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Review

## TREATMENT PROCEDURES FOR ANAL FISTULOUS CRYPTOGLANDULAR ABSCESS — How to Get the Best Results

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#### **Abstract**

Introduction: Up to date anal fistulous cryptoglandular abscess is a subject of controversial scientific discussions and the number of medico legal cases dealing with treatment procedures is growing. In principal, there is a dispute whether it is reasonable to perform a primary fistulotomy at the time of abscess drainage or to wait for a secondary fistulotomy. The purpose of this study was to compare studies focussing on the treatment of anal fistulous abscess with regard to different treatment procedures, their outcome (recurrence, incontinence, follow-up) and factors influencing outcome (primary or recurrent fistulous abscess, comorbidity, exclusion criteria, anaesthesia, microbiology, antibiotics, search for internal opening, classification).

Methods: A Medline search included the terms: fistulous abscess, anal abscess, horseshoe abscess, anorectal sepsis, and perianal infection/abscess.

Results: In 63 (1964-2004) studies we found 35 different treatment methods: the most often used procedures were incision and drainage (I + D; n = 35) and incision and drainage and primary fistulotomy (I + D + pF; n = 23). Only in ten studies the treatment has been restricted for primary anal fistulous abscess; the remaining studies investigated primary and recurrent anal fistulous abscess. There was a considerable lack of information on morbidity, microbiology, and exclusion criteria. In only 16/63 studies patients were routinely diagnosed and treated under general anaesthesia. We found nine different classifications of fistulous abscess. There is a wide range of recurrence after different treatment procedures: up to 88% after 1+D and 21% after I + D + pF. The incontinence rate after 1 + D ranged from 0-26%, after 1 + D + pF 0-52%. However, in many studies there was no information on incontinence available.

Conclusion: A true comparison of different treatment methods is not available. This is mainly due to either a lack of information on important factors influencing outcome, even unclear definitions in some instances. Recent randomized studies have been criticized for missing information and flaws in the randomization procedure. The choice of treatment, e.g., primary or secondary fistulotomy, depends on the clinical experience of the surgeon on duty, the hospital structure (staff, equipment, and anaesthesia), the patient's history and the local anatomical circumstances. On the ba-

sis of up to date knowledge there is no reason to condemn primary or secondary fistulotomy without more clinical studies and without knowing the individual situation.

#### Introduction

Anal fistulous abscess poses a challenge to the treating physician and surgeon since ancient times (Aderne 1983). Lockart-Mummery noted in 1929 that probably more reputations had been damaged by unsuccessful treatment of cases of fistula than by excision of the rectum (Lockart-Mummery 1929).

Complex anorectal conditions are difficult to diagnose because clinical features overlap (Gilliland and Wexner 1997). "It is often stated that our knowledge of gross anatomy has reached its ultimate peak of perfection and apotheosis. This is far from true." (Harkins 1965) The actiology of anorectal abscess and fistula appears to be diverse. However, in 1958 Eisenhammer proposed the anal gland/intermuscular abscess theory causing 97 per cent of anorectal abscesses. Parks wrote in 1961: perhaps the most widely held theory concerning the cause of fistula is that infection penetrates the wall of the anal canal through a fissure or other wound and that the infected tract, once established, is maintained by faecal contents entering the internal opening. "The present concept of pathogenesis strongly suggests that both abscess and fistula are one and the same disease: abscess is the acute phase, fistula the chronic" (Parks et al. 1976). Treatment of the fistulous abscess like the lay-open procedure is based on this concept (Parks 1961); the problem is that not all acute abscesses seem to be followed by a chronic fistula (Parks et al. 1976). Goligher et al. (1967) who performed a careful dissection in sixty patients with either an abscess or a fistula were unable to demonstrate an internal opening in most patients. "In fact, a fistula-inano is virtually a sinus secondary to a diseased anal gland, though the minute duct opening into the anal crypt makes it technically a fistula. This would fit with the practical observation that about half the cases of anal fistula do not have a clinically detectable opening." (Parks 1961) And Parks stated: our understanding of the pathogenesis of fistula is still incomplete and unsatisfactory, the results of treatment, though good in most cases, still leave much to be desired. Even in the most expert hands, fistulas still recur after operation, and surgery for high fistulas often is complicated by interference with normal sphincter activity (Parks 1963). The dispute how to treat a fistulous abscess seems to be closely related to this concept of pathogenesis.

There are two principal ways to manage the fistulous abscess: the more conservative approach by incision and drainage followed by a second operation, if necessary, and the more aggressive technique of incision and drainage together with primary fistulotomy. A recent meta-analysis was unable to solve the controversy (Quah et al. 2005). Sphineter-cutting procedures for ano-rectal abscesses resulted in an 83% reduction in recurrence rate, but there was a tendency to higher risk of faecal incontinence (Quah et al. 2005). Unfortunately, there were problems with regard to methodology according to the authors of the meta-analysis (e.g., randomization process, sample size) and the meta-analysis was performed for five studies only.

The purpose of this study was to compare studies focussing on the treatment of anal fistulous abscess with regard to different treatment procedures, their outcome (recurrence, incontinence, follow-up) and factors influencing outcome (primary or recurrent fistulous abscess, comorbidity, exclusion criteria, anaesthesia, microbiology, antibiotics, search for internal opening, classification).

#### MATERIAL AND METHODS

A Medline® search was performed for the terms anal abscess, horseshoe abscess, anorectal sepsis, fistulous abscess, perianal infection or abscess. The last search has been performed in May 2006. We included papers published in English or German, which could be retrieved in Medline and which reported on the treatment of anal fistulous cryptoglandular abscess. Papers reporting the results of treatment of anal fistula without fistulous abscess were excluded as were reports on perianal infection in children, Crohn's disease, ulcerative colitis and hidradenitis suppurativa. The reports were then evaluated for the type of study, definition of anorectal sepsis, comorbidity, exclusion criteria, general anaesthesia, microbiology, search for internal opening, classification of fistulous abscess, use of antibiotics, procedures, recurrence of abscess and/or fistula, and incontinence and follow-up. Results on recurrence and incontinence were given in range.

#### RESULTS

Sixty-three studies were included for evaluation. There were five prospective studies, nine randomized controlled studies (Table 1) and 49 retrospective studies or case reports. The studies were published in the years 1964 to 2005 and had a study population ranging from 1 to 1023.

Only in ten studies the authors have given a clear definition of the anal fistulous abscess studied: primary fistulous abscess, 53 studies included patients with primary fistulous abscess, chronic fistulous abscess, or previous surgical treatment for fistulous abscess.

30 studies reported on the *comorbidity* of patients with fistulous abscess, in the remaining 33 studies in-

Table 1. Treatment groups used in most studies.

Treatment	Number of Studies
Incision+Drainage (I+D)	35
Incision+Drainage+primary Fistulotomy (I+D+pF)	23
Incision+Drainage+secondary Fistulotomy (I+D+sF)	3
Incision+Drainage+Sphincterotomy (I+D+Sp)	6
Incision+Drainage+pS (primary suture)	3
I+D+Se (setch)	6
I+D+U (unroofing)	9
I+D+pI <sup>2</sup>	4
I+D+sF	5

cluding the randomized controlled studies data on comorbidity were not available.

