ORIGINAL ARTICLE

Predictive Factors and Timing of Developing Anal Fistula after Drainage of Cryptoglandular Anorectal Abscess: A Retrospective Cohort Study

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Background: Cryptoglandular infection is one of the main causes of common anorectal infections that presents in conjunction with abscess following anal fistula after drainage.

Objective: To evaluate the rate and predictive factors of fistula formation following anorectal abscess drainage, and the timing of fistula diagnosis.

Materials and Methods: The present study was a retrospective study of 232 patients with cryptoglandular anorectal abscess that underwent drainage in the operating room under anesthesia between 2010 and 2019. The predictive factors of fistula development were analyzed using Cox's proportional hazard.

Results: Seventy out of 232 patients (30%) developed anorectal fistula after drainage of anorectal abscess. Median follow-up time was 35.5 months, and 25.02% (95% CI 19.89 to 31.19) of patients developed fistula within 12 months after the surgery. Independent factors in developing anal fistula after drainage were female gender (HR 2.17, 95% CI 1.15 to 4.14, p=0.017), alcohol consumption (HR 2.24 95% CI 1.20 to 4.22, p=0.012), and driver (HR 2.80, 95% CI 1.08 to 7.25, p=0.034). The protective factors are gauze packing (HR 0.43, 95% CI 0.23 to 0.82, p=0.009) and identifiable organism from pus culture (HR 0.59, 95% CI 0.36 to 0.99, p=0.046).

Conclusion: After drainage of a cryptoglandular anorectal abscess, there is a need to raise the awareness concerning anorectal fistula in female patient, alcohol drinkers, and those who work as drivers. Bacterial cultures should be taken, and gauze drain should be positioned. The potential fistula formation should be monitored in the first year after the operation with an option of extending to a second year.

Keywords: Anal fistula; Fistula in ano; Abscess; Drainage

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Fistula in ano or anal fistula (FIA) is one of the most common diseases seen by general and colorectal surgeons. There are numerous etiologies of anal fistula. In eastern countries, the most common cause of anorectal abscess is cryptoglandular infection. It differs from western countries where Crohn's disease and cryptoglandular infection are both reported as being common causes of anal fistula[1]. Incidence of developing anal fistula differs in each etiology. Therefore, the present study was focusing on incidence, risk, and time of cryptoglandular anorectal abscess leading to development of anal fistula.

The first stage in the treatment of an anorectal abscess is incision and drainage. Anal fistula occurred in 15% to 56% of individuals after drainage[2,3]. Patients with anal fistula often experience discomfort and discharge, typically requiring surgery for definitive treatment. Complicated cases might need multiple surgeries over time. This raises questions about whether predicting and preventing this condition is possible. The formation of an anal fistula after draining an abscess has been linked to several factors. While studies mention Crohn's disease, trauma, and cancer as causes, the present investigation only looked at the causes of cryptoglandular anal fistulas. A better understanding

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of the overall rate and predictive factors of fistula formation following abscess drainage, as well as the timing confirmation of fistula, is crucial for the identification and classification of patients during abscess drainage in order to determine both the operative plan and surgical follow-up.

Materials and Methods

Study design and setting

The present study was a retrospective cohort study with information collected between January 2010 and December 2019 in Chiang Mai University Hospital. The study was approved by the research committee, Faculty of Medicine, Chiang Mai university, research ID SUR-2563-07756. During this time, 325 patients were diagnosed with anorectal abscess, which were confirmed as the cause of infection from the cryptoglandular infection. Twenty-eight patients were excluded due to bedside drainage of abscess, 30 with spontaneous drainage with no further operations, nine patients had a history of anal fistula, and 26 patients underwent surgery at other hospitals. This resulted in 232 patients that met the eligibility criteria.

Participants

The eligible criteria were patients aged over 15-years-old, diagnosed with anorectal abscess that originated from cryptoglandular infection and who underwent drainage intraoperatively. Exclusion criteria were patients who had history of anal fistula, with or without a history of surgery. Patients who had been operated on at other hospitals, or had bedside drainage were also excluded. If the final etiology was changed to other etiology, the patients were also excluded.

