$).

SUBJECTIVE LONG-TERM OUTCOME

Symptoms related to SPSD, including pain, fluid discharge and itching at the natal cleft, were not significantly different between both treatment groups at long-term follow-up (Table 2). In both groups, there was a significant decrease in severity of these three symptoms at long-term follow-up compared to preoperatively ($p < 0.001$ for all 3 symptoms in both groups). The impact of the whole treatment for SPSD was significantly less after phenolisation compared to excision (Table 2). In addition, 30 patients (83.3%) in the phenolisation group would undergo the same treatment again versus 22 patients (57.9%) in the excision group ($p = 0.024$). With regard to quality of life, there was no significant difference in any of the nine domains of the SF-36 between both treatment groups at long-term follow-up (Figure 2).

Table 2. Subjective long-term outcome

	Phenolisation group (n = 36)	Excision group (n = 38)	p-value
Pain at natal cleft*			
Preoperative	1.6 (±1.2)	1.6 (±1.1)	0.970
Follow-up	0.2 (±0.5)$^{+}$	0.3 (±0.5)$^{+}$	0.490
Fluid discharge at natal cleft*			
Preoperative	1.5 (±1.0)	1.7 (±1.2)	0.423
Follow-up	0.2 (±0.5)$^{+}$	0.1 (±0.3)$^{+}$	0.545
Itching at natal cleft*			
Preoperative	1.2 (±1.1)	1.3 (±1.2)	0.700
Follow-up	0.2 (±0.5)$^{+}$	0.3 (±0.6)$^{+}$	0.278
Personal impact of the whole treatment (VAS, 0-100)	29.2 (±25.8)	48.2 (±33.2)	0.010
Patients that would undergo the same treatment again (%)	30 (83.3)	22 (57.9)	0.024

Values are reported as mean (±standard deviation), unless otherwise stated.
*Items were scored on a six-point scale from 0 (no complaints) to 5 (daily complaints).
$^{+}p < 0.001$ compared to preoperative value.
Abbreviation: VAS, visual analogue scale (the lower the score, the less the impact)

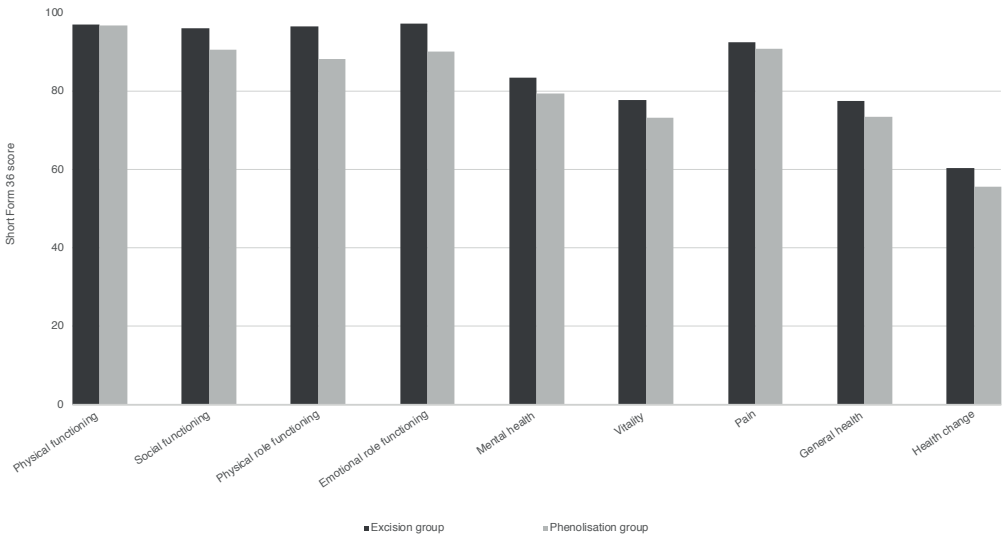

Figure 2. Short Form 36 (SF-36) at long-term follow-up

DISCUSSION

No significant difference in recurrence rate and quality of life between pit excision and phenolisation of the sinus tracts and radical excision with primary wound closure for primary SPSD was found after a follow-up of four years. However, the impact of the whole treatment was significantly less after phenolisation compared to radical excision, but 14% of patients in the phenolisation group required a second phenolisation treatment to reach complete wound healing.

The personal impact of the treatment for SPSD was less in the phenolisation group compared to radical excision and in addition, a remarkably higher percentage of patients in the phenolisation group would undergo the same treatment again (83% versus 58%). Smaller wounds, shorter wound healing times and less pain during the first two weeks after the operation, as reported in the short-term outcome of our randomised controlled trial, have probably contributed to this finding [10]. However, almost 14% of the patients in the phenolisation group required a second phenolisation treatment and that could influence the impact of the whole treatment for SPDS. Subgroup analysis of the patients who required a second phenolisation treatment showed a mean visual analogue scale (VAS) score for the impact of the whole treatment comparable to the VAS-score of the total phenolisation group, although this subgroup may be too small to draw any definitive conclusions. However, the short-term advantages of phenolisation seem to outweigh the downside of a second phenolisation procedure that might be required to reach complete wound healing.

Although this is, to our knowledge, the first randomised controlled trial comparing the phenolisation technique and radical excision with primary wound closure in SPSD, some other studies have been published also reporting on the recurrence rate after phenolisation. Calikoglu et al. published the only other available randomised trial comparing phenolisation and surgical excision. However, after surgical excision they awaited secondary wound healing instead of performing primary wound closure. After a mean follow-up of approximately 40 months, there was no significant difference in recurrence rate reported between both treatment options: 18.6% after phenolisation and 12.5% after surgical excision [11]. Akan et al. reported a retrospective study comparing pit excision and phenolisation versus excision combined with a Limberg flap. Recurrence rate was 8% in the phenol group versus 6% in the excision group after a follow-up of 26 months, with no significant difference between both groups ($p = 0.50$) [14]. Bayhan et al. also reported a retrospective study comparing phenol application

and excision with a modified Limberg flap. They reported a recurrence rate of 18.9% after phenolisation after a mean follow-up of 16.5 months and a recurrence rate of 6.8% 17.9 months after excision, although this was not statistically significant [15]. A study from Gonullu et al. retrospectively analysed 100 patients after phenol treatment (mean follow-up 34 months) versus 100 patients after complete excision with Limberg flap repair (mean follow-up 44 months). Three patients after phenol treatment had a recurrence versus five patients in the excision with flap repair group. No significant difference was found between both treatment groups ($p = 0.721$) [17]. As reported in all these studies, there was also no significant difference in recurrence rate between the phenolisation and excision group in the current study. However, the primary endpoint of the current study was loss of days of normal daily activity, as described in the short-term results of our study and therefore, this study was not powered for recurrence rate [10].

Other studies also reported recurrence rates for phenol application, however without comparing it with another treatment modality for SPSD. Olmez et al. reported a recurrence rate of 2.5% in 83 patients after a mean follow-up of 25.7 ± 8.5 months, although recurrence was not defined in their study. In addition to recurrence, they also reported treatment failure of 13.3%, which was defined as unhealed wounds two months after surgery or recurrence of symptoms identified in an outpatient setting or by phone call [17]. Another study applied phenol in 143 patients with SPSD with a mean follow-up of 24 months. A recurrence rate of 8.3% was reported [9]. Topuz et al. reported no recurrence in 20 patients who received phenolisation as first treatment for SPSD. However, the mean time to follow-up was not reported in the study [18]. In our study, we used at least two years of follow-up to assess whether a recurrence occurred or not after phenolisation or excision for SPSD. In our opinion, this is the least follow-up time needed to determine whether SPSD has been completely cured. In addition, a clear definition of recurrence is often lacking in the studies published in the literature. We defined recurrence as objectified by a physician or an additional surgical procedure after the index operation. In addition, we asked patients whether they had the impression of a recurrence that was not previously objectified by a physician. In that case, we would have invited the patient to evaluate whether there was an objective recurrence, but this was not the case in any of the patients available for long-term follow-up. Ideally, we had invited all patients to assess whether there was an objective recurrence, however, most patients were not willing to visit the out-patient clinic. Therefore, we decided to ask whether the patients had the impression of a recurrence and only asked them to the outpatient clinic if the answer was positive. This was, to our

opinion, acceptable, as the general policy in patients with SPSD is to only treat SPSD if the related symptoms are influencing quality of life. So, in the decision to proceed to surgery, symptoms related to SPSD are more important than an objective recurrence without complaints. Therefore, we defined patients without a subjective impression of a recurrence as no recurrence in the current study.

In the phenolisation group in the current study, 17% of patients needed a second phenolisation procedure. This was required in a slightly higher percentage of patients compared to the randomised trial by Calikoglu et al., in which 11% underwent a second phenolisation procedure [11]. However, in most patients in the current study, no recurrence occurred after the second procedure (5 out of 6 patients, 83%), whilst that was the case in only half of the patients in the study by Calikoglu et al. Since the absolute number of patients who required a second phenolisation procedure is very small in both studies, it is difficult to compare the recurrence rate in this subgroup of patients between both studies. Dag et al. previously described that a second phenolisation procedure has an acceptable chance of success justifying the application of a second phenolisation procedure as was done in the current study [8]. However, Dag et al. reported that in the case of three or more phenolisation procedures almost all will fail and more than two phenolisation procedures should not be performed.

This study has some limitations. First, the response rate was 77%, although the patients were repeatedly contacted by email and phone to participate. The less than 100% response rate could probably have led to an overestimation of the recurrence rate as it is, in our opinion, more likely that patients without complaints did not participate. Second, patients and physicians were not blinded in this study. Both surgical procedures have different appearances at the natal cleft, so blinding for the patient and assessor was not possible. Third, the primary endpoint of this study was loss of days of normal daily activities, as described in the short-term results of this study. So, power calculation was not based on recurrence rate, the most important outcome parameter for long-term follow-up after surgery for SPSD. However, as already described in the study protocol, recurrence rate as primary end-point would require the inclusion of too many patients to reach statistical significance and is unattainable to our opinion [12]. The difference in recurrence rate as found in the current study between phenolisation and excision (5.6% versus 2.6%, respectively) was not statistically significant, but this is, to our opinion, also not relevant from a clinical point of view with two patients versus one patient with a recurrence, respectively. Finally, patients with recurrent SPSD were not included in this study. Although the results of the current study are strictly

only applicable in patients with primary SPSD, it is very likely that the results are also valid in patients with recurrent SPSD. However, the phenolisation technique should be performed in an additional cohort of patients with recurrent SPSD to prove equal outcomes as for primary SPSD, as reported in the current randomised trial.

CONCLUSION

Pit excision with phenolisation of the sinus tract has already been proven as a save treatment option for primary SPSD with less postoperative pain, shorter wound healing times and less loss of days of normal daily activity compared to radical excision with primary wound closure. The current study showed no significant difference with regard to recurrence rate and quality of life between both treatment options after long-term follow-up. Although almost 14% of the patients in the phenolisation group required an additional phenolisation procedure to reach complete wound healing, patients reported the total personal impact of the phenolisation treatment as less compared to excision. Therefore, pit excision with phenolisation should be considered primary treatment option for primary SPSD.

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CHAPTER 6

Phenolisation of the sinus tract in recurrent sacrococcygeal pilonidal sinus disease: *a prospective cohort study*

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ABSTRACT

INTRODUCTION

Phenolisation is a minimally invasive treatment option in patients with primary pilonidal disease. However, most studies focus on patients with primary pilonidal sinus disease, while data of patients with recurrent pilonidal disease are very scarce. The purpose of this study was to evaluate phenolisation of the sinus tract in patients with recurrent pilonidal sinus disease after previous surgery for SPSD.

METHODS

This single-center prospective cohort study included 60 patients with recurrent pilonidal disease. Loss of days of normal daily activities, surgical site infection, wound epithelisation, quality of life and complaints related to pilonidal disease were postoperatively assessed.

RESULTS

A total of 57 patients (95%) were treated with phenolisation and the median daily loss of days of normal activities was 5.0 (1.0– 12.0) days. 51 patients (89.5%) resumed normal daily activities after two weeks. Surgical site infection occurred in five patients (8.8%). Compared to preoperative scores, quality of life was significantly higher after 12 weeks ($p = 0.014$) and pain and itch scores were lower after six and 12 weeks ($p \leq 0.005$). Wounds were completely healed in 45 of 51 patients (89.8%) who were available after 12 weeks of follow-up.

CONCLUSION

Phenolisation for recurrent pilonidal disease is safe with a median complete return to daily activities within five days and complete wound healing after three months in 90%. Therefore, phenolisation should be considered as a treatment option in patients with recurrent pilonidal sinus disease.

INTRODUCTION

Sacrococcygeal pilonidal sinus disease (SPSD) has a high incidence [1]. Different treatment modalities are currently applied for SPSD. In the case of a tense painful abscess, a simple incision and drainage would be sufficient in most cases. However, in patients with symptomatic chronic SPSD, excision with or without primary wound closure is a very often applied definitive management procedure. As a result, wound dehiscence with longer wound healing time is a major problem after this type of surgery. Besides, recurrence is also an important issue in patients surgically treated for SPSD as recurrence rates up to 68% have been reported ten years after surgery, depending on the type of surgery performed [2]. Repeated treatments in the case of recurrence with long recovery times could easily have a large impact on patients' quality of life. Therefore, recently published literature is more focused on minimally invasive treatment modalities such as phenol, laser or endoscopic treatments. In these minimally invasive treatments, wounds are smaller and therefore, wound healing time is shorter.