Exclusion criteria (e.g., inflammatory bowel disease) were announced in 38 studies and were missing in 25 studies including one randomized controlled study. Several reports focussed on complex fistulas only (Hamilton 1975; Hanley et al. 1976; Hanley 1978; Hanley 1979; Held et al. 1986; Inccoglu and Gencosmanoglu 2003; Joy and Williams 2002; Ramanujam et al. 1983) or simple fistula only (Ho et al. 1997; Tang et al. 1996).

Although it is obvious from the descriptions of many authors, that diagnosis and treatment of anal fistulous abscess may be successfully and securely performed in a patient under general anaesthesia, this has been carried out on a routine basis only in 16 studies; in 19 studies general anaesthesia was used in some but not in all patients. Regional anaesthesia only was applied for patients in five studies, local anaesthesia alone in one study, regional and/or local anaesthesia was applied in 5 studies, and in 17 studies the information was missing or unclear, including two randomized controlled studies.

Microbiological investigations were done and reported in 16 studies, in one study microbiological tests were performed in some patients. In 46 studies, including three randomized controlled studies, the microbiological results were not available.

Most authors reported that a search for *internal openings* has been performed (n = 45). In five studies it has been frankly stated that a search for internal opening was never performed. 9 studies, including two randomized controlled studies, did not indicate the search for internal opening. In two studies searching was left to the individual decision of the surgeon, no probing was allowed in one study, and search was prohibited in one study in the incision and drainage group but allowed in the fistulotomy group.

At least nine published *classifications* were used for description of the fistulous abscess: Parks et al. (1976) (n = 34), Milligan and Morgan (1934) (n = 4), Stelzner (1981) (n = 4), Eisenhammer (1954) (n = 4), Goligher (1980) (n = 1), Gabriel (1963) (n = 5), Lilius (1968) (n = 1), Courtney (1949) (n = 1), Goldberg et al. (1980)

Table 2. Recurrence, incontinence and follow-up after incision and drainage.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up	
Abcarian	1976	1.6	0	-	_	
Bernard	1983	66	•	-	-	
Buchan	1973	16	16	-	4-9 years	
Cox	1997	44.1	44.1	20.6	44 months	
Doberneck	1987	4	12	-	1 year	
Fucini	1991	88	88	0	64 months	
Gemsenjäger	1989	-	•	-	•	
Giebel	1991	•	84	0	15 months median	
Goligher	1967	10	•	5 overall	3-5 years	
Grace	1982	14.5 overall	1.8 overall	-	•	
Hämälainen	1998	10	37	-	5.5 years	
Held	1986	60	0	0	3 years	
Но	1997	3.6	25	0	15.5 months	
Knoefel	2000	34	34	3.1 overall	40 months	
Kovalcik	1979	11.2 overall	11.2 overall	2 temporary	•	
Kyle	1990	5.6	10.3	0	•	
Lai	1983	13	27	0	•	
Marks	1973	D	D	D	D	
Maskow	1989	14.3 overall	14.3 overall	26	-	
Nomikos	1997	7.1 overall	7.1 overall	_	19 months	
Oliver	2003	29 overall	29 overall	0	12 months	
Onaca	2001	8.4 overall	8.4 overall	•	2 weeks	
Prasad	1981	2 overall	2 overall	-	2-4 years	
Ramstead	1983	-	18	-	-	
Read	1979	•	•	-	•	
Sangwang	1996	•	0	0	-	
Schouten	1991	40.6 persistence and recurrence	•	21.4	42.5 months median	
Scoma	1974	-	66	-	6 months – 13 years	
Seow-Choen	1993	11	11	0	121/122 weeks	
Fang	1996	14.3	14.3	0	l year	
Vasilevsky	1984	11	37	•	•	
Waggener	1969	61.9 overall	61.9 overall	0	-	
Weber	1982	8	31	0	•	
Whitehead	1982	-	-	-	-	
Winslett	1988	•	•	_	•	

<sup>-</sup> Unclear or missing information

(n = 1). In 8 studies no classification system has been reported. Arbitrary or simple classifications (side of location or deep versus superficial) were used in 5 studies.

In nine studies antibiotics were used routinely, in 18 studies partially. The type of antibiotic is not indicated in most studies. No antibiotics were given in seven studies and use of antibiotics was not communicated in 29 studies.

Treatment procedures for fistulous abscess were used in 35 different treatment procedures. There are six major treatment combinations: incision and drainage =

I+D with variations (unroofing = U; packing = P; incision and drainage plus fistulotomy = F or fistulectomy = Fi with further variations, e.g., counter incision = CI, sphincter reconstruction and/or muscle filling procedure = SRC; incision and drainage with unroofing plus fistulotomy or seton = Se; incision and drainage with sphincterotomy = Sp; incision and drainage with seton or primary suture = pS with variations, e.g., pezzer catheter = PC or Gentacoll antibiotic, and single type of treatment groups fistulotomy, seton, sphincterotomy, fistulectomy, rectal advancement flap = RAF. Incision and drainage (n = 35) and inci-

D death

sion and drainage plus primary fistulotomy (n=23) are the most frequently studied techniques. They are followed in number by incision and drainage plus unroofing (n=9), incision and drainage plus seton (n=6), incision and drainage plus sphincterotomy (n=6), incision and drainage plus secondary fistulotomy (n=5), incision and drainage and unroofing plus primary fistulotomy (n=4), incision and drainage plus secondary fistulotomy (n=3) and incision and drainage plus primary suture (n=3) (Table 1).

Recurrence of abscess and/or fistula is not indicated in all studies. Recurrence rate for abscess is higher after incision and drainage (1.6%-88%) than after incision and drainage plus unroofing (3%-18.6%), incision and drainage plus primary fistulotomy (0-21.1%), incision and drainage plus secondary fistulotomy (0%), incision and drainage plus sphineterotomy (7.1-50%), incision and drainage plus seton (0-12.5%), incision and drainage plus primary suture (15-20%) (Tables 3-11).

Recurrence rate for fistula is highest after incision and drainage (0-84%) when compared to incision and drainage plus unroofing (3%-26%), incision and drainage plus primary fistulotomy (0-21%), incision and drainage plus secondary fistulotomy (0-0.8%), incision and drainage plus sphincterotomy (7.1-13%), incision and drainage plus seton (0-12.5%) or incision and drainage plus primary suture (7-20%) (Tables 2-11).

Incontinence rate after treatment for fistulous abscess is often missed or unclear. Incontinence rate shows large variation in the different treatment groups. Incision and drainage may cause incontinence in 0-26% of patients. The incontinence rate after incision and drainage plus unroofing is 0-5%. Incision and drainage plus primary fistulotomy (0-52%) or secondary fistulotomy (0-4%) differ with regard to incontinence rate. Incision and drainage plus sphincterotomy may cause incontinence, but the incontinence rate is not indicated in four studies. In one study there was no incontinence observed. When a seton is applied after incision and drainage the incontinence rate may vary from 0-37.5% (Table 2-11).

The preoperative assessment of incontinence was practically never performed or left to assessment by questionnaire (Schouten et al. 1991). The time of the follow-up is often not available. The parameter for assessment of the success of the treatment of anal fistulous abscess recurrence and incontinence are missing in many studies.