Variables

Basic data collected included age, gender, body weight, height, occupation, underlying diseases, medication usage, alcohol use, smoker, and history of operation and radiation. Disease data were duration of symptoms, location of abscess, type of anorectal abscess, intraoperative finding, pus culture report, drainage packing type, and antibiotic used. The follow-up time was reviewed in the hospital database and if the patients were lost follow-up for more than six months after surgery, a telephone call was made to interview the patient with regard to the symptoms of fistula. The bacterial culture report was also collected from the hospital database.

Statistical analysis

All Statistical analyses were carried out using Stata Statistical Software, version 16 (StataCorp LLC, College Station, TX, USA). The continuous data were reported as mean and standard deviation or median and interquartile range (IQR). T-test or Mann-Whitney U test was used to compare means between two groups. Categorical data were reported as number of patients and percentage. Chi-square or Fisher's exact test were used to compare between groups. For the identification of the independent factors associated with the development of anal fistula, Cox proportional hazard regression was used in univariable analysis followed by multivariable analysis. A p-value of less than 0.05 was considered a significant level. Time of recurrence was reported using Cox proportional hazard model.

Results

Out of the 232 patients who met the eligible criteria, 70 patients (30.17%) developed anal fistula after drainage of anorectal abscess. As shown in Table 1, there was a higher ratio of females in the fistula group at 24.64% (17/70) versus 12.96% (21/162) in the non-fistula group. There was no statistical difference in the mean age in the groups, 40.85 years in the fistula group in comparison to 42.53 years in the non-fistula group. This was the same as the body mass index (BMI), at 24.64 and 24.11 in fistula and non-fistula group, respectively. There were also no differences between immunocompromised status, which were diabetes and HIV positive. The fistula group demonstrated that patients with alcohol drinking, which included 37 patients (52.86%) had significantly higher rates than non-fistula group with 61 patients (37.65%) (p=0.042), but smoking showed no difference. Radiated history was higher with six patients (3.7%) than in the fistula group with one patient (1.43%). However, there was no statistical significance. There was also no difference in abscess location far from the anal verge, the median location were 2 centimeters from the anal verge in both groups.

It showed abscess types differed significantly across groups (p=0.044). All Supralevator abscess patients developed anal fistula, which was complicated and difficult to cure. Other types had almost identical percentages in both groups.

Patients with drain insertion had a lower incidence of fistula than the non-fistula group after abscess draining with 52/70 patients (74.29%) versus 142/162 (87.65%). It was discovered that the type of

Table 1. Demographic data of 232 patients with cryptoglandular anorectal abscess underwent drainage intraoperatively comparing between developing anal fistula group and non-fistula group

Variable	Fistula group, n=70 (30.17%)	Non-fistula group, n=162 (69.83%)	p-value
Female; n (%)	17 (24.64)	21 (12.96)	0.034*
Age (years); mean±SD	40.85±13.78	42.53±16.74	0.463
BMI (kg/m^2); mean±SD	24.64±5.48	24.11±5.11	0.481
Occupation: driver; n (%)	6 (8.57)	5 (3.09)	0.092
Diabetes mellitus; n (%)	6 (8.57)	27 (16.67)	0.151
HIV infection; n (%)	1 (1.43)	10 (6.17)	0.180
History of radiation; n (%)	1 (1.43)	6 (3.70)	0.678
Smoking; n (%)	17 (24.29)	38 (23.46)	0.868
Alcohol drinking; n (%)	37 (52.86)	61 (37.65)	0.042*
Length from anal verge; median [IQR]	2 [1.5]	2 [1]	0.256
Length from AV >3 cm; n (%)	6 (8.57)	5 (3.09)	0.092
Anterior (10-2 OC); n (%)	19 (27.14)	31 (19.14)	0.223
Drain placement; n (%)	52 (74.29)	142 (87.65)	0.019*
Type of abscess; n (%)			0.044*
Intersphincteric/perianal	50 (71.43)	131 (80.86)	
Ischioanal abscess	16 (22.86)	29 (17.90)	
Supralevator abscess	3 (4.29)	0 (0.00)	
Horseshoes abscess	1 (1.43)	2 (1.23)	
Drain type; n (%)			0.024*
No drain placement	18 (25.71)	21 (12.96)	
Gauze drain	35 (50.00)	109 (67.30)	
Penrose/catheter	17 (24.29)	32 (19.75)	
Culture pus from abscess; n (%)			0.038*
No Identifiable organism	25 (35.71)	35 (21.60)	
Gram positive organism	11 (15.71)	20 (12.35)	
Gram negative organism	34 (48.57)	107 (66.05)	
Identifiable bacteria organism	34 (48.57)	105 (64.81)	0.028*
Drug resistance organism; n (%)	5 (7.14)	9 (5.56)	0.765
Single oral Augmentin; n (%)	14 (20.00)	36 (22.22)	0.862
Length of stay; median [IQR]	2 [4]	2 [3]	0.423