Phenolisation is a minimally invasive treatment modality for patients with symptomatic primary chronic SPSD that has shown to be safe and effective in patients with primary SPSD. Two randomised trials comparing phenol application and excision for primary SPSD have been performed so far, showing less postoperative pain, faster return to normal daily activities, quicker wound healing as well as equal surgical site infection and recurrence rates after phenolisation [3,4]. Several additional cohort studies on phenol application on primary SPSD have been published showing comparable results. However, studies evaluating phenol application in patients with recurrent SPSD after previous surgical excision are very scarce with only two published cohort studies only including 36 and 26 patients, respectively [5,6].

In this prospective cohort study, we evaluated phenolisation of the sinus tract in patients with recurrent SPSD after previously undergoing surgery for SPSD.

MATERIAL AND METHODS

STUDY DESIGN

This was a prospective single-center cohort study conducted in Diakonessenhuis Utrecht (the Netherlands). Patients were considered for participation in this study if they presented with SPSD at the department of surgery. Patients with recurrent SPSD after one or more previous surgical treatments for SPSD and age ≥ 18 years were eligible for inclusion in this study. Patients who presented with no or minimal symptoms related to SPSD, an abscess due to SPSD, a large network of subcutaneous sinus tracts (patients with these conditions are not eligible to undergo phenolisation) or primary SPSD were excluded. This study was approved by the Medical Ethical Committee in Utrecht.

SURGICAL INTERVENTIONS AND DATA COLLECTION

Data about body mass index, smoking, working position, quality of life (QoL), family history, duration of symptoms related to SPSD and previous surgical intervention(s) for SPSD were prospectively collected for all patients before surgery. More detailed questions about symptoms related to SPSD (i.e. itching and pain) were evaluated; each symptom was scored on a six-point scale from 0 to 5 (ranging no complaints to daily complaints). A visual analogue scale (VAS), scored from 0 to 100 (worst to best), was used to measure the QoL.

Phenolisation of the recurrent pilonidal sinus was performed in the operation room. The anesthesiologist and patient decided, depending on their preferences, if the anesthesia was spinal or general. Antibiotics were not administered. Patients were positioned in a prone position and to optimise the view of the area of the natal cleft, plasters were used to separate the buttocks. After cleaning the natal cleft with antiseptic solution (Betadin 100mg/mL), the area was covered with sterile dressings. The pit(s) of the sinus were probed to determine the direction of the sinus(es). All the pit(s) were excised as limited as possible. A curette was introduced in the excised pit(s) to clean the tract. All the hairs, debris and granulation tissue were removed. Hemostasis was reached by using electrocautery and/or external compression. To protect the area of the natal cleft against phenol, a gauze was used to protect the anus and the skin was protected by Vaseline. After secure protection, liquid phenol 85% was injected by using syringes. The amount of injected phenol depended on the volume of the tract. After one minute, phenol was aspirated and a new same amount of phenol was injected once more, again for one minute. After a second time of aspiration, the remaining phenol was washed out with ethanol 70% to neutralise remnants of phenol.

Data on the number of midline and off-midline pits, duration of operation, intraoperative complications and presence of hair and the volume of the sinus were prospectively collected. Postoperative advice to all patients was to keep the buttocks clean and epilate hair of the skin surrounding the wound. Patients were admitted the same day.

Patients were asked to complete a diary for two weeks postoperatively. Data with regard to complaints related to the treatment, i.e. fluid discharge, pain, irritation, itching and burning sensation were scored using the six-point scale as mentioned previously. A VAS score was used to score pain from 0 to 100 (no pain to extremely painful). Patients also indicated every day if they used any painkillers and if they were able to perform normal daily activities, such as working or doing housekeeping work.

Subjective evaluation was obtained by a questionnaire two, six and 12 weeks after surgery containing items about patient's satisfaction (disease scored as cured, improved, unchanged or worsened), complaints related to the phenol treatment (same complaints and scoring system as used in the diary), QoL (VAS) and return to normal daily activities.

Two, six and 12 weeks after surgery, the wound was evaluated in the outpatient clinic by one of the investigators (EF or NS) by using an assessment form, including wound closure (defined as complete epithelisation of the skin), size of the wound(s) in three dimensions (in the case of no complete epithelisation) and surgical site infection (SSI).

STATISTICAL ANALYSIS

Data were analysed using SPSS for Windows version 23.0 (SPSS Inc., Chicago, Illinois, USA). Values were reported as mean (± SD) or as median (interquartile range) in the case of continuous values, depending on whether the data were normally distributed or not. Categorical values were reported as frequencies and percentages of the total number of patients. Differences between continuous pre- and postoperative values were statistically analysed by the paired-samples t-test. When data were not normally distributed, the Wilcoxon signed-rank test was performed. Differences were considered statistically significant with $p\text{-value} < 0.050$.

RESULTS

A total of 60 out of 565 patients who presented with SPSD at the Diakonessenhuis between September 2013 and September 2017 were eligible for inclusion in the current study (Figure 1). Since two patients refused surgical treatment and one patient had no SPSD intra-operatively, 57 underwent phenolisation. Table 1 presents the baseline characteristics of the included patients. Previous surgery for SPSD was performed once in 52 patients (86.7%), twice in three patients (5.0%), three times in three patients (5.0%), four times in one patient (1.7%) and in one patient the number and kind of previous treatment(s) was unknown as this was performed in another hospital a long time ago. A total of 39 previous procedures (65.0%) were incision and drainage of an abscess, in 16 cases (26.7%) excision of the pilonidal sinus disease was performed and four previous procedures were phenolisation. In the remaining cases, the specific procedures were unknown. The median interval between the last surgical procedure and phenolisation for recurrence was 13 (5.8 to 41.3) months.

Table 1. Baseline Characteristics

	Phenolisation n = 60
Male sex (%)	50 (83.3)
Age (years)	29.2 (10.8)
Body mass index (kg/m^2)	25.4 (4.0)
Smoking (%)	22 (36.7)
Family history of pilonidal sinus disease (%)	10 (16.7)
Working in sitting position (%)	37 (61.7)
Duration of preoperative symptoms (months)	17.4 (21.1)
Number of sinus pits midline	2.1 (1.4)
Patients with sinus pit(s) at right side of midline (%)	14 (23.3)
Patients with sinus pit(s) at left side of midline (%)	15 (25.0)

Values are reported as mean ± SD or median (interquartile range), unless otherwise stated.

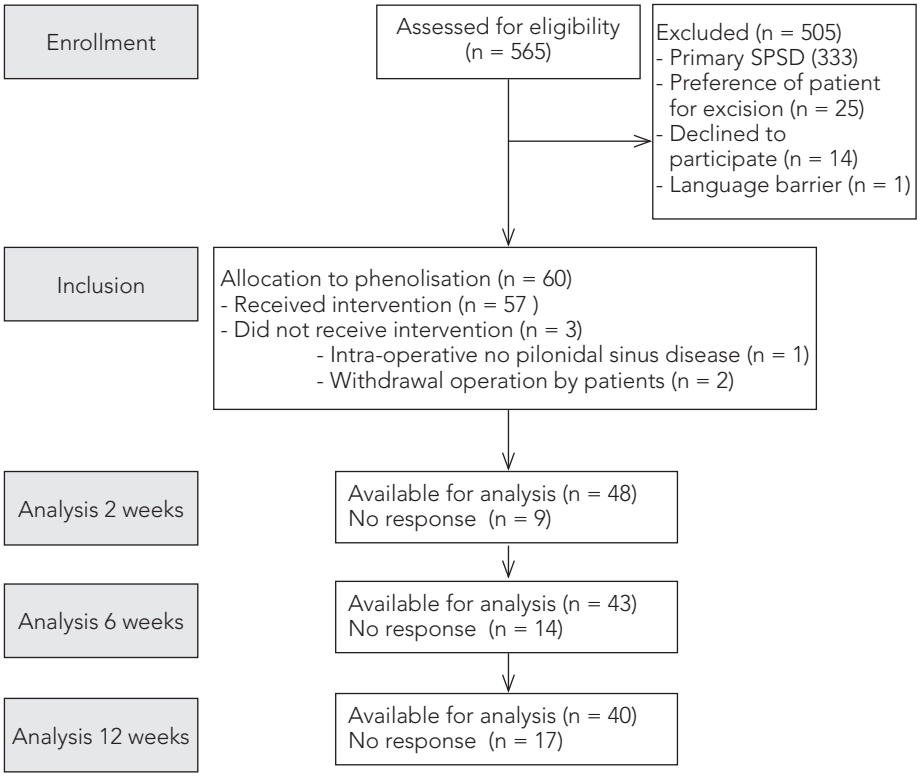

Figure 1. Flow Chart Consort

Abbreviation: SPSD, sacrococcygeal pilonidal sinus disease.

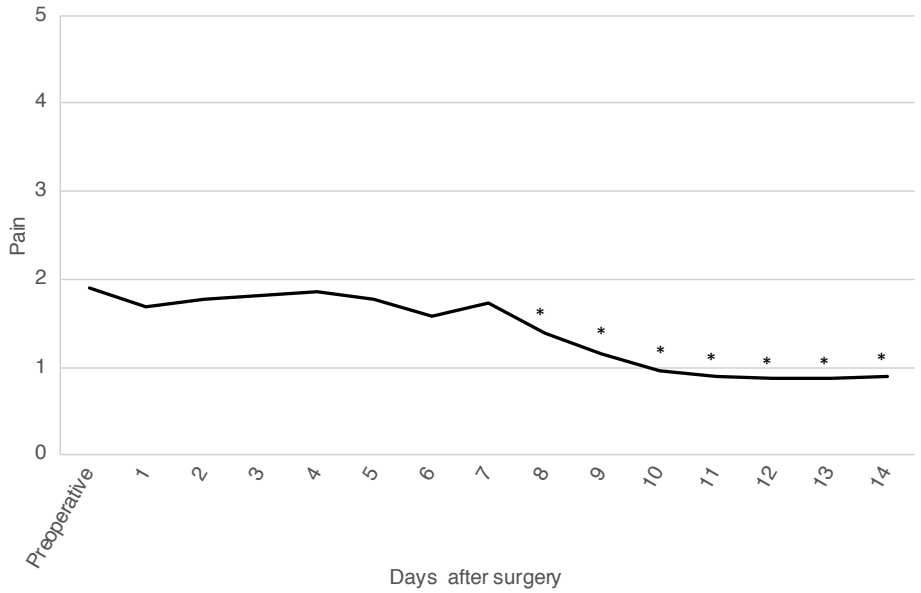

Figure 2. Pain at natal cleft
Items scored on a six-point scale from 0 (no pain) to 5 (daily pain).
*Items showing a statistically significant difference compared to preoperatively ($p < 0.05$)

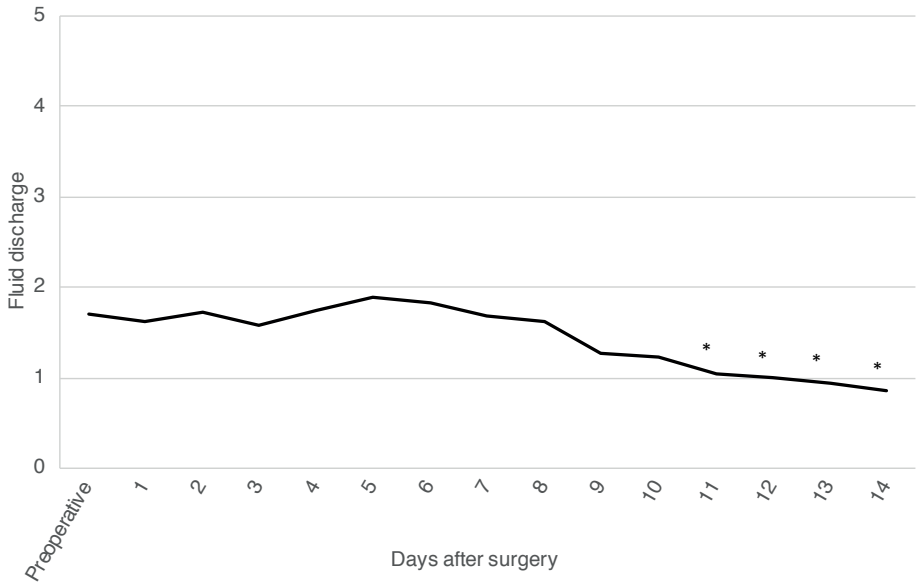

Figure 3.Fluid discharge at natal cleft
Items scored on a six-point scale from 0 (no discharge) to 5 (daily discharge).
*Items showing a statistically significant difference compared to preoperatively ($p < 0.05$)

PERIOPERATIVE DATA

The mean duration of operation was 18.7 (6.4) minutes and there were no intra-operative complications. The mean volume of the sinus was 1.0 (1.0) mL. All patients could be discharged on the same day of surgery. Postoperatively, surgical side infections were seen in five patients (8.8%); one patient developed an abscess and four patients cellulitis. None of the patients was readmitted.