#### Randomized Controlled Studies

There are 9 randomized controlled studies investigating the treatment in patients with fistulous abscess. The study populations range from 38 to 219 patients with three studies having less than 50 patients and 6 studies with less than 100 patients. Four of nine studies enrolled only patients with primary acute abscess, whereas five studies included all types of abscess. There was no information given on comorbidity. In 8 of 9 studies exclusion criteria were reported. In seven studies patients were treated under general anaesthesia, in one study general or spinal anaesthesia, and in one study information was lacking. In six studies no microbiological test was performed. A search for in-

ternal opening was performed in most studies: 6/9 studies. In 2 studies the decision was left to the individual surgeon, in one study it was banned from the group investigating incision and drainage only while it was possible in the fistulotomy group. Antibiotics were not administered in 2 studies and prohibited in one study. In three studies patients received routinely antibiotics, in three studies no information was given on the use of antibiotics. Three studies compared incision and drainage to primary fistulotomy (Ho et al. 1997; Oliver et al. 2003; Tang et al. 1996). Hebjorn et al. (1987) compared incision, drainage and unroofing to incision, drainage and secondary fistulotomy. Schouten et al. compared incision and drainage to sphincterectomy and primary fistulotomy (1991). Tonkin et al. (2004) compared incision, drainage and unroofing to incision, drainage, unroofing and packing. Kronborg and Olsen (1984) compared incision, drainage and primary fistulotomy to incision, drainage, primary fistulotomy, curettage and primary suture. Leaper et al. (1976) compared incision, drainage, primary fistulotomy and packing to incision, drainage, curettage and primary suture; and finally Mortensen et al. (1995) compared incision, drainage, primary suture plus Gentacoll to incision, drainage and primary su-

The recurrence rate for abscess ranges from 0% to 40.6%. The recurrent rate for abscess after incision and drainage is 3.6% (Ho et al. 1997), 29.5 (Oliver et al. 2003), 14.3% (Tang et al. 1996), 40.6% (Schouten et al. 1991), after incision, drainage and unroofing 5.6% (Hebjorn et al. 1987), 13% (Tonkin et al. 2004). Abscess recurrence rate after incision, drainage, primary fistulotomy has been 4.2% (Ho et al. 1997), 29.5% (Oliver et al. 2003), 0% (Tang et al. 1996) or 2.9% when combined with sphincterectomy (Schouten et al. 1991). After incision, drainage and unroofing the abscess recurrence rate was between 5.6% (Hebjorn et al. 1987) and 13% (Tonkin et al. 2004). Hebjorn et al. (1987) reported an abscess recurrence rate of 5.6% when unroofing was combined with secondary fistulotomy; Tonkin et al. (2004) observed a recurrence rate of 5% for abscess. Leaper et al. (1976) found an anal abscess recurrence rate of 26.3% after incision, drainage, primary fistulotomy and packing compared to 9.3% after incision, drainage, and curettage and primary suture. Kronborg and Olsen (1984) reported a recurrence rate of 15% for incision, drainage, primary fistulotomy, curettage and primary suture. Mortensen et al. (1995) did no find an advantage when he added gentacoll to incision, drainage and primary suture compared to the same treatment without gentacoll (22 versus 17%).

In four studies recurrence is used for abscess and fistula (Tang et al. 1996, Schouten et al. 1991, Oliver et al. 2003, Mortensen et al. 1995). Leaper et al. (1976) reported on abscess recurrence only. The recurrence rate for fistula was highest after incision and drainage: 25% (Ho et al. 1997). In descending order the following fistula recurrence rates were reported: incision, drainage, unroofing, packing with 20% (Tonkin et al. 2004), incision, drainage + primary fistulotomy with 12.2% (Kronborg and Olsen 1984), incision, drainage + unroofing with 11.1% (Hebjorn et al. 1987) and

Table 3. Recurrence, incontinence and follow-up after incision and drainage + primary fistulotomy.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up
Abcarian	1976	0	0	-	-
Bernard	1983	0	-	-	-
Cox	1997	21.1 overall		21.1	44 months
Doberneck	1987	0	0	-	1 year
Fucini	1991	0	0	4	64 months
Giebel	1991	•	3	0	15 months median
Grace	1982	14.5 overall	1.8 overall	-	-
Hanley	1976	0	0	0	•
Held	1986	8	0	0	3 years
Но	1997	4.2	0	0	15,5 months
Knoefel	2000	4 overall		3.1 overall	40 months
Kovalcik	1979	11.2 overall		2 temporary	-
Kronborg	1984	7.3	12.2	•	36 months
Lai	1983	0	0	0	•
Maskow	1989	0	0	52	-
Mazier	1971	3.9 overall		-	6 months - 9 years
McElwain	1975	3.6	3.6	3.2	42.7 months
Oliver	2003	5	5	6	12 months
Prasad	1981	2 overall	-	2-4 years	
Seow-Choen	1993	13	13	6.5 minor	121/122 weeks
Tang	1996	0	0	0	12 months
Waggener	1969	0	0	0	-
Weber	1982	6	0	0	•

Table 4. Recurrence, incontinence and follow-up after incision and drainage + secondary fistulotomy.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up
Abcarian	1976	0	0	-	-
Hill	1967	-	0.8 overall	4 overall	Less than 1 year – 20 years
Waggener	1969	0	0	0	-

Table 5. Recurrence, incontinence and follow-up after incision and drainage + sphincterotomy.

Author	Year	ar Recurrence rate Recurrence abscess % fistula %		Incontinence rate %	Follow-up	
Athanasiadis 1990		21-22.2 overall	21-22.2 overall	-	18-44 months	
Bernard	1983	50	-	-	-	
Gemsenjäger	1989	-	-	•	-	
Hanley	1979	-	-	-	-	
Nomikos	1997	7.1 overall	7.1 overall	-	19 months	
Sohn	1980	13	13	0	2-6 years	

Table 6. Recurrence, incontinence and follow-up after incision and drainage + primary suture.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up
Buchan	1973	20	20	-	4-9 years
Mortensen	1995	17	17	-	3 months
Wilson	1964	15	7	-	27 months

Table 7. Recurrence, incontinence and follow-up after incision and drainage + seton.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up
Cox	1997	12.5	12.5	37.5	44 months
Fucini	1991	0	0	0	64 months
Hanley	1978		-	-	-
Held	1986	0	0	0	3 years
Pearl	1993	3 overall	3 overall	5 overall	23 months
Sangwang	1996	•	0	0	-

Table 8. Recurrence, incontinence and follow-up after incision and drainage and unroofing.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up	
Buchan	1973	18.6	15.1	-	4-9 years	
Chrabot	1983	•	•		•	
Hebjorn	1987	5.6	11.1	0	12 months	
Henrichsen	1986	26 overall	26 overall	-	6 months	
Lindell	1973	•	•	•	-	
Pearl	1993	3 overall	3 overall	5 overall	23 months	
Ramanujam	1984	3.7	3.7	•	36 months	
Schouten	1987	•	-	0	1-5 years	
Tonkin	2004	13	8.7	-	-	

Table 9. Recurrence, incontinence and follow-up after incision and drainage and unroofing + primary fistulotomy.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up
Henrichsen	1986	26 overall	26 overall	-	6 months
FGII	1967	-	0.8 overall	4 overall	Less than 1 year – 20 years
Lindell	1973		-		-
Ramanujam	1984	1.8	1.8	•	36 months

Table 10. Recurrence, incontinence and follow-up after incision and drainage and unroofing + secondary fistulotomy.