BMI=body mass index; AV=anal verge; IQR=interquartile range; SD=standard deviation

* Statistical significance, p<0.05

drain insertion differed significantly in each group (p=0.024). The fistula group had a lower incidence of detectable bacterial culture from abscess than the non-fistula group in 34/70 (48.57%) versus 105/162 (64.81%). Colorectal experts attended 59/232 (21.12%) of the operations at the authors' institution, when the study indicated abscess complexity. The median length of stay (LOS) in both groups was two days, with no significant differences.

Oral antibiotics were usually prescribed for at least two weeks following surgery. Single oral Augmentin pills were offered, as well as combinations of cefixime or ciprofloxacin plus metronidazole or clindamycin. Oral Augmentin had no effect in either group with 20% in fistula and 22% in non-fistula.

From the 144 reports of bacteria identified from the pus culture, *Escherichia coli* was the most common bacterium from laboratory reports at 72.34% followed by *Klebsiella* spp. at 32.62% and *Streptococcus* spp. at 18.44%. Other bacteria were less than 10%. Antibiotic resistance identified had no difference between the two groups.

Predictive factors for the development of anal fistula

Anal fistula developed in 30.17% of the 232 patients. In univariable and multivariable Cox proportional hazard analyses, eleven factors from previous studies were shown in Table 2, to be related with development of anal fistula following abscess

Table 2. Univariable and multivariable Cox proportional hazard analysis of predictive factors for anal fistula development after drainage anorectal abscess

Variables	Univariable analysis			Multivariable analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Female	1.61	0.91 to 2.87	0.103	2.17	1.15 to 4.14	0.017*
BMI	1.02	0.98 to 10.7	0.364	1.02	0.96 to 1.09	0.360
Diabetes mellitus	0.52	0.22 to 1.20	0.125	0.51	0.21 to 1.21	0.127
Driver	2.22	0.89 to 5.52	0.087	2.80	1.08 to 7.25	0.034*
Smoking	1.13	0.65 to 1.95	0.673	0.86	0.43 to 1.71	0.669
Alcohol drinking	1.72	1.06 to 2.79	0.027*	2.24	1.20 to 4.22	0.012*
Abscess form AV >3 cm	1.12	0.59 to 2.14	0.729	0.85	0.43 to 1.68	0.631
Type of abscess						
Intersphincteric/perianal	-	Ref.	-	-	Ref.	-
Ischioanal abscess	1.44	0.82 to 2.55	0.202	1.49	0.79 to 2.80	0.211
Supralevator	3.83	1.19 to 12.34	0.024*	2.09	0.55 to 7.95	0.275
Horseshoe abscess	1.71	0.24 to 12.42	0.827	2.90	0.35 to 23.8	0.322
Pus culture						
Identification of organism	0.55	0.34 to 0.89	0.014*	0.59	0.36 to 0.99	0.046*
Type of drain						
No drain placement	-	Ref.	-	-	Ref.	
Gauze drain	0.47	0.26 to 0.83	0.010*	0.43	0.23 to 0.82	0.009*
Penrose/catheter	0.74	0.37 to 1.47	0.390	0.65	0.29 to 1.42	0.276
Augmentin oral	0.91	0.51 to 1.65	0.761	0.97	0.52 to 1.83	0.935