From eight days after surgery, pain was significantly less compared to preoperatively (Figure 2). In addition, fluid discharge was significantly less compared to preoperatively from day 11 after surgery (Figure 3). Itching, irritation and a burning sensation at the natal cleft was rarely present with a maximum score of one during the first two weeks after surgery.

FOLLOW-UP DATA

Figure 1 shows the number of patients available for follow-up two, six and 12 weeks after surgery. Median loss of days of normal daily activities was 5.0 (1.0 – 12.0) days. A total of 51 patients (89.5%) resumed normal daily activities after two weeks after surgery; after six and 12 weeks postoperative, normal daily activities were resumed in 52 (91.2%) and 53 patients (93.0%) respectively.

The pain and itch scores were significantly lower two, six and 12 weeks after surgery compared to preoperatively (Table 2). QoL dropped two weeks after surgery but was significantly higher 12 weeks after surgery compared to preoperatively (Table 2). A total of 36 patients (90.0%) reported SPSD as fully cured or significantly improved 12 weeks postoperatively compared to before surgery. Two patients (5.0%) reported SPSD as unchanged and one patient (2.5%) as worsened. In addition to the 17 patients who did not respond (Figure 1), one patient (2.5%) did not complete this item in the questionnaire.

Table 2. Pre- and postoperative subjective and objective data

	Preoperative	2 weeks postoperative	p-value compared to preoperatively	6 weeks postoperative	p-value compared to preoperatively	12 weeks postoperative	p-value compared to preoperatively
Subjective data							
Pain (VAS, 0-100)	15.0 [6.0 – 36.5]	8.0 [0.50 – 19.0]	0.091	5.0 [1.0 – 10.0]	0.010	9.0 [0.0 – 19.0]	<0.001
Pain*	2.0 [1.0 – 3.0]	1.0 [0.0 – 2.0]	<0.001	0.0 [0.0 – 1.0]	<0.001	0.0 [0.0 – 2.0]	0.005
Itch*	2.0 [1.0 – 2.0]	1.0 [0.0 – 1.0]	<0.001	0.0 [0.0 – 1.0]	<0.001	0.0 [0.0 – 1.25]	<0.001
Fluid*	2.0 [1.0 – 2.5]	1.0 [0.0 – 1.0]	0.013	0.0 [0.0 – 1.0]	<0.001	0.0 [0.0 – 1.0]	0.248
Irritation*	N.R.	0.0 [0.0 – 1.0]	N/A	0.0 [0.0 – 1.0]	0.851**	0.0 [0.0 – 1.0]	0.074**
Burning sensation*	N.R.	0.0 [0.0 – 1.0]	N/A	0.0 [0.0 – 1.0]	0.546**	0.0 [0.0 – 1.0]	0.480**
Quality of life (VAS, 0-100)	73.0 [50.0 – 80.0]	66.0 [50.0 – 79.5]	0.182	75.0 [65.0 – 83.0]	0.072	75.0 [68.0 – 83.0]	0.014
Objective data							
Length of wound (mm)	N/A	8.0 [3.0 – 15.0]	N/A	3.1 [1.7 – 9.3]	0.019**	0.0 [0.0 – 8.4]	0.011**
Width of the wound (mm)	N/A	3.0 [2.0 – 5.0]	N/A	2.0 [1.0 – 4.8]	0.018**	0.0 [0.0 – 3.0]	0.030**
Depth of the wound (mm)	N/A	5.0 [2.0 – 10.3]	N/A	2.0 [1.0 – 9.0]	0.123**	0.0 [0.0 – 5.3]	0.059**

Values are reported as median and interquartile range (IQR), unless otherwise stated. *Items scored on a six-point scale from 0 (no complaints) to 5 (daily complaints), **p-value compared with values two weeks after surgery.
Abbreviations: N/A, not applicable; N.R., not reported; VAS, visual analogue scale.

Complete wound healing was achieved in nine patients two weeks after surgery. Six weeks after surgery, the wound was completely healed in an additional of 26 patients and an additional ten patients 12 weeks after surgery. In six patients, it was not possible to assess complete wound healing as those patients dropped-out during follow-up before the wound was completely healed. So, complete anatomic wound healing was reached in 45 of 51 patients (89.8%) after 12 weeks of follow-up. The dimensions of the open wounds two, six and 12 weeks after surgery are reported in table 2.

DISCUSSION

This is, to our knowledge, the largest prospective cohort study reporting on the outcome of phenolisation for recurrent SPSD. The results showed a median of five days of loss of normal daily activities after phenolisation of the sinus tracts in patients with recurrent SPSD. Although quality of life dropped two weeks after surgery, it was significantly higher 12 weeks after surgery compared to the quality of life preoperatively. In addition, pain was also significantly decreased 12 weeks after surgery. The operation wounds were completely healed in 90% of patients 12 weeks after surgery.
Comparing the loss of days of daily activities after phenolisation in patients with recurrent SPSD and patient with primary SPSD showed comparable results (five days versus five days, respectively) [4] a randomised-controlled trial (RCT. Two previous studies investigated crystallised phenol in patient with recurrent SPSD. One study was retrospective, including 26 patients and a cure rate of 92.3% was achieved [5]. Another study had a prospective study design and included 36 patients [6]. Patients had minimal pain and most patients reported no complaints. Wounds were completely healed after a median of 48 days. The loss of daily activities was not reported in both studies.

Comparing the loss of days of daily activities after phenolisation with excision in patients with recurrent SPSD showed different results. Two randomised controlled trials compared Limberg flap and Karydakis flap in patients with recurrent SPSD. One study included 71 patients; treating 37 patients with Limberg flap and 34 patients with Karydakis flap. Median loss of days of daily activities was eight (range 6-12) and 17 (range 14-20) days, respectively [7]. The second trial included 120 patients, 60 patients were treated with Karydakis flap and 60 with Limberg flap. Time to return to work was 20 (± 6.01) and 22.35 (± 4.8) days, respectively [8]. So, excision of the pilonidal sinus results in a longer time to return to normal daily activities compared to the phenolisation

technique as was shown in the current study. There are also other minimally invasive techniques to treat SPSD available, including the endoscopic pilonidal sinus treatment (EPSiT) and laser technique. EPSiT has been investigated in a prospective multicenter study including 122 patients with recurrent SPSD [9]. Return to work was after three days, even faster compared to the phenolisation technique. The laser technique was also evaluated in a mixed group with both primary and recurrent SPSD by Pappas et al [10]. In this study, 92.8% of all patients resumed daily activities immediately, a little faster compared to the results in the current study for the phenolisation technique.

The benefits of phenolisation are due to the minimal invasive character; smaller wounds leading to less postoperative pain and quicker skin epithelisation at the natal cleft. The benefits of phenolisation have been reported before in patients treated for primary SPSD, but not for patients who presented with recurrent SPSD [4]. Our current study showed that phenolisation of the sinus tract in patients with recurrence SPSD is safe as no major perioperative complications occurred along with only a SSI rate of 9%. Two other studies reported results of phenolisation in patients with recurrent SPSD reported a SSI rate of 15.4% and 0% without any major complications [5,6]. The results of the current study also proved the clear benefits of smaller wounds with the phenolisation technique in recurrent SPSD; patients experienced less pain with a quick return to normal daily activities and complete wound healing achieved in almost 90% of patients 12 weeks after surgery.

SPSD has a high prevalence and recurrence is still a major problem in patients with SPSD. Currently, no consensus exists on the best treatment modality for recurrent SPSD. Almost no data have been reported on the outcome of the different traditional treatment modalities in patients with recurrent SPSD. In addition, there is a trend towards minimally invasive techniques in patients with primary SPSD, including phenolisation, laser and endoscopic treatments [9,10]. However, in almost none of the reported studies, is there focus on treatment with a minimally invasive modality in patients with recurrent SPSD. Therefore, we performed the current study on a minimally invasive technique in recurrent SPSD, i.e. phenolisation of the sinus tract. The results of the current study on phenolisation in recurrent SPSD are promising and therefore, we have increasingly utilised the minimally invasive treatment with phenolisation, also in patients with recurrent SPSD.

Although this is, as far as we know, the largest prospective study reporting on the outcome of phenolisation in recurrent SPSD, there are some limitations that needs to be

addressed. Loss of patients during follow-up was relatively high in the current study. The relative high drop-out rate could be explained by the fact that the patients in the current study mainly include the young and healthy working population. Patients without symptoms easily cancel their appointment because of their focus on work and social life, especially if the reasons for complaints are not present anymore. This has probably resulted in worse results in the current study as it is more likely that patients with persisting symptoms respond to follow-up. In addition, the recurrence rate was not reported in the current research. Since the aim of the current study was to focus on the short-term benefits of the minimally invasive phenolisation technique, especially on loss of days of normal daily activity, the duration of follow-up was 12 weeks. Therefore, we were not able to report the reliable recurrence rate as this would require a follow-up of at least 12 months.

CONCLUSION

In conclusion, this is the largest prospective cohort study on phenolisation of the sinus tract in patients with recurrent pilonidal sinus disease showing less pain, improvement of quality of life with only five days of loss of normal daily activities and complete wound healing in 90% of patients after 12 weeks. In addition, phenolisation in recurrent SPSD appeared to be safe without the occurrence of major complications. Since the results of this study are very promising, surgeons should also consider phenolisation of the sinus tracts as a treatment option in patients with recurrent SPSD.

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CHAPTER 7

Sexual function in patients suffering from sacrococcygeal pilonidal sinus disease

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ABSTRACT

INTRODUCTION

Sexual function is one of the aspects upon which quality of life (QoL) is based. Although previous studies have evaluated the influence of sacrococcygeal pilonidal sinus disease (SPSD) on QoL, no data are available on the influence of SPSD on sexual function in a highly active sexual population based on the age range. The aim of this prospective study was to evaluate whether SPSD has a negative impact on sexual function and whether this is influenced by the surgical treatment of SPSD.

METHODS

Sexual function was pre- and postoperatively assessed by the Sexual Self-Consciousness Scale (SSCS, score range 0-48), subdivided into the sexual embarrassment (SE, score range 0-24) and sexual self-focus subscale (SFF, score range 0-24). The higher the score, the higher is the sexual dysfunction. Patients were also asked whether SPSD influenced their sexual functioning.

RESULTS

A total of 88 male patients who underwent surgical treatment for SPSD were included in the study. The mean (± SD) preoperative SSCS score was 14.5 ± 9.1 and 13.9 ± 8.4 two weeks postoperatively ($p = 0.394$). Six and twelve weeks after surgery, there was a significant reduction to 12.2 ± 9.0 ($p = 0.002$) and 12.3 ± 8.8 ($p = 0.013$), respectively. SE decreased from 5.5 ± 5.1 preoperatively to 5.1 ± 4.6 ($p = 0.258$), 4.2 ± 4.7 ($p = 0.004$) and 4.0 ± 4.6 ($p = 0.013$) two, six and 12 weeks after surgery. For SFF, there was a decrease from 9.0 ± 5.0 to 8.9 ± 4.9 ($p = 0.717$), 7.8 ± 5.2 ($p = 0.004$) and 8.2 ± 5.3 ($p = 0.168$), respectively. Preoperatively, 70% of the patients totally or partially disagreed that SPSD influenced their sexual functioning and this increased to 80% of the patients twelve weeks after surgery.

CONCLUSION

This prospective study showed a significant decrease in sexual dysfunction both six and twelve weeks after surgery compared to preoperatively in patients suffering from SPSD.

INTRODUCTION

Sacrococcygeal pilonidal sinus disease (SPSD) is an acquired disorder of the natal cleft. SPSD affects around 0.7% of the population and is twice more common in men. SPSD is most commonly found between the age of 15 and 30 years, affecting women at a younger age than men [1,2]. SPSD might present either as an acute abscess or chronic disease. In the acute stage, patients mainly complain of pain, while patients with chronic SPSD often present with intermittent discharge, irritation, itching or a burning sensation at the natal cleft [1,3]. Subjective perception of symptoms and the influence of the symptoms on quality of life (QoL) is increasingly taken into account in patients with benign diseases. In SPSD, symptoms have proven to have a negative impact on quality of life [4].

Sexual function is one of the aspects upon which quality of life is based. Therefore, impairment of sexual function can have a substantial negative impact on quality of life. Previous studies have shown a significant increase in the prevalence of sexual dysfunction in patients with chronic pain as well as in patients suffering from chronic diseases such as Parkinson's disease, epilepsy, chronic renal failure, multiple sclerosis and dermatological diseases [5]. Although several studies have evaluated the effect of SPSD on general quality of life, there are currently no data available on the relationship between sexual (dys)function and SPSD. In addition, specific data concerning the change of sexual function after treatment of SPSD have never been investigated. However, since patients affected by SPSD are within the age range of a sexual active population, data on sexual function is highly relevant [6].

The prospective study aimed to evaluate whether SPSD has a negative impact on sexual function and whether this is influenced by the surgical treatment of SPSD.