Author	Year	Recurrence rate abscess %	Recurrence rate fistula %	Incontinence rate %	Follow-up
Chrabot 1983 Hebjorn 1987		5,6	- 5.6	44.4	- 12 months
Henrichsen	1986	26 overall	26 overall	-	6 months
Ramanujam	1983	0	2.2	2.2 temporary	3 months minimum
Ramanujam	1984	3.1	3.1	•	36 months

8.7% (Tomkin et al. 2004), incision, drainage, primary fistulotomy, curettage + primary suture with 10% (Kronborg and Olsen 1984), incision, drainage, unroofing + secondary fistulotomy with 5.6% (Hebjorn et al. 1987) and incision and drainage + primary fistulotomy with 0% (Ho et al. 1997).

4 studies have not reported on incontinence rates (Kronborg and Olsen 1984, Leaper et al. 1976, Mortensen et al. 1995, Tonkin et al. 2004). There was no incontinence rate observed after incision and

drainage in three studies (Ho et al. 1997; Oliver et al. 2003; Tang et al. 1996); however, Schouten et al. (1991) reported an incontinence rate of 21.4% after incision and drainage. There was a low incontinence rate following primary fistulotomy in two studies: 0% (Ho et al. 1997), 6% (Oliver et al. 2003), but when primary fistulotomy was combined with sphincterectomy it rose to 39.4% (Schouten et al. 1991). Unroofing did not increase the incontinence rate in one study: 0% (Hebjorn et al. 1987).

Table 11. Randomized controlled trials and fistulous abscess.

Author	Year	N	P/M	Com	Excl	Anest	Micro	I.O.	Class	A	т	RA	RF	Inc	Foll
Hebjorn	1987	38	P	-	-	G	-	+	P		IDU IDUsF	5.6 5.6	11.1 5.6	0 44.4	12
Но	1997	52	М	-	+	G	-	+	P	No	ID IDpF	3.6 4.2	25 0	0	15.5
Kronborg	1984	83	P	-	+	G	+	+	P	+	IDpF IDpFCpS	7.3 15	12.2 10	-	36
Leaper	1976	219	М	•	+	G	+	+	ММ	+	IDpFP IDCpS	26.3 9.3		-	3
Mortensen	1995	107	М	-	+	G	+	(+)	Р	+	IDpSGe IDpS	22 17	22 17	-	3
Oliver	2003	200	М	-	+	G	-	+	Р	None	ID IDpF	29.5 29.5	29.5 29.5	0	12
Schouten	1991	70	Р	-	+	G/S		- +	Р	None	ID IDSppF	40.6 2.9	40.6 2.9	21.4 39,4	42.5
Tang	1996	45	Р	•	+		-	+	P		ID IDpF	14.3 0	14.3 0	0	12
Tonkin*	2004	43	М	-	+	G	-	(+)	0	-	IDU IDUP	13 5	8.7 20	-	-

<sup>\*</sup> fistulotomy is decision of individual surgeon

N number of patients in study

P primary acute fistulous abscess M mixed: recurrent and primary

Com Comorbidity indicated yes + or no -

Exclusion criteria indicated yes + or no -

Anaesthesia G General anaesthesia S Spinal anaesthesia – information missing

Microbiology indicated + or missing -

Search for internal opening yes + or no -

Classification: P Parks, MM Milligan-Morgan, O other (superficial/deep)

A Antibiotics: missing information -, yes +, none

T Treatment: IDU Incision Drainage Unroofing; IDUsF Incision Drainage Unroofing secondary fistulotomy; ID Incision Drainage; IDpF Incision Drainage primary fistulotomy; IDpFCpS Incision Drainage primary Fistulotomy; IDpFCpS Incision Drainage primary Fistulotomy; IDpFCpS Incision Drainage Sphincterotomy primary fistulotomy; IDUP Incision Drainage Unroofing Packing

RA recurrent abscess rate in % RF recurrent fistula rate in %

Inc Incontinence rate in %

Foll Follow-up in M months

Follow-up information is available in 8/9 studies with a follow-up time ranging from 3 months to 42.5 months. I year or less follow-up has been reported for five studies: (Hebjorn et al. 1987; Leaper et al. 1976; Mortensen et al. 1995; Oliver et al. 2003; Tang et al. 1994). Only three studies followed the patients for more than a year: Ho et al. (1997), Kronborg and Olsen 1984; Schouten et al. 1991 (Table 11).

#### DISCUSSION

63 studies were analyzed for factors which may influence the outcome of the treatment of fistulous abscess: treatment of acute abscess or recurrent abscess, comorbidity, exclusion criteria, anaesthesia, microbiological cultures, search for internal opening, used classification of fistula/abscess and antibiotics.

#### PRIMARY ACUTE ABSCESS

Only ten studies focussed on the treatment of primary acute abscess, whereas 53 studies included primary fistulous abscess, chronic fistulous abscess or patients which have been treated several times for anorectal suppuration.

Parks noted already in 1961 that "the operation may be difficult if much fibrous tissue has been deposited in the sphincter muscles; the features distinguishing between smooth and striated muscle are destroyed by repeated infection." More than 10 years later he stated that "differentiation of various muscle groups was a matter of some difficulty" in case of fibrous tissue formation (Parks et al. 1976). This may also affect the ability to locate properly the primary opening, which will be discussed later.

Primary acute abscess may have a better healing rate when compared to patients with recurrent abscess. Fistula development has been associated with a past history of anorectal sepsis (Isbister 1987). In fact, 60-70% of patients with complex fistula-in-ano suffered already from anal abscess (Scoma et al. 1974; Perez et al. 2005). The recurrence rate was also significantly higher for patients who had been treated previously for ischiorectal abscess (44.1%) compared to patients treated initially (19.6%; p<0.05) (Cox et al. 1997). 35% of anorectal abscesses of non-specific origin developed into a fistula. The mean incidence per 100,000 population is 8.6 for non-specific anal fistula, but this study was concerned with in-hospital patients only (Sainio 1984). In 1998 Hämäläinen and Sainio did not find an association of previous abscess and fistula formation.

#### COMORBIDITY

In 30 studies we found information on comorbidity of the patients. In 33 studies, including randomized controlled studies there was no information on comorbidity available. Associated illness (alcoholism, diabetes, syphilis) and patient's delay to contact a doctor were the main reasons for prolonged hospitalization (Lindell et al. 1973). "It would seem that there are a number of etiologic factors, including trauma, fissures with abscess, crypt abscess, and altered host resistance factors, which account for this group of diseases." (Lindell et al. 1973).

Fistula development and treatment have been considered to be a different entity in Crohn's disease (Buhr et al. 2003). Recurrence rate of fistulous abscesses were higher in patients with diabetes (40%) and Crohn's disease (41.7%) (Cox et al. 1997). It is unclear whether a more conservative approach in the treatment of anal fistula in these patients caused this recurrence rate. Several authors recommend incision and drainage in all abscesses in Crohn's disease (Fucini 1991; De Dombal et al. 1966).