BMI=body mass index; AV=anal verge; HR=hazard ratio; CI=confidence interval
* Statistical significance, $p<0.05$

drainage and these were used for further analysis as shown in Table 2. There were five independent variables found to be statistically significant. First, HR 2.17 (95% CI 1.15 to 4.14, p=0.017) for female gender. Second, patients with prolonged sitting career, like truck and bus drivers had an HR 2.80 (95% CI 1.08 to 7.25, p=0.034). Third, patients with alcohol consumption had an HR 2.24 (95% CI 1.20 to 4.22, p=0.012). Fourth, when compared to no drain placement, packing the abscess with a gauze drain demonstrated a protective benefit (HR 0.43, 95% CI 0.23 to 0.82, p=0.009), but it was not significant when compared to Penrose drain or catheter drain inserted after surgery. The fifth factor was the identification of organism from pus culture, which revealed a lower risk of developing an anal fistula when compared to patients who had no growth or no culture from the abscess (HR 0.59, 95% CI 0.36 to 0.99, p=0.046). Cox proportional hazard regression of each independent factor was shown in Figure 1.

Timing of development of fistula

After the anorectal abscess was drained, it took approximately three months to assess anal fistula formation. If there was an external opening with discharge from the lesion, the diagnosis of anal fistula may be established. In the authors' practice, they follow up with the patients after surgery for the first two or three months, then six months, and one year after the drainage. If the patients had other illnesses and visited the hospital, the anal fistula symptoms of the patients might be reviewed from the hospital database to perform this research. The median follow-up time was 35.5 months, as Figure 2. There were 25.02% (95% CI 19.89 to 31.19) of the patients had recurrence in the 12 months after surgery and 30.04% (95% CI 25.27 to 37.76) in the 48 months.

Discussion

Developing of an anal fistula after drainage of an anorectal abscess is common. The present study found this occurred in 30.17% of patients, which showed a correlation with the previous studies[4-6]. However, the present study included patients in which it was confirmed that the etiology of the abscess was cryptoglandular infection and did not include Crohn's disease.

Over the last ten years, predictors for the development of anal fistula have been reported.