MATERIALS AND METHODS

Patients with SPSD were identified from a randomised controlled trial (RCT) comparing two different treatment modalities for primary SPSD, including phenolisation of the sinus tract and radical excision [7]. Patients over the age of 18 with symptoms due to primary chronic SPSD were included in the RCT. Exclusion criteria were no or minimal symptoms related to SPSD, suspicion of an extensive subcutaneous network of sinus tracts as this is a contra-indication for phenolisation, presence of an abscess or previous surgery related to SPSD. Since only a few female patients were included in the RCT due to the lower incidence of SPSD in the female population, only male patients were included in the current analysis to obtain the results on sexual function in a more homogenous group of patients. Since the aim of this study was to evaluate sexual function in patients with SPSD, sexual function was analysed independently of the type of surgery.

DATA COLLECTION

Preoperatively, baseline characteristics were prospectively collected, including age, body mass index, smoking, relationship status and family history of SPSD. Information regarding sexual function was preoperatively obtained and in addition, two, six and twelve weeks postoperatively by the Sexual Self-Consciousness Scale (SSCS) [8]. The SSCS is a 12-items questionnaire, assessing sexual function based on sexual self-consciousness. The questions included in the SSCS are shown in table 1. The SSCS can be subdivided into two six-items subscales, including Sexual Embarrassment (SE) subscale and Sexual Self-Focus (SSF) subscale. All items were answered on a five-points scale (score range: 0–4), resulting in a minimum score of zero and maximum score of 24 points per subscale, and a cumulative maximum score of 48 points on the complete SSCS. Increasing test scores correlate with more sexual self-consciousness and therefore higher sexual dysfunction. In addition, participants were also asked to indicate to what extent they agree with the statement 'Pilonidal sinus disease influences my sexual functioning' with available answers 'totally disagree' 'partially disagree' 'I don't know', 'partially agree' or 'totally agree'.

Quality of life was pre- and postoperatively evaluated by the Short Form 36 (SF-36), consisting of 36 questions comprising nine different domains of quality of life: physical functioning, physical role limitation, emotional role limitation, bodily pain, vitality, mental health, social functioning, general health and health change [9]. For every domain, a score between 0 and 100 can be obtained; the higher the score, the better quality of life.

Table 1. Sexual Self-Consciousness Scale questionnaire [8]

Sexual Embarrassment subscale
It takes quite some time for me to overcome my shyness in sexual situations
I quickly feel embarrassed in sexual situations
I feel uncomfortable in sexual situations
I find it difficult to sexually let myself go in front of the other person
When I see myself during sex, I am irritatingly aware of myself
I continuously feel being observed by the other person during sex
Sexual Self-Focus subscale
I am aware during sex of the impression I make on the other person
I pay much attention to my sexual thoughts and feelings
I often wonder during sex what the other person thinks of me
I am preoccupied by the way I behave sexually
During sex, I pay much attention to what happens inside my body
I often imagine how I behave during sex

Score range 0-4 per item: strongly disagree = 0, disagree a little = 1, neither agree or disagree = 2, agree a little = 3, and strongly agree = 4

Additionally, wound closure, defined as complete epithelisation of the skin at the natal cleft and fluid discharge from the surgical wound, scored on a six-point scale from 0 (no complaints) to 5 (daily complaints), were postoperatively assessed.

STATISTICAL ANALYSIS

Data were analysed using SPSS for Windows version 23.0 (SPSS Inc., Chicago, IL, USA). Categorical data were presented as frequencies with percentages. Continuous values were expressed as mean ± standard deviation (SD). The paired samples t-test and Wilcoxon signed-rank test were used for statistical analysis of continuous pre- and postoperative values. Statistical analysis of values between groups was performed using Mann-Whitney U tests. All tests were two-tailed and were considered statistically significant with $p < 0.05$.

To identify independent predictors of SSCS-scores twelve weeks after surgery, univariate regression analysis was performed by linear regression analysis for correlations between individual variables and SSCS scores. Variables that were analysed included age, body mass index (BMI), smoking, relationship status, family history of SPSD, number of preoperative sinus pits and postoperative bodily pain, fluid discharge and wound epithelialisation at twelve weeks. Variables with $p \leq 0.200$ in univariate analysis were all together entered into a multivariate regression model. Variables with $p \geq 0.100$ in multivariate analysis were excluded until only significant independent variables left ($p < 0.100$).

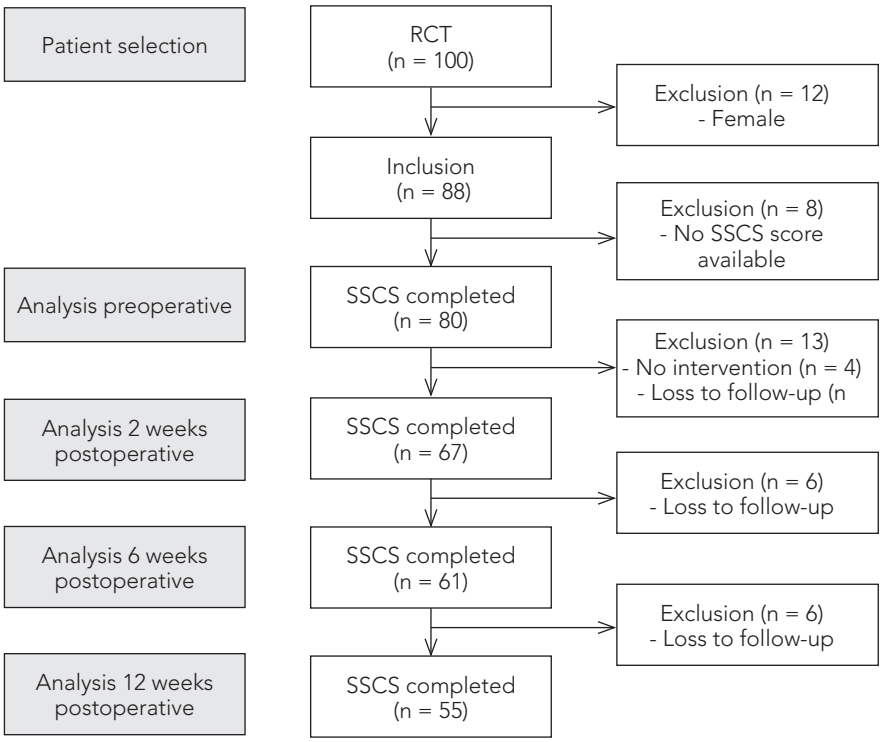

Figure 1. Flowchart

Abbreviations: RCT, Randomised control trail; SSCS, Sexual Self-Consciousness Scale.

Table 2. Baseline characteristics

	Total (n = 88)
Age (years)	27.6 (8.5)
Body mass index (kg/m^2)	24.9 (3.6)
Smoking (%)	30 (34.1)
Relationship (%)	51 (58.0)
Positive family history of SPSD (%)	20 (22.7)
First degree family member	15 (17.0)
Number of preoperative sinus openings	3.56 (1.96)
Type of surgery	
Phenolisation (%)	45 (51.1)
Radical excision (%)	43 (48.9)
Fluid discharge*	
Preoperative	1.8 (1.2)
2 weeks postoperative	1.3 (1.2)
6 weeks postoperative	0.6 (0.9)
12 weeks postoperative	0.5 (1.1)
Complete wound epithelialisation	
2 weeks postoperative (%)	11 (12.5)
6 weeks postoperative (%)	40 (45.5)
12 weeks postoperative (%)	52 (69.1)

Values are reported as mean ± SD, unless otherwise stated. *Score range 0 (no complaints) - 5 (daily complaints).
Abbreviation: SPSD, sacrococcygeal pilonidal sinus disease

RESULTS

Between September 2013 and September 2017, a total of 100 patients were included in the randomised trial. Since 12 of these patients were females, 88 male patients were included in the current analysis. The baseline characteristics and postoperative fluid discharge and wound epithelialisation rate of the included patients are shown in table 2. The flow chart indicating the number of patients who completed the SSCS questionnaire preoperatively and two, six and twelve weeks after surgery is shown in figure 1.

Table 3. Pre- and postoperative sexual self-consciousness scores (SSCS)

	Preoperative (n = 80)	2 weeks postoperative (n = 67)	p-value*	6 weeks postoperative (n = 61)	p-value*	12 weeks postoperative (n = 55)	p-value*
SSCS (range 0-48)	14.5 (9.1)	14.0 (8.3)	0.394	12.1 (8.9)	0.002	12.3 (8.8)	0.013
Sexual embarrassment subscale (range 0-24)	5.5 (5.1)	5.1 (4.6)	0.258	4.2 (4.7)	0.004	4.0 (4.6)	0.003
Sexual self-focus subscale (range 0-24)	9.0 (5.0)	8.9 (4.9)	0.717	7.8 (5.2)	0.004	8.2 (5.3)	0.168
Total SSCS score in patients with							
Complete wound epithalialisation	NA	14.7 (8.2)	0.709†	12.0 (9.3)	0.839†	11.7 (8.2)	0.768†
No complete wound epithalialisation	NA	13.7 (8.4)		12.4 (8.9)		13.4 (10.6)	

Values are reported as mean ± SD, unless otherwise stated.
Increasing scores on the Sexual Self-consciousness Scale indicates higher sexual self-consciousness and consequently more sexual dysfunction. *compared to preoperative value; †comparing SSCS score for complete versus no complete wound epithelialisation.
Abbreviations: SPSD, sacrococcygeal pilonidal sinus disease; NA, not applicable

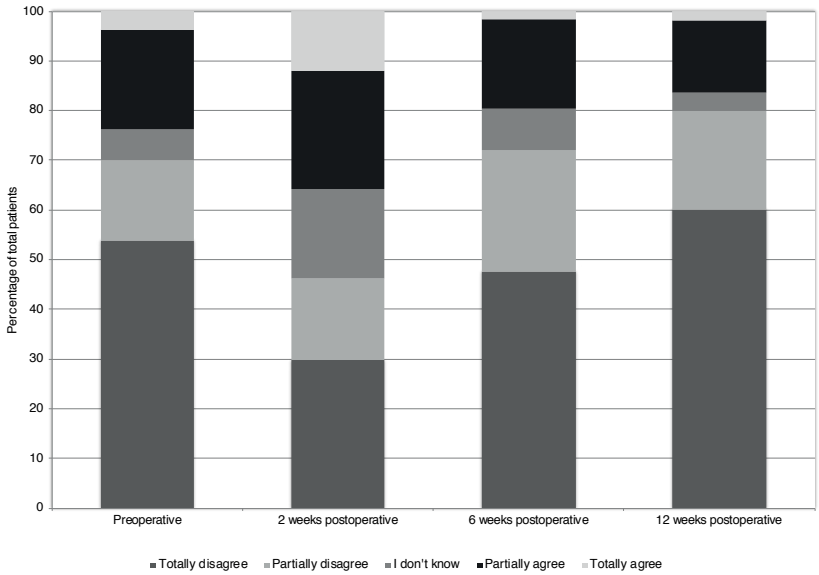

Figure 2. (Dis)agreement with statement 'Sinus pilonidal disease influences my sexual functioning'

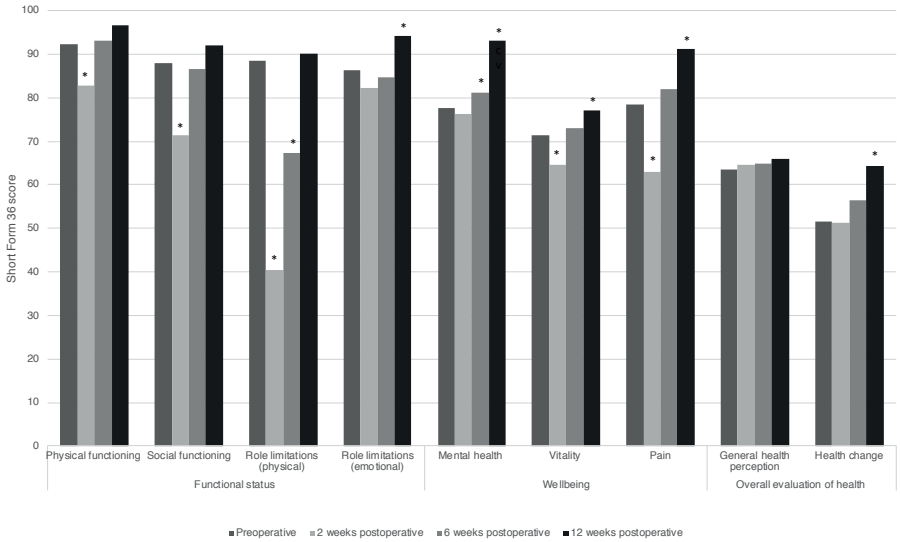

Figure 3. Quality of life (Short Form 36)

* $p < 0.05$ compared to preoperatively

Table 4. Uni- and multivariate analysis of Sexual Self-Conscious Scale 12 weeks after surgery

Variable	Univariate analysis				Multivariate analysis			
	Coefficient	95% CI		p-value	Coefficient	95% CI		p-value
Age	-0.263	-0.512	-0.014	0.039				ns
BMI	0.347	-0.276	0.970	0.268				
Family history	-0.718	-6.249	4.813	0.795				
Smoking	0.279	-4.699	5.256	0.911				
Relationship status	-5.826	-10.881	-0.772	0.025	-4.068	-8.897	0.760	0.097
Preoperative number of sinus pits	0.200	-1.069	1.468	0.753				
Pain	-0.227	-0.367	-0.087	0.002	-0.201	-0.341	-0.061	0.006
Wound epithelialisation	0.001	-0.006	0.009	0.758				
Fluid discharge score	2.432	0.310	4.553	0.025				ns

Abbreviations: CI, confidence interval for coefficient; BMI, Body mass index; ns, not significant

SEXUAL FUNCTION

Two weeks after surgery, the SSCS score was not significantly different compared to preoperatively (Table 3). However, six and twelve weeks after surgery, the SSCS score was significantly lower compared to preoperatively, indicating a better sexual function. The SE subscale showed the same trend as the total SSCS score with a significant decrease from 5.5 ± 5.1 preoperatively to 4.2 ± 4.7 six weeks and 4.0 ± 4.6 twelve weeks after surgery. The SSF subscale also showed a significant reduction six weeks after surgery, however, twelve weeks after surgery there was no significant difference in comparison with the preoperative score. At all three postoperative follow-up points, there was no significant difference in the total SSCS score between patients with and without complete wound epithelialisation (Table 3).