#### **EXCLUSION CRITERIA**

Exclusion criteria, e.g., inflammatory bowel disease, were indicated in 38 studies and were not available in 25 studies including one randomized controlled study. Exclusion criteria are known to have a significant impact on clinical studies and may affect the validity of a study (Rothwell 2005). Several studies were performed in patients with complex fistula (Hamilton 1975; Hanley et al. 1976; Hanley 1978; Hanley 1979; Held et al. 1986; Inceoglu and Gencosmanoglu 2003; Joy and Williams 2002; Ramanujam et al. 1983) or simple fistula only (Ho et al. 1997; Tang et al. 1996). According to Thomson (1986), each type of fistula (intersphincteric, transsphincteric, suprasphincteric and extrasphincteric) should be considered as a separate entity. Comparison of similar fistulas is more meaningful (Sangwang et al. 1994).

#### Anaesthesia

Only in 16 studies the examination and surgical treatment of patients with anal abscess/fistula were done

under general anaesthesia; in 19 studies general anaesthesia was applied for some but not all patients. In five studies patients received regional anaesthesia, regional and/or local anaesthesia in another five studies, local anaesthesia in one study. In 17 studies the information concerning anaesthesia was missing or unclear.

It is important that patients with anorectal sepsis have complete medical and surgical assessment at the time of their first admission (Winslett et al. 1988). The use of local anaesthesia has been accused for missed fistula and subsequent recurrence (Chrabot et al. 1983) and even lethal outcome (Marks et al. 1973). Especially high abscesses may be difficult to diagnose (Lockart-Mummery 1975). Although the type of anaesthesia had no effect on fistula formation, the known difficulties in diagnosis and treatment of patients with anorectal suppuration favour the use of general anaesthesia or at least spinal anaesthesia (Hawley 1975; Kovalcik et al. 1979; Lindell et al. 1973).

#### MICROBIOLOGY

In 16 studies we were able to obtain information on microbiological cultures, partially in one study. In 46 studies including three randomized controlled studies microbiological testing was either not done or not reported.

Looking at the studies with information on microbiology the effect of microbiology on outcome or treatment is not completely clear. Virulence of the organism, bacteraemia and occurrence of metastatic infections together with underlying disorders may be the cause of lifethreatening anorectal suppurations (Abcarian 1976). Skin-derived bacteria were considered to be the sign of a superficial fistula and lead to the conclusion that no further operation for fistula treatment may be necessary (Grace et al. 1982; Henrichsen and Christiansen 1986, Whitehead et al. 1982). Mortensen et al. (1995) doubted the prognostic significance of Staphylococcus aureus. Seow-Choen and Nicholls (1992) did not see evidence that chronic inflammation in anal fistula is maintained by excessive numbers of organisms or organisms of an unusual type.

#### SEARCH FOR INTERNAL OPENING

Most authors agree on a search for internal opening (n = 45). In five studies the search has never been done. In nine studies, including two randomized controlled studies, there was no information on this important step in diagnosis. In two studies the decision to search for an internal opening has been left to the individual surgeon; in one randomized controlled study, the search was not allowed for patients treated with incision and drainage.

Parks stated in 1961 "First step ... identify internal opening," and Hill added in 1967: Yet, determination of the point of origin of a fistulous process obviously is of utmost importance. It is not possible to be consistently successful in the treatment of fistula unless the source of infection can be located consistently, although it may be sometimes extremely difficult to define anatomical structures in the presence of infection or scarring (Hill 1967). The incidence of unidentified

primary openings at first surgery can vary from 12% to 28% (Adams and Kovalcik 1981, Bennett 1962, Mazier 1971, Rosen 1994). There is no difference in the success rate of consultants or research fellows to identify openings or tracks (Seow-Choen et al. 1991) which is in contrast to the statement of Marks et al. (1973): "Since treatment does not require invasion of a major body cavity it ordinarily falls to the most junior surgical resident to release the rectolent pus. In short, fistula in ano with abscess has no surgical clan" (Marks et al. 1973). Careful search is recommended by several authors (Chrabot et al. 1983; Cox et al. 1997; Girona and Denkers1996; Kyle and Isbister 1990; Waggener 1969), whereas some surgeons are unwilling to search for internal opening during the acute phase (Zuffery 2005). "It is a greater sin to create a false passage than to overlook a fistula." (Doberneck 1987). The inability to locate the primary opening may imply a circuitous track or false passages, spontaneous closure of the primary opening or microscopic opening (Eisenhammer 1978; MCLeod 1991; Milligan and Morgan 1934, Rosen 1994; Seow-Choen and Nicholls 1992; Scoma et al. 1974; Lockart-Mummery 1975). Simple fistula-inano may not have readily detectable primary openings and may possess secondary tracks (Sangwang et al. 1994). However, missed openings or tracks during the first operation may be the leading cause in 31.8 to 73.3% of recurrences (McElwain et al. 1975, Vasilevsky and Gordon 1985, Rosen 1994, Sainio and Husa 1985, Mazier 1971; Sangwang et al. 1994). Sainio and Husa were able to demonstrate an internal opening in 198 of 199 fistulas (Sainio and Husa 1985). In contrast, Seow-Choen et al. (1993) claimed that the finding of an internal opening does not reduce the recurrence rate, whereas Waggener reported on successful immediate fistulotomy in 73% of patients and complete wound healing without recurrence in 94% (Waggener 1969).

#### CLASSIFICATION OF FISTULOUS ABSCESS

There were nine different published classifications in use for the description of the fistulous process: Parks et al. (1976), Milligan and Morgan (1934), Stelzner (1981), Eisenhammer(1954), Goligher(1980), Gabriel(1963), Lilius(1968), Courtney(1949), Goldberg et al. (1980). Eight studies did not use or report a classification and in five studies a simple classification (e.g., deep versus superficial; left, right) or arbitrary classification were used.

It is obvious that the failure to appreciate the anatomy will likely result in recurrence or persistence of anal fistulous abscess (Nelson 2002).

Milligan and Morgan (1934) classified fistula according to the relationship of their tracks to the anorectal ring with anal fistula below the level of the (sphincter) ring and anorectal fistulas extending above the (sphincter) ring.

High intermuscular abscess has been first described by Eisenhammer in 1953. In 1954 he postulated that anal abscess and fistula were different stages of the same disease. Eisenhammer found that 97% of fistulas have a cryptoglandular origin with the following distribution: high intermuscular 10%, low intermuscular 81%, ischiorectal 2%, subcutaneous 1%, intermuscular ischiorectal 4% (Eisenhammer 1958). Parks reported on his investigations on the cryptoglandular origin of anal abscesses in 1961 and later published a classification which summarized the previous concepts as well as his own clinical and surgical experience: intersphincteric, transsphincteric, suprasphincteric, extrasphincteric (Parks et al. 1976). Stelzner (1981) classified fistulas into three main groups: intermuscular, transsphincteric, and extrasphincteric.

Goligher (1980) modified the Milligan-Morgan (1934) classification by dividing the high anorectal fistula into ischiorectal and pelvirectal.