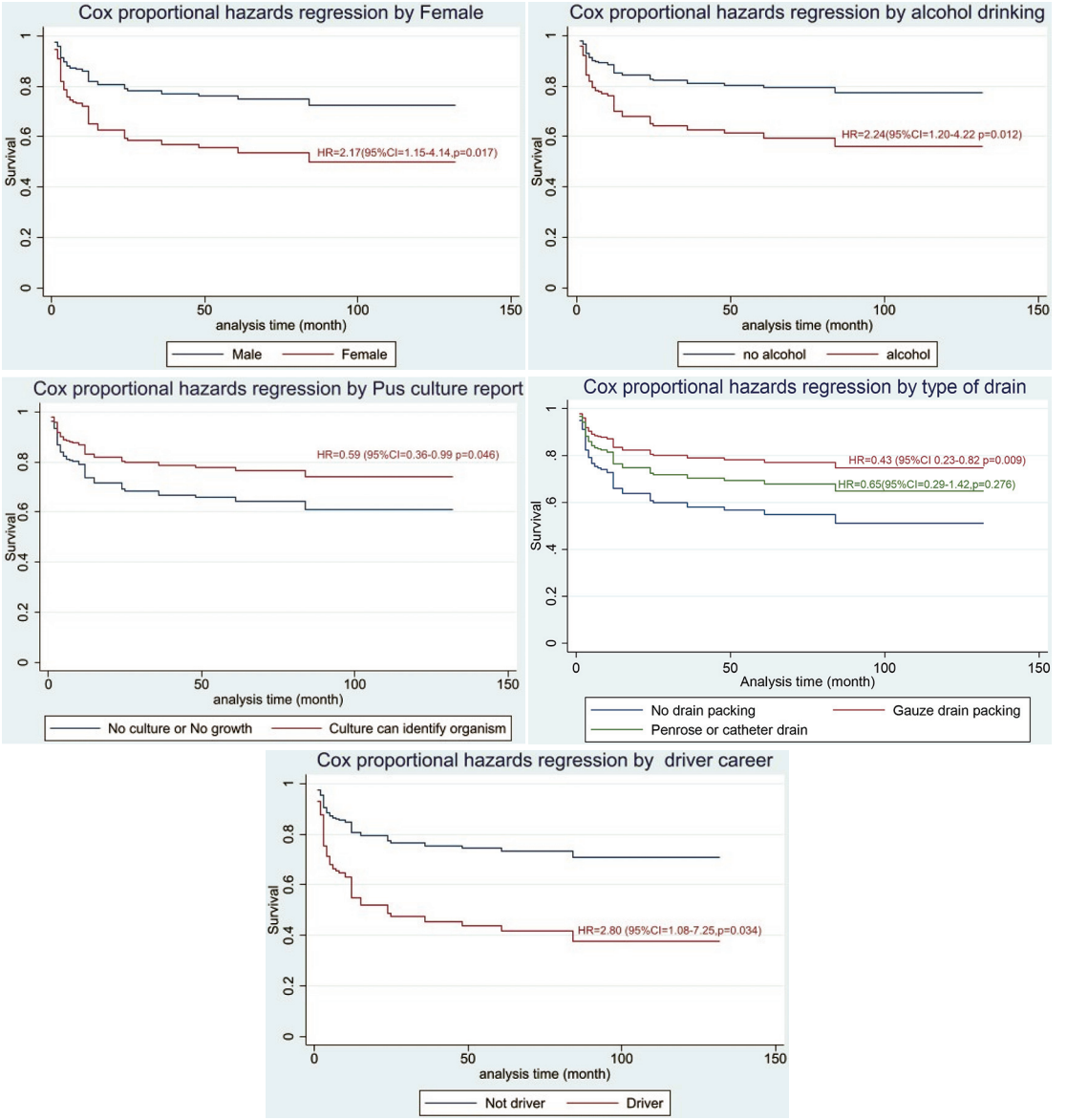

Figure 1. Cox proportional hazard regression by factors of anal fistula development after drainage of anorectal abscess.

Being female is one of the independent factors in the present research that is associated with an increased risk of developing anal fistula. This was similar to a large study by Sahnan et al.[2] that found that male patients had a lower incidence of anal fistula than female patients with 32.6% in female versus 14.9% in male (OR 2.5, 95% CI 1.7 to 3.7, p<0.001). Although, Crohn's disease was also included in Hamadani et al.'s report, gender made no significant impact[7].

Interestingly, the report by Hamadini et al. classified patients under 40 years old as more prone to developing a fistula after the initial drainage of anorectal abscesses. However, this particular tendency was not observed in the present study. Hamadini et al.'s findings could be explained by the inclusion of patients with Crohn's disease in their sample, as this condition tends to be more active in younger adolescents[7].

BMI did not show any correlation with developing anal fistula in the present study. This differed from the study by Lu et al.[8] in 2019, which included 790 patients categorized in three groups according to their BMI. Patients with high BMI, at 26.0 to 40.6 kg/m², showed a higher risk of developing FIA (HR 1.75, 95% CI 1.10 to 2.40, p=0.002).

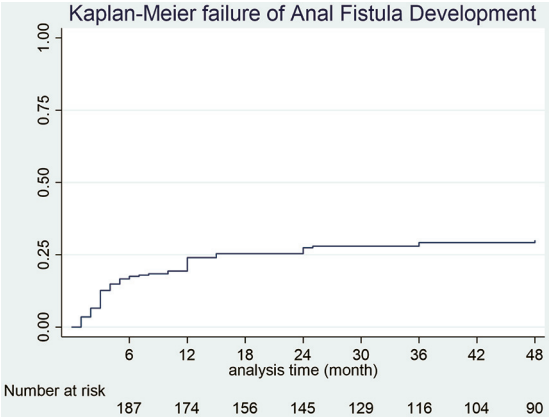

Figure 2. Kaplan-Meier failure curve of anal fistula development after drainage abscess.

In studies, diabetes and HIV, which are considered as indicating immunocompromised status, were found to be associated with developing anal fistula. However, these two factors did not show any significance in the present study, as was the case in the study by Hamandi et al[7]. These differences can be explained by, nowadays, in practice antibiotics are prescribed in almost all patients with anorectal abscess included immune competent and immunocompromised patients. Administering antibiotics was found to provide advantages for patients dealing with anal fistulas[9].