Preoperatively, 56 patients (70.1%) indicated that their SPSD did not or only partially influenced their sexual functioning (Figure 2). However, two weeks after surgery, patients significantly more often agreed with the statement 'Pilonidal sinus disease influences my sexual functioning' compared to preoperatively (totally disagree 53.8% and totally agree 3.8% preoperatively versus. totally disagree 29.9% and totally agree 11.9% two weeks after surgery, $p = 0.002$). Compared to preoperatively, six and twelve weeks after surgery 2.0% and 9.9% more patients totally or partially disagreed that SPSD influenced their sexual functioning ($p = 0.861$ and $p = 0.129$, respectively).

QUALITY OF LIFE

The SF-36 domains 'physical and social functioning', 'physical role limitations', 'vitality' and 'pain' all decreased significantly two weeks after surgery (Figure 3). However, twelve weeks after surgery, the scores on these domains came back to preoperative levels ('social functioning' and 'physical role limitations') or were significantly improved ('physical functioning', 'vitality' and 'pain'). Three other domains, including 'emotional role limitations', 'mental health' and 'health change' were also significantly improved twelve weeks after surgery compared to preoperatively, without a drop two or six weeks after surgery. The domain 'general health perception' did not significantly differ on any moment after surgery compared to preoperatively.

UNI- AND MULTIVARIATE ANALYSIS OF SSCS SCORE TWELVE WEEKS AFTER SURGERY

The results of uni- and multivariate analysis for the SSCS score twelve weeks after surgery are shown in table 4. A total of four variables, including age, relationship status, pain and fluid discharge, found in the univariate analysis were entered into

the multivariate analysis. Finally, two variables were identified as significant predictors of the SSCS score twelve weeks after surgery; patients with a relationship and pain independently predicted a higher SSCS score, i.e. more sexual dysfunction.

DISCUSSION

This is, to our knowledge, the first prospective study evaluating the influence of SPSD on sexual functioning. The results of this study showed that treatment of SPSD improved sexual function six and twelve weeks after surgery. A relationship and pain were independent predictors of more sexual dysfunction twelve weeks after surgery. In addition, although there was some decrease two weeks after surgery, quality of life also significantly improved twelve weeks postoperatively on most dimensions.

Although sexual function improved six and twelve weeks after surgery, there was initially, two weeks postoperatively, no influence on sexual function. However, we would have expected an increase in the SSCS score two weeks after surgery due to wound pain, fluid discharge and a wound at the natal cleft. This finding, the absence of a reduction in the SSCS score two weeks after surgery, supports that symptoms related to SPSD do have the same impact on sexual function as complaints due to surgery for SPSD. On the contrary, compared to preoperatively, significantly more patients indicated that SPSD influenced their sexual function two weeks after surgery. This implies that the surgical wound has a higher impact on sexual function than symptoms related to SPSD. So, it is unclear from our data whether surgery for SPSD has a negative impact on sexual functioning during the first two postoperative weeks.

It has previously been reported that pain and chronic diseases have a negative impact on sexual function, while sexual activity has been associated with health benefits and longevity [5,6]. Therefore, it is surprising that no data were available on sexual function in patients with SPSD so far. Some studies on sexual function with regard to perianal diseases that are located around the same body area like SPSD, have been published, although data on this subject is also limited. Riss et al. [10], investigated sexual function in patients after surgical treatment for perianal fistulas in Crohn's disease. The authors concluded that postoperative sexual function, measured by the International Index of Erectile Functioning (IIEF), was not different compared to the general population. On the contrary, Lin et al. found a significant higher incidence of sexual dysfunction in women after surgery for haemorrhoids [11]. Since data on sexual functioning in

patients with disorders close to the urogenital area, i.e. the anal region, are scarce and also inconsistent, a plea for additional studies focussing on this subject is justified.

The SSCS questionnaire is divided into two subscales; the Sexual Embarrassment (SE) subscale representing a feeling of inhibition and discomfort in sexual situations and the Sexual Self-Focus (SSF) subscale representing self-consciousness behaviour without affective connotation [8]. The current study showed a significant decrease of the SE subscale six and twelve weeks after surgery compared to preoperatively, while the SSF subscale only showed a significant reduction six weeks after surgery. Since the final SSF subscale score twelve weeks after surgery did not show a difference compared to preoperatively and the SE subscale score did, SPSD might have more impact on sexual embarrassment. This might be explained by the fact that the SSF subscale is about 'self-focus', which might be less influenced by a physical disorder than sexual embarrassment.

Preoperative QoL scores measured by the SF-36 health survey questionnaire were, compared to the normal healthy male population as reported by Van der Zee et al., below average on the domains 'social functioning', 'emotional role limitations', 'mental health', 'pain', 'general health perception' and 'health change' [9]. In more than half of the domains, QoL reduced two weeks after surgery, probably due to the consequences of surgery, including, pain, fluid discharge and a wound at the natal cleft. However, in six of the nine domains of the SF-36, values significantly improved twelve weeks after surgery and were, compared to the normal healthy population, at least equal on all domains, except for 'general health perception'. Since Jenkinson et al. showed decreased SF-36 scores for patients with a long-lasting illness, the lower scores twelve weeks after surgery in 'general health perception', compared to healthy male adults as reported by Van der Zee et al., could probably be explained by the history of the chronic illness SPSD [9,12].

This prospective study has some limitations that needs to be considered. First, the loss of follow-up was relatively high. Despite reminding phone calls, patients failed to return the questionnaire. This might be due to the subject of the questionnaire as patients feel embarrassed to complete sexual-related questions. In addition, some patients only completed the quality of life questionnaire and refused to complete the SSCS. This has contributed to the relatively high loss to follow-up. Second, the follow-up period is relatively short. However, even after twelve weeks of follow-up a significant decrease in SSCS score was found. Since about 70% of patients had

complete wound healing after twelve weeks of follow-up, longer follow-up is finally expected to lead to complete wound healing in all patients and this might result in an even higher improvement in sexual function. However, a significant difference in SSCS score between patients with or without complete wound healing was not detected during any of the postoperative follow-up points. So, a further decrease of the SCSS score in the long run is speculative. Third, data on the SSCS in the normal healthy population are lacking, so we were not able to compare patients suffering from SPSD at baseline with healthy individuals. In addition, the minimal clinically important change of the SCSS score is also unknown. For that reason, we also obtained from all patients to what extent they agreed with the statement 'Pilonidal sinus disease influences my sexual functioning'. Since there was an increase from preoperatively to twelve weeks after surgery of 10 % of patients who totally or partially disagreed, we considered the significant increase of the SCSS score as clinically relevant. Finally, female patients were excluded from the analysis, so no data on sexual function are available in the female population. This was decided as only 12% of the included patients were women and excluding them resulted in a more homogeneous study population with only male patients. However, future research should also focus on sexual (dys)function in female patients suffering from SPSD.

CONCLUSION

In conclusion, this is, as far as we know, the first study evaluating sexual function after surgery in patients with SPSD, including a patient population in a highly active sexual age range. This prospective study showed a significant decrease in sexual dysfunction six as well as twelve weeks after surgery for SPSD. The significant improvement of sexual function as shown in this study supports surgical treatment in the case of symptomatic SPSD and contributes to the preoperative counselling of patients facing surgery for SPSD.

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CHAPTER 8

General discussion and future perspectives

Sacrococcygeal pilonidal sinus disease (SPSD) is a common disease and a surgical procedure is often prescribed for treatment. Excision techniques are most commonly applied, but a 'gold standard' treatment does not exist [1]. The principle of the excision techniques is to excise the sinus and all associated subcutaneous tracks. 'The American society of colon and rectal surgeons' and 'the Italian society of colorectal surgery' both stated that surgical excision with or without wound closure, is the standard treatment for SPSD [2]. Additionally, the American Society strongly recommends a minimal invasive technique, phenolisation, as an effective treatment that may result in rapid and durable healing, while the recommendation by Italian society was weaker [2,3]. A Dutch guideline for SPSD is lacking, but one is currently under development. High infection rates and high risks of recurrence are major problems in patients after a treatment for SPSD. Identifying an optimal treatment for SPSD would provide significant benefits to society as a whole as it is a common disease mainly seen in young working men, and both the disease and the treatments can have high social and economic impacts. Minimally invasive techniques are being applied more frequently, and these techniques are being investigated for safety and efficacy.
When focusing on optimising treatment of SPSD, it is important to take the entire spectrum of SPSD into account. This implies not only focusing on minimising the risk of recurrence, but also on the impact of the various treatment options on quality of life (QoL) and the recovery process.

As mentioned above, radical excision is still the most frequently applied treatment. The main disadvantage of radical excision is that surgical site infection is reported in up to 24% of patients [4]. Systematic antibiotics have not shown to be of any benefit in the reduction of surgical site infection rates, whereas gentamicin collagen sponges have been shown to significantly reduce the risk of surgical site infections after other surgical procedures [5]. In **chapter 2**, the effect of local intra-operative administration of a gentamicin collagen sponge after excision of SPSD was assessed. In this systematic review, a trend towards a reduced incidence of surgical site infections was found. The lack of significance is probably caused by the small number of patients included in the various studies. In addition, negative effects of gentamicin on wound healing and recurrence rates were not encountered. Remarkably, in the included studies the wound was closed in the midline, whereas extensive reports in literature conclude that off-midline closure is preferable [5,6]. The studies reviewed in this meta-analysis showed a high heterogeneity and did not include details on whether the gentamicin sponge was inserted as a whole or in pieces, and whether this resulted in different outcomes [7-10]. We hypothesised that wounds will recover quicker if the gentamicin sponge

is cut in small pieces before insertion in the wound, because a whole gentamicin sponge could act as a barrier in the wound cavity. However, this hypothesis needs investigation. Further research, i.e. a large randomised controlled trial including at least 400 patients, is needed to make a definitive determination on the effectiveness of gentamicin collagen sponges for the healing of SPSD related wounds.

In addition to a high risk of surgical site infection, high recurrence rates have been reported after surgical treatment of SPSD [5]. A common theory is that body hair after surgical treatment may contribute to recurrent SPSD. Razor shaving, cream depilation and laser treatment are different methods used for hair removal. In **chapter 3** all available literature regarding the effect of hair removal on the recurrence rate of SPSD after surgical treatment is summarised. Recurrence was seen in 9.3% of the patients treated with laser hair removal, in 19.7% after no hair removal and in 23.4% after razor shaving and cream depilation. However, the methodological quality of the included studies was poor, and in addition, substantial heterogeneity was seen between studies; study population, type of surgical treatment and definition of outcomes were all different. The highest risk of recurrence after razor shaving and cream depilation is probably due to the effect of the largest included study (113 patients) of Petersen et al [11]. A significant difference in favour of no hair removal (19.7%) versus razor depilation (30.1%) after surgical resection of SPSD was found after 11 years. The lowest recurrence rate was found after laser depilation. One favourable aspect of laser depilation is the permanent nature of the treatment compared to shaving and cream depilation. However, an important factor of the laser treatment is that it has to be performed at an experienced treatment center, treatment has to be performed more frequently, possibly up to eight times, and that the costs are relatively high with rarely reimbursed by the health care insurance, at least in the Netherlands. Two guidelines give advice about hair epilation, both with rather weak advice; the American Society of colon and rectal surgeons advises elimination of hair from the gluteal cleft by shaving or laser epilation [2,3]. The Italian guideline states that shaving along the gluteal cleft can be used to prevent recurrence and that laser epilation also results in positive outcomes. Based on the results in **chapter 3**, patients should be discouraged to shave the gluteal cleft and instead be advised to use laser hair removal as a means of preventing recurrence. However, this advice should be interpreted with caution because of the methodological low quality of the included studies. More high-quality studies are needed to give patients evidenced-based advice with regard to whether hair removal is beneficial to reduce the risk on recurrence after surgical treatment of SPSD, and what method of hair removal should be preferred.