The Lilius classification of fistula largely resembles Golighers system, which is a modification of the Milligan Morgan classification (Sainio and Husa 1985). Nowadays, the fistula may be classified as simple or complex (Thompson 1966), intersphincteric, transsphincteric, suprasphincteric or extrasphincteric (McLeod 1991). A simple fistula shows an easily identifiable track and primary opening, while a complex fistula is characterized by the presence of a secondary track and unidentified primary opening (Sangwang et al. 1994). Complex fistula may be mistaken for a simple fistula in case the secondary tracks were not identified (Sangwang et al. 1994). Anorectal abscesses are usually classified by the site of origin, but the inflammatory process may prevent a clear division (Scoma et al. 1974). Abscesses and fistula-in-ano may present difficulties for the surgeon confronted with such an unusual type as the high intermuscular variety (Bernard et al. 1983). Fucini (1991) confirmed Eisenhammer's view of the non-existence of supra- or extrasphincteric tracks.

#### ANTIBIOTIC USE

The information on antibiotics use was not given in 29 studies. Antibiotics were used in nine studies routinely, in 18 studies partially without telling what type of antibiotic was used in most studies. In seven studies antibiotics were not allowed or considered unnecessary.

Antibiotics may influence outcome in septic or toxic patients (Abcarian 1976) or in patients with immune suppression (Lindell et al. 1973). Perioperative antibiotics do not affect the development of fistula (Hämäläinen and Sainio 1998).

#### TREATMENT GROUPS

There are 35 different treatment variations: incision and drainage, incision and drainage with unroofing or packing; incision and drainage plus primary fistulotomy or fistulectomy with or without counter incision, sphincter reconstruction, muscle filling procedure; incision and drainage plus unroofing with sphincterotomy or sphincterectomy; incision and drainage with seton or primary suture with/without pezzer catheter, gentacoll antibiotic; fistulotomy, seton treatment; sphincterotomy; fistulectomy; rectal advancement flap.

Incision and drainage (n = 35) and incision and drainage plus primary fistulotomy (n = 23) are the most frequently studied techniques. They are followed in number by incision and drainage plus unroofing (n

= 9), incision and drainage plus seton (n = 6), incision and drainage plus sphincterotomy (n = 6), incision and drainage plus secondary fistulotomy (n = 5), incision and drainage and unroofing plus primary fistulotomy (n = 4), incision and drainage plus secondary fistulotomy (n = 3) and incision and drainage plus primary suture (n = 3) (Table 1).

In 1990 Grace emphasized that the principles of cold fistula surgery should still hold good during the acute episode: There is a lot of personal experience which speaks for the more conservative approach. "After 21 years, I now believe a staged procedure, incision and drainage, preserving all of sphincters of the lower posterior anorectum should give better results than the lay open fistulotomy technique."(Hanley 1985) Or: "Since 34% of the patients in our study have not yet gone to develop anal fistulas, we feel that this speaks for the conservative management of the problem, i.e., incision and drainage of anal abscess in the office using local anaesthesia." (Scoma et al. 1974) Or: No fistulotomy in perianal fistula producing pus - it may cause incontinence (Stelzner 1986). Some authors have emphasized the fistulotomy should be used only in selected cases (Hebjorn et al. 1987; Lockart-Mummery 1975; Sangwang et al. 1996; Seow-Choen et al. 1993; Sohn et al. 1980; Tang et al. 1996) or they recommend staged fistulotomy for complicated anorectal fistulas (Pearl et al. 1993; Ustynoski et al. 1990). It is, however, accepted in general that overzealous attempts at primary fistulotomy should be banned (Koyalcik et al. 1979; Buchan and Grace 1973). However, the argumentation that only 35% - 48% patients after incision and drainage suffer from recurrence and/or persistence and the majority of patients may not need a fistulotomy should be re-evaluated (Vasilevsky and Gordon 1984; Sainio 1984). According to Eisenhammer (1978) there were only a few good reasons not to perform simultaneously incision and drainage with fistulotomy: the only true indication for surgical drainage (alone) of the primary anorectal crypto-glandular abscess is where the surgeon lacks experience and where extreme personal affairs take precedence.

"The most important surgical concept is that the initial acute abscessal stage of the fistulous abscess is the correct time to perform a radical cure or fistulectomy and prevent the formation of the chronic stage, or anal fistula" (Eisenhammer 1978). And Parks added: "The crux of the operation is the removal of the infecting source - the infected anal gland and its surrounding tissue which lies deep to the internal sphincter in the midportion of the anal canal" (Parks 1961). However, Parks argues against the laying-open procedure and for the partial internal sphincterotomy (Parks 1963). Goligher et al. (1967) did not find an intersphincteric abscess and concluded that internal sphincterotomy would not have cured the patients. Since that time several investigators have pleaded for simultaneous primary fistulotomy and incision and drainage (Abcarian 1976;Lai et al. 1983; Maskow and Kirchner 1989; McElwain et al. 1975; Waggener 1969; Ho et al. 1997; Kyle and Isbister 1990; Knoefel et al. 2000; Fucini 1991; Lindell et al. 1973). Selected primary fistulotomy, e.g., in low fistula or subcutaneous intersphincteric or transsphincteric fistula, has been proposed by others (Ramanujam et al. 1984; Tonkin et al. 2004; Oliver et al. 2003). Total fistulectomy is either impossible (Mazier 1971) and/or associated with a larger wound, more separation of the sphincter, longer healing time and a greater chance of incontinence (Hill 1967). Lay open of the fistula was superior to excision in a study presented by Kronborg (1985). Waggener (1969) advocated primary fistulotomy for the following indications: 1. abscess in perianal subcutaneous tissue secondary to fistula-in-ano, 2. fistulous tract not deep to the anorectal ring, 3. positive identification of internal opening, 4. abscess in proximity to anal canal. "A false opening should never be created in an effort to complete the fistulotomy" (Waggener 1969). "In a teaching hospital a fistulotomy should only be performed if the track can be easily identified and the opening is not above the dentate line"(Weber and Buchmann 1982).

McCleod emphasized that a simple fistula can be treated without major risk with fistulotomy. A more conservative approach may be better in case of elderly patients, poor anal sphincter tone, and women with anterior fistula (McLeod 1991) "In all instances, the objectives should be to eradicate the fistula without compromising continence" (McLeod 1991).

Several authors recommend primary suture after incision and drainage when intraoperative antibiotics were given in a large dose (Kroborg and Olsen 1984; Wilson 1964; Ellis 1960; Mortensen et al. 1995). The study by Leaper et al. (1976) has been criticized for incompleteness of follow-up by Nelson (2002). Kronborg and Olsen admitted that concomitant low fistula may be treated simultaneously or during healing of abscess, but suture may not be advantageous in these patients and the recurrence rate higher (Kronborg and Olsen 1984). Lindell et al. (1973), Held et al. (1986) and Hamilton (1975) saw an advantage in unroofing or saucerisation of the abscess.

In 1978 Eisenhammer stated: "Both closure and unroofing have no place in surgical treatment of the acute cryptoglandular fistulous abscess."