Use of a packing drain after drainage is a controversial issue. Packing with a gauze drain in the present study showed less potential to develop anal fistula compared to non-packing drain group. This was not supported by a report by Mohamedahmed et al.[10] that found that there was no significant difference between groups and there was a concern about pain during the changing of the gauze. It also reported that patients suffered from pain while dressing the wound with packing gauze drain[11]. Perera et al.[12] also conducted an RCT evaluating post-operative packing that reported no difference in risk of developing anal fistula between groups with 37.5% in the packing group versus 33.3% in the non-packing group (p=0.580). In a Cochrane review, packing drain did not show any benefit, but the author concluded that despite the lack of high-quality evidence regarding packing, the packing of abscess cavities is a common practice[13]. Drainage without drain packing, the abscess's opening usually involves early closure when there is still fluid collection beneath the wound. However, when the wounds were dressed with gauze, the new gauze is changed once daily or every other day until the wound base was shallow, and the base of abscess can be identified. This differs from the Penrose and catheter drain, which were normally removed early or the formation of fibrous track along the drain would remain in the skin opening.

The type of abscess did not show to be statistically significant in the adjusted model. Even though, if looking in the table, a Supralevator abscess is 100% likely to turn into anal fistula after the drainage. Due to the complexity, and location of Supralevator abscess, there were few cases of this type available in the present study. Further studies and reports might help to confirm the outcome.

The use of antibiotics after drainage is also a debatable issue. There have been reports pro and against the giving of antibiotics as some showed benefit in preventing fistula development. In a randomized trial in Iran, only 14% of patients in a group taking antibiotic developed a fistula compared to 33% of a non-antibiotic group[14]. However, there is an argument that antibiotics had no effect on the establishment of anal fistulas as the result was published following randomized placebo-controlled research that excluded Crohn's disease and immunocompromised individuals[15]. In the authors' investigation, taking single oral Amoxycillin-Clavulanic acid had no effect on fistula formation. An Amoxycillin-Clavulanate combination showed a minimum inhibitory concentration value of 0.5 to 4.0 µg/mL for *Bacteroides fragilis*[16]. There were only 3.3% to 9.8% Ampicillin-resistance of *E. coli* found to be resistant to Augmentin[17], This may provide comfort to individuals who are taking a large number of antibiotics as part of a combination of antibiotics.

The development of a fistula and the recovery from an anorectal abscess were found to be related to occupational and lifestyle factors. In the present study, patients with prolonged sitting, for example truck or bus drivers, had more frequency of anal fistula formation. This discovery may not have been mentioned in previous studies. An occupation or activity that requires sitting for lengthy periods without adjusting posture, such as driving a car, riding a bicycle, or riding a motorcycle, may increase the chance of getting fistula and recurrent fistula. Patients should be encouraged to alter their posture more often and avoid activities that require sitting for lengthy periods. The long-time sitting factors may be difficult to change due to its feature. Surgeon might explore these activities in patients with anorectal abscess and anal fistula for better outcome of the treatment.

Conclusion

Following the treatment of draining the cryptoglandular-cause perianal abscess, patient recommendations should encompass lifestyle modifications, including abstinence from alcohol consumption and avoiding prolonged sitting, especially relevant for individuals involved in driving occupations. Additionally, the strategic use of gauze packing within the drainage cavity may be considered to mitigate the likelihood of subsequent anal fistula development. Female patients, in particular, should be informed about the potential occurrence of an anal fistula post-treatment. Vigilant postoperative surveillance during the first year is imperative for individuals who underwent anorectal abscess drainage, warranting comprehensive monitoring and follow-up care.

Limitation

The present study was a single institutional retrospective study. Therefore, the transferability of the findings is limited. A multicenter study would increase confidence in the identification of risk factors and facilitate provision of a prediction score. It became evident that long-term sitting related to the patients' occupation was a risk factor. Information from a habit such as bicycling may be useful to collect. This hypothesis may need further confirmation for prospective research.

What is already known on this topic?

Predictive factors that can develop FIA after drainage anorectal abscess.

What does this study add?

1. Prolong sitting career such as bus driver or truck driver is a new independent factor that can develop FIA. This finding can be used as advice for patients prone to have prolong sitting. Avoiding prolonged sitting can prevent fistula development.

2. Timing for FIA development after drainage abscess seems to be about one year after the drainage.

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Conflicts of interest

The authors declare no conflict of interest.

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