Radical excision is known for its protracted wound healing time and high risk of surgical site infections. In recent years, an increasing trend towards less invasive treatment modalities has been observed for the treatment of SPSD. 'Endoscopic pilonidal sinus treatment' (EPSiT), 'Video-assisted ablation of pilonidal sinus' (VAAPS), laser ablation treatment and pit excision with phenolisation of the sinus tracts are minimal invasive treatments for SPSD. Many cohort studies on phenolisation in patients with primary SPSD focusing on pain, wound healing and surgical site infection have been published. However, no data is available regarding the time to return to normal daily activities. In addition, this technique has never been compared to the most commonly applied treatment for SPDS, i.e. radical excision with primary wound closure, in a randomised controlled trial. Since SPSD mainly occurs in the young, healthy, working population, time to return to normal daily activities is a highly relevant endpoint, with other outcomes, like pain, wound healing and surgical site infection, all contributing to this endpoint. In **chapter 4**, the outcomes of a randomised controlled trial (RCT) comparing the phenolisation technique with radical excision in patients with primary SPSD are described, focusing on time to return to normal daily activities. A significant reduction in time until return to daily activities was found; 5.2 days after phenolisation versus. 14.5 days after radical excision. Operation time was shorter, patients had significantly less pain and wound epithelisation was significantly quicker after phenolisation. Phenolisation is safe as judged by only minor complications occurring in 4% of patients. Based on the results of this RCT we advocate phenolisation.

'Endoscopic pilonidal sinus treatment' (EPSiT), 'Video-assisted ablation of pilonidal sinus' (VAAPS) and laser ablation treatment are other minimal invasive treatment modalities. Results of EPSiT and VAAPS are from four prospective cohort studies [12-15]. Both treatments are safe, and no postoperative wound infections have been reported. Risk of recurrence varied from 3.7 - 14.8%. Laser treatment has been investigated in three small cohort studies [16-18]. The treatment was safe, wound infections were reported in 5-7% and 3-10% developed a recurrence. However, length of follow-up was only 15 months and preferable would be at least three years. The limited available results of these other minimal invasive techniques seem comparable with those of the phenolisation technique as reported in this thesis. However, we reported as well in this thesis the available evidence of phenolisation versus excision. Based on that results is phenolisation the currently preferred therapy.

Since recurrence is another main problem after surgery for SPSD and short-term results of phenolisation were found to be superior, **chapter 5** focused on the long-

term outcome. The long-term results of the randomised trial described in chapter 4 revealed no significant differences in recurrence rate and quality of life after a follow-up of four years (2.6% versus 5.6%, p = 0.604). The available literature also reported no significant differences in recurrence rates between phenolisation and excision: Calikoglu et al., performed the only other randomised trial comparing phenolisation versus excision with secondary wound healing, after a follow-up op 40 months , no significant difference in recurrence rate was reported (18.6% after phenolisation and 12.9% after surgical excision (p = 0.92) [19]. Other retrospective case-control studies compared phenolisation with excision and flap reconstruction, and did not find any significant differences in recurrence rates either [20-22]. In our randomised trial, recurrence was defined and objectified by a physician. Although a small group of 14% of patients treated with phenolisation required a second treatment, a remarkably higher percentage of patients would still undergo the same treatment again in this group (83%) compared to excision (58%). Here, the small impact of repeat phenolisation appears to outweigh the downsides of undergoing a second treatment to reach complete wound healing. In addition, the total personal impact of phenolisation was significantly less compared to excision. Therefore, after promising short-term results published in chapter 4, the success of phenolisation was confirmed in this long-term study. Hence, we propose that phenolisation should be considered as first treatment option for primary SPSD.

Recurrence rates of up to 68% have been reported up to 10 years after surgery [23]. Because of this high percentage and the promising results of the phenolisation technique in primary SPSD as described in chapter 4 and 5, phenolisation in patients with recurrent SPSD was performed in a prospective cohort study in chapter 6 focusing on short-term results (3 months of follow-up). A mean of five days of loss of normal daily activities after phenolisation was found in 57 patients with recurrent SPSD. This is similar to the data on patients treated with phenolisation for primary SPSD (chapter 4). Again, the treatment was safe, and no major complications occurred. After twelve weeks pain reduction and improvement of QoL were found compared to preoperative. Only two cohort studies focusing on results of phenolisation in patients with recurrent SPSD have previously been published: one retrospective study, including 26 patients, reported a cure rate of 92.3% and one prospective study, with 36 patients, reported completely healed wounds in all patients after a median of 48 days [20-24]. However, the main outcome measure of the cohort study described in chapter 6, loss of days of daily activities, was not assessed in these studies. The recurrence rate was not reported in the study reported in chapter 6 as a longer follow-up is required than the current

definition of three months used in this study. Two previous RCT's have compared two non-minimal invasive procedures in patients with recurrent SPSD; Limberg flap and Karydakis flap. Bali et al., reported a median loss of daily activities of eight (range 6-12) and 17 (range 14-20) days, respectively [25]. El Hadidi et al., registered time to return to work of 20 (± 6.01) and 22.35 (± 4.8) days, respectively [26]. Excision of recurrent SPSD therefore leads to longer times required to return to normal daily activities compared to the findings of our current cohort study on phenolisation. Other minimal invasive techniques have been investigated in recurrent SPSD as well. EPSiT was studied in in a prospective cohort in 122 patients with recurrent SPSD and patients returned to work after three days [14]. A laser technique was evaluated in prospective mixed cohort of primary and recurrent patients; 92.8% of patients resumed daily activities immediately [17]. So, both techniques lead to slightly faster return to normal daily activities compared to phenolisation. However, RCT's comparing the different minimal invasive techniques in patients with recurrent SPSD are lacking, but should definitely be the subject of future studies to prove whether the outcome of one is superior to the others. Since our large prospective cohort study on phenolisation in recurrent SPSD showed promising results, comparable with the results of our RCT focusing on primary SPSD, phenolisation is increasingly being applied in patients with recurrent SPSD in our institution. However, long-term results, especially with regard to recurrence rate, should be assessed before a final determination on the most effective treatment for patients with recurrent SPSD can be justified.

As stated repeatedly that SPSD mainly occurs in the young, male working population, we hypothesised that SPSD might have a negative impact on sexual functioning. Several studies evaluated the effect of SPSD on general QoL, but no results are available about the impact of SPSD on sexual functioning. In **chapter 7** the first prospective study evaluating the influence of SPSD on sexual function in male patients is described. Following treatment of 88 patients with SPSD with either phenolisation or excision, overall the sexual function improved after six to twelve weeks postoperatively compared to preoperatively. Sexual function was assessed by the sexual self-consciousness scale (SSCS), subdivide in the sexual embarrassment subscale (SE) focusing on feeling of inhibition and discomfort in sexual situations) and the sexual self-focus subscale (SFF) representing self-consciousness behaviour without affective connotation). The SE scale significantly decreased six weeks after surgery (indicating better sexual function), but there was no significant difference twelve weeks after surgery compared to preoperatively. Treatment of SPSD apparently had more impact on sexual embarrassment, since the sub-scale focusing on sexual embarrassment decreased at six weeks postoperatively

and this persisted twelve weeks after surgery, indicating a better sexual function. Only male patients were included in this study as SPSD occurs more commonly in male patients, but also in order to create a more homogenous patient group. Comparing sexual function after phenolisation versus excision was not performed because of the small number of patients included in both treatment groups. The follow-up time was relatively short (12 weeks) in this study and loss to follow-up (31%) might be due to the subject of the questionnaire; patients might have felt embarrassed to complete sexual-related questions. Unfortunately, data on the SSCS in the normal healthy population is lacking, so we were not able to compare our results with healthy individuals. On the other hand, an increase of 10% of patients who totally or partially disagreed 'Pilonidal sinus disease influences my sexual function' 12 weeks after surgery was reported compared to preoperatively, which would appear clinically relevant. Patient reported outcomes (PROMS) are becoming more and more important including data on sexual functioning in patients with disorders in the urogenital area. The results of this study could aid in preoperative counselling of patients who are preparing for treatment for SPSD.

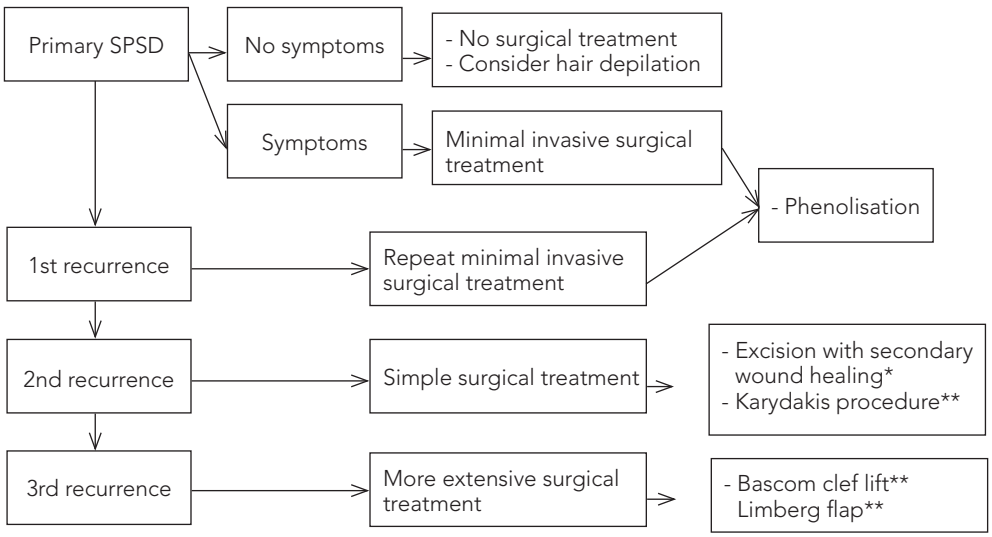

Figure 1. Treatment strategy for patients with sacrococcygeal pilonidal sinus disease
* Vacuum-assistant therapy can be considered
** No evidence about the administration of gentamicin collagen sponge exists

Based on the results of the studies described in this thesis as well as the additional available literature, the treatment protocol according to the flowchart in figure 1 is recommended.

FUTURE PERSPECTIVES

Even though a shift from excision towards minimal invasive techniques has been observed over the past years, developments aiming to optimise treatment of SPSD are still relevant.

Optimising treatment starts with understanding of the etiology of a disorder. Although, the etiology of SPSD is still not fully understood, the latest findings suggest that hair found in the pilonidal sinus stems from hair originating on the head [28]. One potential flaw of this hypothesis is that bald people may also present with SPSD. Future studies should focus on further elucidation of this etiology. Hair from the head, gluteal cleft and cyst should be compared and microscopically analysed as this could help in prevention recurrence after surgery for SPSD.

If a surgeon decides to perform a radical excision in a patient with SPSD, the Cochrane review strongly advises to close the wound off-midline which leads to a reduction of infection and recurrence rates [4]. The advice to apply a gentamicin collagen sponge cannot be given based on the systematic review and meta-analysis described in chapter 2, so larger well-designed RCT's are required. Cutting the sponge into small pieces before insertion in the wound is supposed to promote wound healing; however, this hypothesis needs further investigation.

In the review on hair depilation it was found that laser hair removal seems to be the most effective treatment for hair depilation and that it decreases recurrence risk. Based on this review, patients should be advised to use laser hair depilation as opposed to razor shaving. However, the methodological quality of the included studies was limited while heterogeneity among the studies was pronounced. An RCT is required to be able to make an evidence-based decision on whether laser depilation prior to surgery for SPSD is of additional value. Main outcome parameters should include recurrence rate, pain, adverse events of laser and cost.

Return to daily activities remains an important outcome parameter of SPSD as it particularly compromises a young working population. Based on the RCT described in chapters 4 and 5, surgeons are encouraged to consider phenolisation as treatment of choice for primary SPSD. However, the different minimal invasive techniques should be compared directly in RCT's to finally assess which one is superior focusing on a broad range of outcomes; short-term outcomes, long-term outcomes and costs.

Although the short-term results from the prospective cohort study of phenolisation in recurrent SPSD are favourable and comparable to the short-term outcome of phenolisation in primary SPSD, the long-term results are also required to identify whether the recurrence rate in patients with recurrent SPSD is the same as in patients with primary SPSD. In that case, phenolisation could also be considered the first choice of treatment in patients with recurrent SPSD.

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CHAPTER 9

Nederlandse samenvatting

Sinus pilonidalis, ook wel een haarnestcyste genoemd, is een veel voorkomende aandoening en komt voornamelijk voor in de bilspleet. Indien een behandeling is geïndiceerd is dit vaak een chirurgische behandeling. Een radicale excisie is de meest toegepaste techniek, maar een 'gouden standaard' bestaat er niet. Met een radicale excisie wordt gepoogd om de gehele sinus en de verbonden subcutane gangetjes in zijn geheel te verwijderen. 'The American society of colon and rectal surgeons' en 'the Italian society of colorectal surgery' stellen beide dat een chirurgische excisie met of zonder het sluiten van de wond de standaardtherapie voor een sinus pilonidalis zou moeten zijn. Tevens adviseert 'the American society of colon and rectal surgeons' sterk dat een minimaal invasieve techniek zoals fenolisatie een effectieve behandeling is welke kan leiden tot snellere genezing. 'The Italian society of colorectal surgery' geeft over een minimaal invasieve techniek enkel een zwak advies. Een Nederlandse richtlijn voor de behandeling van een sinus pilonidalis bestaat er momenteel niet maar is onder ontwikkeling. Belangrijke postoperatieve risico's na een chirurgische behandeling zijn een infectie en een recidief. Zowel het hebben van een sinus pilonidalis als de behandeling ervan kunnen grote sociale en economische gevolgen hebben. Het identificeren van een optimale behandeling kan voordelen opleveren voor de samenleving aangezien een sinus pilonidalis een veel voorkomende ziekte is die vooral voorkomt bij jonge werkende mannen. Minimaal invasieve technieken worden steeds vaker toegepast en deze technieken worden onderzocht op veiligheid en werkzaamheid.