A clear description or definition of the treatment procedure is missing in many studies. It is often not clear what the authors exactly meant when they used terms like fistulotomy and sphincterotomy or fistulectomy and sphincterectomy. A comparison of the outcome of different studies using imprecise definitions is very unlikely.

#### RECURRENCE

Unfortunately not all investigators accounted for recurrence in their study. Some author reported only a recurrence rate for abscess or fistula or a combined rate for both abscess and fistula.

The recurrence rates show a high variation. Recurrence rate for abscess may range from 1.6-88% after incision and drainage, 3-18.6% after incision and drainage plus unroofing, 0-21.1% after incision and drainage plus primary fistulotomy, 0% after incision and drainage plus secondary fistulotomy, 7.1-50% after incision and drainage with sphincterotomy, 0-12.5% after incision and drainage plus seton, and 15-20% after incision and drainage with primary suture.

Similarly the recurrence rate for fistula is ranging from 0-84% after incision and drainage, 3-26% after incision and drainage with unroofing, 0-21% after incision and drainage with simultaneous primary fistulotomy, 0-0.8% after incision and drainage with secondary fistulotomy, 7.1-13% after incision and drainage with sphincterotomy, 0-12.5% after incision and drainage with seton, and 7-20% after incision and drainage with primary suture.

Recurrence has been observed when 1. Correct diagnosis was made but the primary opening was not identified 2. Incorrect diagnosis was made (missed horseshoe fistula, occult secondary extension, extrasphincteric source), 3. Previous iatrogenic injury, 4. Occult Crohn's disease was present, 5. Incomplete laving open of the fistula, 6. Lacking surgical experience and knowledge, 7. miscellaneous (foreign body, immunosuppression, poorly controlled diabetes; premature closure of fistulotomy wounds, 8. packing with Iodoform gauze, 9. special types of high intermuscular abscess or fistula, 10. missing common signs of anal abscess and fistula were present (Rosen 1994; Sainio and Husa 1985; Sangwang et al. 1994; Mazier 1971, Onaca et al. 2001; Ramstead 1983; McElwain et al. 1975; Vasilevsky and Gordon 1985; Bernard et al. 1983). There is a high incidence of recurrent abscesses (48-62%) after simple incision and drainage which is said to be reduced to 0-3.6% following immediate fistulotomy (Seow-Choen and Nicholls Waggener 1969, Chrabot et al. 1983; Hebjorn et al. 1987; Ramanujam et al. 1984; McElwain et al. 1975; Doberneck 1987; Abcarian 1982; Fucini 1991). The incidence of missed fistula during abscess drainage is 18-95% (Seow-Choen and Nicholls 1992; Waggener 1969, Chrabot et al. 1983; Hebjorn et al. 1987; Ramanujam et al. 1984; McElwain et al. 1975; Doberneck et al. 1987; Abcarian 1982; Fucini 1991; Sainio 1984; Henrichsen and Olsen1986).

Cox et al. (1997) reported that recurrence rates were higher in patients with diabetes (40%) and Crohn's disease (41.7%) or when the patients were previously treated for ischiorectal abscess. The incidence of fistula in recurrent anorectal abscess may by as high as 76% (Chrabot et al. 1983). Patients often do not recognize fistulas (Henrichsen and Christiansen 1986) or do not return for follow-up (Lindell et al. 1973). Seow-Choen and Nicholls (1992) proposed that "three factors tend to perpetuate the process in complicated fistula: first, the presence of a disease focus within the anal intramuscular gland or elsewhere within the anal canal, second, the constant contamination resulting from a high intrarectal pressure ... and repeated surgery which may create complicated tracks."

Some authors accepted a recurrence rate of 40.6% (Schouten et al. 1991), 66% (Scoma et al. 1974), or 48% (Vasilevsky and Gordon 1984) as reason enough not to advocate a primary fistulotomy. However, the analysis in these papers may be different after a thorough re-evaluation.

Recurrence rate may also be influenced by the localization of the fistulous abscess. High transsphincteric or suprasphincteric fistulous abscesses may have a higher recurrence rate (Athanasiadis et al. 1990).

#### INCONTINENCE

The incontinence rate after treatment of fistulous abscess is even more difficult to analyze. Many investigators have not reported on the incontinence rate. There is further a large variation between and within treatment groups which makes a comparison unhelpful as is the case for recurrence. Incision and drainage may cause incontinence in 0-26% of patients. Incision and drainage plus unroofing are associated with an incontinence rate of 3-26%, incision and drainage with primary fistulotomy or secondary fistulotomy with 0-52% or 0-4%. Incontinence rate for sphincterotomy was 0 in one study but not reported in the other studies. Seton treatment after incision and drainage may be associated with an incontinence rate of 0-37.5%.

Several authors have discussed the possibility that primary fistulotomy may cause incontinence (Seow-Choen and Nicholls 1992, Scoma et al. 1974, Ramstead 1983, Schouten et al. 1991). However, there is no real evidence demonstrating a causal relationship. "As a general rule the whole of the internal and most of the external sphincter can be cut with the exception of the puborectalis muscle, without any serious loss of function."(Parks et al. 1976) This has been supported by Sainio and Husa in 1985 who stated that the amount of sphincter muscle division did not seem to be an important factor in the development of postoperative anal incontinence. Parks demanded, however, that it is essential to assess the state of the sphincter preoperatively (Parks et al. 1976). During operation differentiation of various muscle groups may be difficult and bleeding will stain the internal sphincter (Parks et al. 1976; Parks 1963). Pearl et al. (1993) suggested that the degree of incontinence is probably related to the patient's preoperative state. In patients with idiopathic anorectal incontinence, mostly women, authors found histological evidence of denervation of the external anal sphincter and also of the puborectal and levator ani muscles which may have been caused by stretch injury either during child birth or by excessive straining at defecation (Parks et al. 1976; Sainio and Husa 1985). Also the increasing ratio of connective tissue to muscle in advancing age may play a part in the development of sphincter weakness (Haas and Fox 1980; Sainio and Husa 1985). This sheds some light on the reported incontinence rate of 44% in the fistula therapy group reported by Schouten et al. (1991). 21% per cent of patients had a defecation disorder before surgery which is almost ten times higher than population prevalence in this age group according to Nelson (2002). In an earlier study by Schouten et al. (1987) the exact state of anal continence prior to primary partial sphincterectomy was unknown (Schouten et al. 1987). It is virtually impossible to document accurately the exact amount of undamaged sphincter mechanism remaining after each procedure (Mazier 1971).

Incontinence rate is not reliable because patients don't tell (Joy and Williams 2000). Objective and subjective assessment may vary according to Hill (1967). "There is, unquestionably, a psychological element: some patients are unwilling to say this type of difficulty exists unless, of course, it becomes unduly annoying; conversely, certain fastidious persons will com-

plain of soilage or leakage even if it is slight" or "In the matter of faecal control the personality of the patient and his bowel habit are almost as important (if not equally so) as the amount of sphincter musculature severed during surgical procedure" (Hill 1967).