Bij het optimaliseren van de behandeling is het belangrijk om rekening te houden met het gehele spectrum van een sinus pilonidalis. De aandacht moet niet alleen gevestigd zijn op het minimaliseren van een recidief maar ook de impact van verschillende behandelopties op kwaliteit van leven en het herstelproces.

Zoals in de vorige alinea genoemd is een radicale excisie de meest toegepast behandeling. Een belangrijk nadeel van deze behandeling is het risico op een infectie, wat kan oplopen tot 24%. Er is aangetoond dat het toedienen van postoperatief systemische antibiotica niet leidt tot een afname van het risico op een infectie. Na het aanbrengen van een met gentamicine geïmpregneerd oplosbaar matje (gentamicine matje) in de wond zou het risico wel afnemen. In **hoofdstuk 2** werd het effect van de lokale toediening van een gentamicine matje onderzocht. In de systematische review vonden we een milde afname van postoperatieve wondinfecties na de achterlaten van een gentamicine matje. Deze afname was echter niet significant, wat waarschijnlijk het gevolg is van het lage aantal patiënten in de geïncludeerde studies. In de studies

werden na het aanbrengen van het gentamicine matje geen nadelige effecten op wondgenezing en recidief risico's gerapporteerd. Wat opmerkelijk was is dat in de studies de wond in de mediaanlijn werd gesloten. Wetenschappelijk is er echter bewezen dat de voorkeur uitgaat naar het sluiten van de wond buiten de mediaanlijn. De geïncludeerde studies in onze review hebben een hoge heterogeniteit en bevatten geen details over het gentamicine matje. Onze hypothese luidt dat wonden sneller herstellen als het gentamicine matje in kleine stukjes wordt gesneden voordat deze in de wond wordt ingebracht. Mogelijk zou een matje als geheel als barrière in de wond kunnen werken. Deze hypothese zou moeten worden onderzocht. Voor een definitief antwoord op de vraag of het aanbrengen van een gentamicine matje een positief effect heeft op de genezing na een chirurgische behandeling van een sinus pilonidalis is een gerandomiseerd gecontroleerde studie (RCT) nodig met ongeveer minimaal 400 patiënten.

Naast een hoog risico op een wondinfectie bestaat er ook een hoog risico op een recidief na een chirurgische behandeling van een sinus pilonidalis. Een veel voorkomende theorie is dat onder andere lichaamshaar hieraan bijdraagt. Scheren, epileren, ontharingcrème en laserbehandeling zijn verschillende ontharingstechnieken. In **hoofdstuk 3** is alle beschikbare literatuur over het effect van ontharing op het recidiefpercentage van een sinus pilonidalis na chirurgische behandeling samengevat. Na een laserbehandeling werd bij 9.3% van de patiënten een recidief gevonden, indien er niet werd onthaard bij 19,7% en na scheren en ontharingscrème bij 23.4%. De kwaliteit van de geïncludeerde was echter matig. Op gebied van studiepopulatie, type chirurgische behandeling en definitie van uitkomsten was er heterogeniteit tussen de studies. Het hoogst gevonden percentage recidieven werd gevonden na scheren of ontharingscrème en was waarschijnlijk het gevolg van de grootst geïncludeerde studie van Petersen et al. met 113 patiënten. 11 jaar na chirurgische resectie van een sinus pilonidalis werd een significant verschil gevonden in recidiefkans in het voordeel van niet ontharen (19,7%) vergeleken met scheren of ontharingscrème (30,1%). De recidiefkans was het laagste na laserbehandeling. Een voordeel van deze behandeling is het permanente karakter in vergelijking met scheren en ontharingscrème. De therapie moet wel in een ervaren behandelcentrum worden uitgevoerd en vaak moet de behandeling herhaald worden; mogelijk tot wel acht keer. Daarnaast zijn de kosten relatief hoog en worden ze zelden vergoed door de zorgverzekering. Twee richtlijnen geven een zwak advies ten aanzien van ontharing; 'the American Society of colon and rectal surgeons' adviseert om de haren uit de bilnaad te verwijderen door middel van scheren of laserontharing. 'The Italian society of colorectal surgery'

stelt dat scheren in de bilnaad kan worden toegepast om een recidief te voorkomen en dat laserontharing ook tot positieve resultaten leidt. Op basis van de resultaten in **hoofdstuk 3** moeten patiënten worden ontmoedigd om de bilnaad te scheren en in plaats daarvan is het advies om de recidief kans te verlagen door laserbehandeling. Dit advies moet met de nodige voorzichtigheid worden geïnterpreteerd vanwege de lage kwaliteit van de geïncludeerde studies. Er is meer wetenschappelijk onderzoek nodig om patiënten een sterk advies te kunnen geven ten aanzien van ontharen en het verlagen van het risico op een recidief. Daarnaast moet worden onderzocht naar welke ontharingsmethode de voorkeur uitgaat.

In de afgelopen jaren wordt er een trend gezien naar minimaal invasieve behandeling-modaliteiten voor de behandeling van een sinus pilonidalis. Verschillende minimaal invasieve behandelingen zijn: 'Endoscopische pilonidale sinusbehandeling' (EPSiT), 'Video-assisted ablation of pilonidal sinus' (VAAPS), laserablatiebehandeling en pit excisie met fenolisatie van de sinusholte. Er zijn veel cohort studies gepubliceerd over fenolisatie bij patiënten met een primaire sinus pilonidalis met uitkomsten gericht op pijn, wondgenezing en postoperatieve wondinfecties. Er zijn echter geen data beschikbaar over de tijd die nodig is na een behandeling om dagelijkse activiteiten weer te kunnen hervatten. Bovendien is fenolisatie nooit in een gerandomiseerde gecontroleerde studie vergeleken met de meest toegepaste behandeling, namelijk radicale excisie met primaire wondsluiting. Aangezien een sinus pilonidalis voornamelijk voorkomt bij de jonge, gezonde werkende bevolking, is de tijd die nodig om normale dagelijkse activiteiten te kunnen hervatten een zeer relevant eindpunt. Uitkomsten zoals pijn, wondgenezing en chirurgische wondinfectie dragen allemaal bij aan dit eindpunt. In **hoofdstuk 4** worden de resultaten beschreven van een RCT waarin fenolisatie wordt vergeleken met radicale excisie bij patiënten met primaire sinus pilonidalis. De belangrijkste uitkomstmaat is het aantal dagen dat nodig is om de normale dagelijkse activiteiten te kunnen hervatten. Er werd een significante verkorting van deze uitkomst gevonden; 5,2 dagen na fenolisatie versus 14,5 dagen na radicale excisie. Na fenolisatie was de operatieduur korter, de patiënten hadden significant minder pijn en de epithelialisatie van de wond was significant sneller na fenolisatie. Bij slechts 4% van de patiënten werden milde complicaties geregistreerd. Op basis van de resultaten van deze RCT stellen we dat fenolisatie veilig is en pleiten we voor fenolisatie.

Zoals genoemd zijn andere minimaal invasieve behandelingen EPSiT, VAAPS en laserablatiebehandeling. Resultaten van EPSiT en VAAPS zijn afkomstig van vier pro-

spectieve cohortonderzoeken. Beide behandelingen zijn veilig en er werden geen postoperatieve wondinfecties gerapporteerd. Het risico op een recidief varieerde van 3,7 en14,8%. De laserbehandeling is onderzocht in drie kleine cohortstudies. Ook deze behandeling was veilig en wondinfecties werden bij 5-7% gerapporteerd en 3-10% ontwikkelde een recidief. De follow-up van deze studies was echter slechts 15 maanden. Bij voorkeur zou de follow-up ongeveer minimaal 3 jaar zijn. De beperkte beschikbare resultaten van de andere minimaal invasieve technieken lijken vergelijkbaar met die resultaten van fenolisatie zoals vermeld in dit proefschrift. Echter hebben wij in dit proefschrift ook de resultaten van fenolisatie versus excisie gerapporteerd. Op basis van die resultaten heeft fenolisatie op dit moment de voorkeur.

Na een chirurgische behandeling van een sinus pilonidalis wordt een recidief frequent gezien. Na de succesvolle korte termijn resultaten van fenolisatie, hebben wij ons gericht op de lange termijn resultaten in **hoofdstuk 5**. De lange termijn resultaten van de RCT in hoofdstuk 4 werden na een follow-up van vier jaar geanalyseerd. Er werd geen significant verschil gevonden in recidieven (2,6% versus 5,6%, p = 0,604) en in de kwaliteit van leven. In de beschikbare literatuur werden ook geen significant verschillende risico's op een recidief gevonden tussen fenolisatie en excisie. Calikoglu et al., is de enige andere gerandomiseerde studie waarin fenolisatie vergeleken werd met secundaire wondgenezing. Na een follow-up van 40 maanden werd geen significant verschil in aantal recidieven gerapporteerd (18,6% na fenolisatie en 12,9% na chirurgische excisie (p = 0,92). Enkele retrospectieve case-control studies vergeleken fenolisatie met excisie en een flapreconstructie. Deze studies vonden ook geen significante verschillen in recidiefpercentages. In onze RCT werd een recidief gedefinieerd en geobjectiveerd door een arts. Een kleine groep patiënten (14%) had na fenolisatie een tweede behandeling nodig. Ondanks een tweede behandeling kiest een opmerkelijk hoger percentage patiënten nog steeds voor dezelfde behandeling na fenolisatie (83%) vergeleken met excisie (58%). De kleine impact van herhaalde fenolisatie lijkt dus op te wegen tegen de nadelen van een tweede fenolisatie. Daarnaast was de totale persoonlijke impact van fenolisatie significant minder in vergelijking met excisie. Na de veelbelovende korte termijn resultaten in hoofdstuk 4 werd in deze lange termijn studie het succes van fenolisatie bevestigd. Daarom is ons advies om fenolisatie als eerste behandeloptie te overwegen voor de behandeling van een sinus pilonidalis.

Na een ingreep van een sinus pilonidalis worden recidieven gerapporteerd tot 68% en tot na 10 jaar na de operatie. Vanwege dit hoge percentage en de veelbelovende

resultaten van fenolisatie bij een primaire sinus pilonidalis (zoals beschreven in hoofdstuk 4 en 5) werd fenolisatie bij patiënten met een recidiverende sinus pilonidalis uitgevoerd. In **hoofdstuk 6** is de prospectieve cohortstudie gerapporteerd welke gericht is op korte termijn resultaten (follow-up van 3 maanden). Na fenolisatie van 57 patiënten met recidiverende sinus pilonidalis konden patiënten na gemiddeld vijf dagen dagelijkse activiteiten hervatten. Dit resultaat is vergelijkbaar met de patiënten die met fenolisatie behandeld werden met een primaire sinus pilonidalis (hoofdstuk 4). Nogmaals, de behandeling was veilig en er traden geen grote complicaties op. In onze cohortstudie was na twaalf weken de pijn afgenomen en kwaliteit van leven verbeterd ten opzichte van preoperatief. Slechts twee cohortstudies met resultaten gericht op fenolisatie bij patiënten met een recidiverende sinus pilonidalis werden eerder gepubliceerd: één retrospectieve studie met een inclusie van 26 patiënten welke een genezingspercentage van 92,3% rapporteerde en één prospectieve studie met 36 patiënten welke volledige genezing rapporteerde na een mediaan van 48 dagen. In de genoemde cohortstudies werd echter de uitkomstmaat 'hervatten van dagelijkse activiteiten' niet gerapporteerd. In de cohortstudie in hoofdstuk 6 werd het recidiefpercentage niet gerapporteerd aangezien een langere follow-up vereist is dan 3 maanden die in de studie werd gehanteerd.

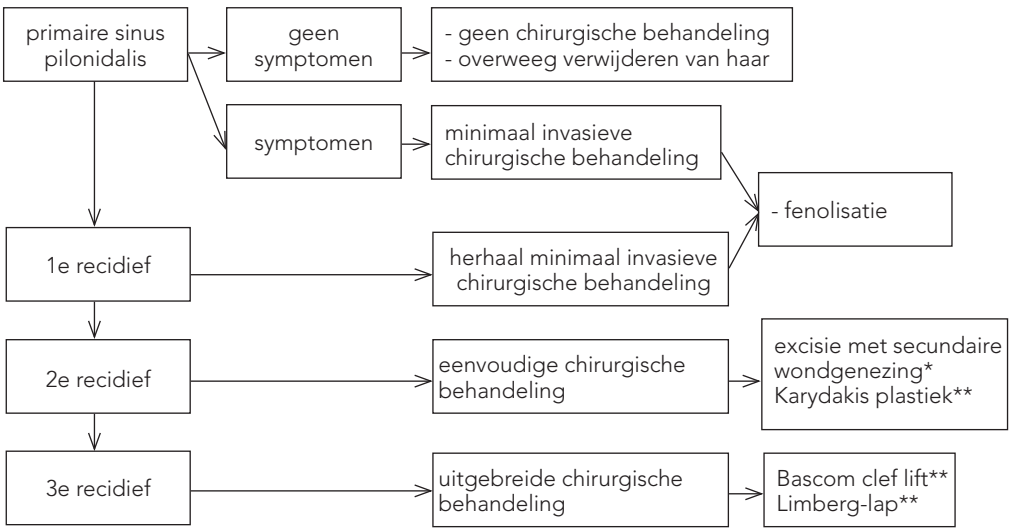
Twee eerder gepubliceerde RCT's vergeleken twee niet-minimaal invasieve procedures vergeleken bij patiënten met recidiverende sinus pilonidalis; de Limberg-lap en de Karydakis-plastiek. Bali et al., rapporteerden een mediaan verlies van respectievelijk acht (range 6-12) en 17 (range 14-20) dagen met dagelijkse activiteiten. El Hadidi et al., rapporteerde dat na respectievelijk 20 (± 6,01) en 22,35 (± 4,8) dagen na de ingreep het werk weer kon worden hervat. In vergelijking met onze bevindingen in de cohortstudie leidt excisie bij recidiverende sinus pilonidalis tot latere hervatting van dagelijkse activiteiten in vergelijking met fenolisatie. Andere minimaal invasieve technieken zijn ook onderzocht bij recidiverende sinus pilonidalis. EPSiT werd onderzocht in een prospectief cohort van 122 patiënten met recidiverende sinus pilonidalis. De patiënten hervatte na drie dagen het werk. De lasertechniek werd onderzocht in een prospectief cohort met patiënten met een eerste en een recidief sinus pilonidalis. Na de lasertechniek hervatte 92,8% van de patiënten de dagelijkse activiteiten onmiddellijk. Na beide technieken lijkt dus een iets sneller herstel van dagelijkse activiteiten mogelijk te zijn in vergelijking met fenolisatie. Echter ontbreken RCT's die de verschillende minimale invasieve technieken bij patiënten met recidiverende sinus pilonidalis met elkaar vergelijke. Dergelijke onderzoeken zouden gedaan moeten worden om te bewijzen of er een minimale invasieve techniek superieur is. Fenolisatie wordt in onze instelling steeds vaker toegepast bij patiënten met recidiverende sinus pilonidalis,

aangezien onze grote prospectieve cohortstudie naar fenolisatie bij recidiverende sinus pilonidalis veelbelovende resultaten liet zien en tevens vergelijkbaar is met de resultaten van onze RCT gericht op primaire sinus pilonidalis. Voordat een definitief advies gegeven kan worden over de meest effectieve behandeling voor patiënten met recidiverende sinus pilonidalis moeten de lange termijn resultaten van deze cohort studie beoordeeld worden met als primaire uitkomst het recidiefpercentage.

In dit proefschrift wordt herhaaldelijk genoemd dat een sinus pilonidalis voornamelijk voorkomt bij de jonge werkende mannen. Onze hypothese was dat het hebben van een sinus pilonidalis een negatieve invloed zou hebben op het seksueel functioneren. In verschillende onderzoeken is het effect van een sinus pilonidalis op de algemene kwaliteit van leven geëvalueerd, echter zijn er geen resultaten beschikbaar over de impact van een sinus pilonidalis op het seksueel functioneren. In **hoofdstuk 7** wordt de eerste prospectieve studie beschreven die de invloed van een sinus pilonidalis op het seksuele functioneren bij mannelijke patiënten evalueert. Vergeleken met voor de operatie verbeterende de seksuele functie na zes tot twaalf weken na fenolisatie of excisie bij 88 patiënten. De seksuele functie werd beoordeeld met de SSCS ('sexual self-consciousness scale'). Deze vragenlijst is verdeeld in twee sub schalen, namelijk de SE ('sexual embarrassment subscale') gericht op gevoel van remming en ongemak in seksuele situaties en de SFF ('sexual self-focus subscale') gericht op het zelfbewustzijn. Zes weken postoperatief nam de SE sub schaal significant af, wat duidt op een betere seksuele functie. Echter was er na twaalf weken geen significant verschil met de preoperatieve score. Aangezien de SFF sub schaal zes weken na de operatie afnam en deze tot twaalf weken na de operatie aanhield concludeerde wij dat een behandeling van een sinus pilonidalis meer invloed had op het seksuele zelfbewustzijn. Omdat een sinus pilonidalis vaker voorkomt bij mannelijke patiënten en om een meer homogene patiëntengroep te creëren werden alleen mannelijke patiënten in deze studie geïncludeerd. Vanwege het kleine aantal patiënten in beide behandelgroepen werden de uitkomsten van verschillende behandelingen (fenolisatie en excisie) op seksueel functioneren niet vergeleken. De follow-up van 12 weken was relatief kort en er was een relatief lage response van 69%. Dit zou het gevolg van het onderwerp van de vragenlijst kunnen zijn. De patiënten voelden zich mogelijk beschaamd om seksuele vragen te beantwoorden. De resultaten van de studie kunnen helaas niet vergeleken worden met de gezonde individuen omdat er geen data beschikbaar is over de uitkomst van deze vragenlijst bij de normale gezonde populatie. Na 12 weken zagen we wel een toename van 10% ten opzichte van preoperatief van patiënten die het geheel of gedeeltelijk oneens waren met de stelling: 'sinus pilonidalis beïnvloedt

mijn seksuele functie'. Gezien de toename van 10% lijkt deze toename klinisch relevant. Patiënt-gerapporteerde uitkomsten (PROMS) worden steeds belangrijker, inclusief gegevens over seksueel functioneren bij patiënten met aandoeningen in het urogenitale gebied. De resultaten van deze studie kunnen helpen bij preoperatieve counseling van patiënten die zich voorbereiden op een behandeling van een sinus pilonidalis.

Op basis van de resultaten van de studies in dit proefschrift en de aanvullende beschikbare literatuur wordt het behandelprotocol in figuur 1 aanbevolen.



Figuur 1. Behandelstrategie voor patiënten met een sinus pilonidalis
* Vacuüm therapie kan overwogen worden
** Er is geen bewijs voor het toevoegen van een met gentamicine geïmpregneerd oplosbaar matje

TOEKOMSTPERSPECTIEVEN

De afgelopen jaren is er een verschuiving geweest van excisie naar minimaal invasieve technieken. Ondanks deze ontwikkeling is het optimaliseren van de behandeling van een sinus pilonidalis nog steeds relevant.

Het optimaliseren van de behandeling begint met het begrijpen van de etiologie van de aandoening. De etiologie van een sinus pilonidalis is nog altijd niet volledig duidelijk. Nieuwe bevindingen suggereren dat het haar dat in de sinus wordt aangetroffen, afkomstig is van haar van het hoofd. Deze hypothese kan in twijfel getrokken worden omdat kale mensen ook een sinus pilonidalis kunnen hebben. Toekomstige studies zouden zich moeten richten op verdere opheldering van de etiologie. Haar van het hoofd, de bilspleet en de sinus zouden moeten worden vergeleken en microscopisch geanalyseerd. Dit zou kunnen helpen bij het verlagen van de kans op een recidief na een operatie van een sinus pilonidalis.

Als een chirurg besluit om een radicale excisie uit te voeren bij een patiënt met een sinus pilonidalis adviseert een Cochrane review sterk om de wond buiten de mediaanlijn te sluiten. Dit leidt tot een vermindering van infectie- en recidiefpercentages. Op basis van het systematische review en meta-analyse in hoofdstuk 2 kan er geen advies worden gegeven om een gentamicine matje aan te brengen. Een grotere opgezette RCT is daarvoor vereist. Verder moet onderzocht worden of de wondgenezing bevorderd wordt door het gentamicine matje in kleine stukjes snijden alvorens deze in de wond te brengen.

In ons review concludeerde we dat laserontharing de meest effectieve behandeling lijkt te zijn om het risico op een recidief van een sinus pilonidalis te. Op basis van die conclusie moeten patiënten worden geadviseerd om laserontharing te ondergaan in plaats van scheren. De methodologische kwaliteit van de geïncludeerde studies was echter beperkt, terwijl de heterogeniteit tussen de studies uitgesproken was. Om te beoordelen of laserontharing voorafgaand aan chirurgische behandeling van een sinus pilonidalis van toegevoegde waarde is moet worden onderzocht in een RCT. Belangrijkste uitkomstparameters zouden recidiefpercentages, pijn, bijwerkingen en kosten moeten zijn.

Aangezien vooral de jonge werkende beroepsbevolking een sinus pilonidalis heeft is het hervatten van dagelijkse activiteiten na een ingreep een belangrijke uitkomst-

parameter. Op basis van de RCT beschreven in de hoofdstukken 4 en 5, worden chirurgen aangemoedigd om fenolisatie te beschouwen als voorkeursbehandeling voor een primaire sinus pilonidalis. De verschillende minimaal invasieve technieken moeten echter direct in RCT's worden vergeleken om uiteindelijk te beoordelen welke minimaal invasieve techniek superieur is.

In de prospectieve cohortstudie zijn de korte termijn resultaten van fenolisatie bij patiënten met een recidief sinus pilonidalis gunstig en vergelijkbaar met de korte termijn resultaten van fenolisatie bij patiënten met een primaire sinus pilonidalis. Om te beoordelen of het recidief percentage bij patiënten met recidiverende sinus pilonidalis hetzelfde is als bij patiënten met primaire sinus pilonidalis na fenolisatie zijn ook lange termijn resultaten noodzakelijk. Indien het recidief percentage gelijk is kan fenolisatie ook worden beschouwd als de eerste keuze behandeling bij patiënten met recidiverende sinus pilonidalis.

CHAPTER 10

Review committee

List op publications

Dankwoord

Curriculum Vitae

REVIEW COMMITTEE

Prof. dr. M.R. van Dijk
Prof. dr. R.L.A.W. Bleys
Prof. dr. T.J.M. Verheij
Prof. dr. M.R. Vriens
Prof. dr. J.F. Lange

LIST OP PUBLICATIONS

Nguyen LA, **Pronk AA**, Furnée EJB, Pronk A, Davids PHP, Smakman N. Local administration of gentamicin collagen sponge in surgical excision of sacrococcygeal pilonidal sinus disease: a systematic review and meta-analysis of the literature. *Tech Coloproctol. 2016 Feb;20(2):91-100.*

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DANKWOORD

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Geachte **Prof. Dr. I.H.M. Borel Rinkes, beste Inne**. Wij hebben in de afrondende fase van mijn promotietraject samengewerkt. Uw enthousiasme voor dit algemene chirurgische onderwerp gaf mij veel vertrouwen en werkte motiverend. Uw heldere commentaar en input heeft het afronden van mijn proefschrift enorm bevorderd. Veel dank voor uw rol als promotor.

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CURRICULUM VITAE

Anne Akke Pronk werd op 8 augustus 1991 geboren te Utrecht. In diezelfde stad behaalde ze haar VWO-diploma op het St. Bonifatiuscollege en startte zij haar studie Geneeskunde aan de Universiteit Utrecht. In 2016 behaalde ze haar arts-examen.

Gedurende het einde van de opleiding Geneeskunde raakte Akke overtuigd van haar passie voor de urologie en startte zij als ANIOS urologie in het UMC Utrecht. In het UMC Utrecht heeft ze met veel plezier haar eerste ervaringen als toekomstig uroloog opgedaan. Na zes maanden in de academie stapte Akke over naar het Tergooi Ziekenhuis in Blaricum om daar haar kennis en ervaring verder uit te breiden.

In 2019 werd Akke aangenomen voor de opleiding urologie (opleider prof. dr. L.M.O. de Kort). Haar vooropleiding bij de chirurgie volbracht ze in het Meander Medisch centrum in Amersfoort (opleider prof. dr. E.C.J. Consten). Momenteel vervolgt Akke haar opleiding urologie in het St. Elisabeth Tweesteden Ziekenhuis (opleider dr. J.H. van Roijen). In de loop van 2021 zal ze haar opleiding voorzetten in het UMC Utrecht.

Interesse in de wetenschap werd tijdens haar studie geneeskunde aangewakkerd door deelname aan het Honoursprogramma. Dit programma volgde zij bij de interventieradiologie waar zij onderzoek deed naar de kwaliteit van leven na radioembolisatie. Door haar nieuwsgierigheid naar de snijdende vakken besloot ze verder onderzoek te doen naar een algemeen chirurgisch onderwerp. Ze kreeg de kans het

onderzoek naar de behandeling van een haarnestcyste (sinus pilonidalis) op te starten onder leiding van N. Smakman en E.J.B. Furnée. Naast een klinische studie, waarin twee behandelingen voor een haarnestcyste met elkaar werden vergeleken, schreef ze verschillende artikelen op dit gebied. Alle artikelen bundelde Akke in dit proefschrift.

Naast studeren en werken was Akke van 2013 tot 2017 actief als marathonschaatster op nationaal niveau. Als hoogtepunt schaatste ze tweemaal de alternatieve Elfstedentocht uit op de Weissensee in Oostenrijk en reed ze wedstrijden op het Zweedse natuurijs. Na het stoppen met schaatsen op nationaal niveau is Akke altijd sportief gebleven. Zo doet ze af en toe een triatlon, maakt ze vele kilometers op de racefiets en haalt ze graag haar schaatsen nog uit het vet.