The difference in continence may not be explained by different technique but by different types of fistula or different methodology to determine functional outcome (Rothenberger 1993; Garcia-Aguilar et al. 1998). Some kind of functional disturbance is obvious after almost any type of operation of anorectal surgery (Rothenberger 1993). Multiple operations may have an impact on anal control (Sainio and Husa 1985). In a direct comparison of incision and drainage, incision and drainage with primary fistulotomy or incision and drainage with seton Cox et al. (1997) have not revealed a significant difference in incontinence rate. The extent and the localisation of the anal fistulous abscess may have an impact on the development of incontinence. However, the data presented in these reviewed studies do not reveal any evidence that this is true.

#### RCT AND META-ANALYSIS

We have searched 9 studies for criteria which may have an impact on outcome of surgical treatment of anal fistulous abscess. The generally small study populations may not allow for a generalization. In addition, these were mainly specialized centres for the treatment of anal fistula and abscess. It is obvious that different enrolment criteria, e.g., primary acute abscess, were used. There is no clear and evident information on comorbidity. The exclusion criteria focus on inflammatory bowel disease, suppurative hidradenitis or carcinoma. The surgical treatment is mainly performed under general anaesthesia. The search for an internal opening was performed in 6 of 9 studies. Microbiology or antibiotic administration was not considered to be important for most studies. There is a distinct variation in the treatment modalities which does not allow comparison between most groups. The criteria for success of the surgical treatment, e.g., recurrence and/or persistence of abscess and/or fistula, or indicator for possible interference with the continence, e.g., incontinence, were reported not in all studies or the information was rather vague. The short follow-up period of 3-12 months in most instances did not allow a firm conclusion with regard to recurrence.

In a recent meta-analysis some additional problems were discussed regarding randomized controlled trials in the treatment of fistulous abscess. There was no conclusive evidence if simple drainage or sphincter cutting procedure is the better treatment for anal fistulous abscess (Quah et al. 2005). Some of the randomized controlled studies had methodological flaws: Hebjorn et al. (1987), Schouten et al. (1991) and Ho et al. (1997) did the randomization before the surgery and had a fistulotomy done in the majority of cases, where one would have expected only one third of internal openings to be found (Nelson 2002). According to Nelson (2002) the only study in which randomization occurred after operative exploration and discovery of an internal opening has been reported by Tang et al. (1996).

No prior sample size calculation was described in any of the five studies included in the meta-analysis. There was also no information available on the anatomical localisation of the fistula with regard to the sphincter continence muscles which may have an impact on the development of incontinence. The operations were performed by surgeons with different experience. Only two of the five trials gave an account on the grade of the participating surgeons. The randomization process was not described in two studies. The terminology used to describe the outcome measures varied from report to report, e.g. recurrence of abscess and/or fistula, postoperative incontinence. Wound healing was described in two studies (Quah et al. 2005).

#### Conclusion

Even highly specialised centres have difficulties to recruit an expressive number of patients with fistulous abscess and to continue a follow-up for at least 1 year. The treatment of fistulous abscess has been a matter of dispute for the last fifty years. From the beginning there was a conflict between a more conservative (only incision and drainage and staged procedure when a fistula develops) approach versus a more decisive intervention (single stage procedure).

There are good arguments for each side. However, it seems that it is impossible to compare the different treatment modalities in face of different patient characteristics, variation in treatment and follow-up in the yet published studies. Even the randomized controlled trials do not help to make a decision which treatment (single stage procedure or staged procedure) is better. The studies differ in enrolment criteria (primary acute abscess versus unrestricted enrolment, comorbidity, exclusion criteria, microbiological test, anaesthesia, antibiotic administration). There are 35 treatment modalities and 9 different fistula classifications in use. Reporting of recurrence or incontinence is, even in randomized controlled studies, often lacking. RCTs did not perform the correct procedure of randomization, or there was no information available. The incontinence rate differs highly, some studies obviously have not examined the patients before, and there is evidence that in some of the studies with a high incontinence rate many patients were incontinent before the operation. Reporting the relative risk of incontinence, standard continence assessment and uniform timing of continence assessment is warranted for further well-planned and properly conducted RCTs. A consensus should be reached which control group could be used. With regard to the complexity of this disease and the possible medico legal consequences of the treatment the decision for treatment and the procedure itself may be reserved to the senior surgeon with longstanding experience in coloproctology.

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# Consensus Meeting on "Relevance of Parenteral Vitamin C in Acute Endothelial Dependent Pathophysiological Conditions (EDPC)"

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#### Abstract

The 22<sup>nd</sup> Hohenheim Consensus Workshop took place in at the University of Stuttgart-Hohenheim. The subject of this conference was vitamin C and its role in the treatment of endothelial dysfunction. Scientists, who had published and reviewed scientific and regulatory papers on that topic were invited, among them basic researchers, toxicologists, clinicians and nutritionists. The participants were presented with eleven questions (bold letters), which were discussed and answered (italic letters) at the workshop, with the aim of summarising the current state of knowledge. The explicatory text accompanying the short answers was produced and agreed on after the conference and was backed up by corresponding references.

The therapeutic relevance of administration of the physiological antioxidant vitamin C in high parenteral doses in Endothelial Dependent Pathophysiological Conditions (EDPC) was discussed. Endothelial dysfunction is defined as including disturbed endothelial dependant relaxation of resistance vessels, breakdown of the microvascular endothelial barrier and/or loss of anti-adhesive function. It occurs in severe burn injury, intoxications, acute hyperglycemia, sepsis, trauma, and ischemic-reperfusion tissue injury and is induced by oxidative stress. Reduced plasma ascorbate levels are a hallmark of oxidative stress and occur in severe burns, sepsis, severe trauma, intoxication, chemotherapy/radiotherapy and organ transplantation. Vitamin C directly enhances the activity of nitric oxide synthase, the acyl CoA oxidase system and inhibits the actions of proinflammatory lipids. There is experimental evidence that parenteral high-dose vitamin C restores endothelial function in sepsis. In vitro, supraphysiological concentrations (> 1mM) of ascorbate restore nitric oxide bioavailability and endothelial function. Only parenterally, can enough vitamin C be administered to combat oxidative stress. There is no evidence that parenteral vitamin C exerts prooxidant effects in humans. Theoretical concerns in relation to competitive interactions between vitamin C and glucose cellular uptake are probably only relevant for oxidised vitamin C (dehydroascorbate).

Key words: endothelial dysfunction, vitamin C, parenteral, shock, trauma, oxidative stress

### 1. DEFINITION OF ENDOTHELIAL DYSFUNCTION

Consensus: Depending on vessel type: resistance vessels: disturbance of endothelial relaxation as a result of a stimulus (either physiological or pharmacological). Microcirculatory dysfunction of the endothelial barrier. Loss of anti-adhesive function.

With a weight of 1.5 kg and surface area of 700 m<sup>2</sup>, the endothelium can be seen to represent a major organ of the body. The main function of an intact endothelium is to maintain blood flow in order to supply tissues and organs with oxygen and nutrients and to remove metabolites. In addition, it serves an endocrine function. It generates a number of extracellular messenger molecules that mediate a variety of vital functions [1]. The physiological function of the endothelium varies depending on the type of vessel. As the vital regulator of arterial vascular tone, it controls local blood flow in response to changes in the metabolic demands of the surrounding tissue but in certain tissues this function is subordinate to its role in contributing to the maintenance of the organism's blood pressure. The endothelium is also vital for maintaining