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Dialkylcarbamoyl chloride-coated *versus* alginate dressings after pilonidal sinus excision: a randomized clinical trial (SORKYSA study)

B. Romain^{1,3} , M. Mielcarek², J. B. Delhorme¹ , N. Meyer², C. Brigand¹ and S. Rohr¹, on behalf of the SORKYSA group*

Departments of ¹Digestive Surgery and ²Public Health, Strasbourg University Hospital, and ³Laboratory of Stress Response and Innovative Therapies, Institut National de la Santé et de la Recherche Médicale (INSERM) IRFAC UMR_S1113, University of Strasbourg, Strasbourg, France

Correspondence to: Dr B. Romain, Department of Digestive Surgery, Strasbourg University, 1 Avenue Molière, 67000 Strasbourg, France (e-mail: benoit.romain@chru-strasbourg.fr)

Background: Disease of the pilonidal sinus is a common condition that affects mainly young adults. Options for management include excision of the sinus tracts, leaving the wound open to heal by secondary intention. The aim of this study was to compare wound healing with dialkylcarbamoyl chloride (DACC)-coated dressings *versus* alginate dressings.

Methods: This multicentre trial randomized consecutive patients undergoing surgery for pilonidal disease to postoperative wound care with either DACC-coated or alginate dressings. The primary outcome was the proportion of wounds healed after 75 days. Secondary outcomes were the local status of wounds during the healing process, the quality assessment of the dressings by the patient, and the time needed to return to usual activities.

Results: A total of 246 patients were included: 120 in the DACC-coated group and 126 in the alginate group. In per-protocol analysis, there were significantly more patients with completely healed wounds after 75 days in the DACC group than in the alginate group: 78 of 103 (75.7 per cent) *versus* 58 of 97 (60 per cent) respectively (odds ratio 2.55, 95 per cent c.i. 1.12 to 5.92; $P = 0.023$). During follow-up, wounds with alginate dressings had more fibrin than those with DACC-coated dressings, but the difference was not significant ($P = 0.079$). There was no difference between the two arms in patients' assessment of the dressings.

Conclusion: The number of wounds completely healed at 75 days was significantly higher for DACC-coated compared with alginate dressings. However, the preplanned, clinically significant improvement in healing of 20 per cent was not reached. Registration number: NCT02011802 (<https://clinicaltrials.gov/>).

*Other members of the SORKYSA group can be found under the heading Collaborators

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Introduction

Pilonidal sinus is a common disease with an estimated incidence of 26 per 100 000 population, affecting men twice as often as women¹. It arises in the hair follicles of the natal cleft of the sacrococcygeal area¹, causing infection, discomfort, pain, immobility, and time lost from work or school².

There is no consensus on the management of chronic pilonidal disease^{2,3}. The principle of treatment is to eradicate the sinus tract. The surgical wound may be left open to heal by secondary intention, with the wound packed daily with dressings until complete healing is achieved. Alternatively, the wound may be closed either immediately after surgical treatment or after a delay. The advantage of primary wound closure is faster healing, allowing an earlier

return to work; however, it is also associated with a higher risk of recurrence of around 35 per cent³.

There is heterogeneity in the reported duration of wound healing after pilonidal sinus surgery, with studies showing that wounds left open to heal by secondary intention are usually healed by 70 days³. Much effort has been spent developing new procedures to accelerate wound healing. In France, alginate dressing is one of the most commonly used treatments, particularly after pilonidal excision. Alginate consists of soft, unwoven fibres composed of cellulose-like polysaccharides derived from the calcium salts of seaweed. The gel formed is highly hydrophilic, which limits wound secretions with strong absorbency. Dialkylcarbamoyl chloride (DACC)-coated dressings are new, without pharmacological effect or the use of an active inhibitory agent. DACC is a fatty acid derivative that is highly hydrophobic. The microorganisms commonly responsible for surgical-site infection, or that colonize chronic wounds, generally have hydrophobic extracellular surfaces and therefore adhere irreversibly to the DACC coating⁴. Two groups^{5,6} have recently shown a reduction in infection rates when DACC-coated dressings were used, and this property could be particularly valuable for wounds prone to infection, such as pilonidal sinus wounds.

The aim of this RCT was to determine whether DACC-coated dressings improved healing rates after pilonidal sinus surgery compared with alginate dressings.

Methods

The SORKYSA (SORbact et KYste SAcrococcygien) trial is a multicentre open RCT. The French medical ethics committee approved the trial (ClinicalTrials.gov identifier NCT02011802). Four hospitals participated (Centre Hospitalier de Mulhouse, Centre Hospitalier de Colmar, Centre Hospitalier de Saverne and Centre Hospitalier Universitaire de Strasbourg (Hôpital de Haute-pierre)). Consecutive patients requiring surgical treatment for symptomatic pilonidal sinus between December 2013 and September 2017 were evaluated for inclusion. Indications for surgery were a symptomatic pilonidal sinus with or without previous abscess. Patients with recurrent pilonidal sinus and who had undergone previous excision could be included. There was no restriction in size or chronicity. Exclusion criteria were: age less than 18 years; concomitant pathology – current treatment for cancer with chemotherapy, uncontrolled hypertension (systolic BP above 180 mmHg or diastolic BP above 110 mmHg), severe co-morbidity reducing life expectancy to less than 12 months, acute cardiovascular disease (myocardial infarction, stroke, recent heart surgery); participation in another

clinical trial; known intolerance to one of the dressings; pregnancy; and uncontrolled diabetes (fasting glucose level above 2 g/l). No patient with active pilonidal infection was included.

Randomization

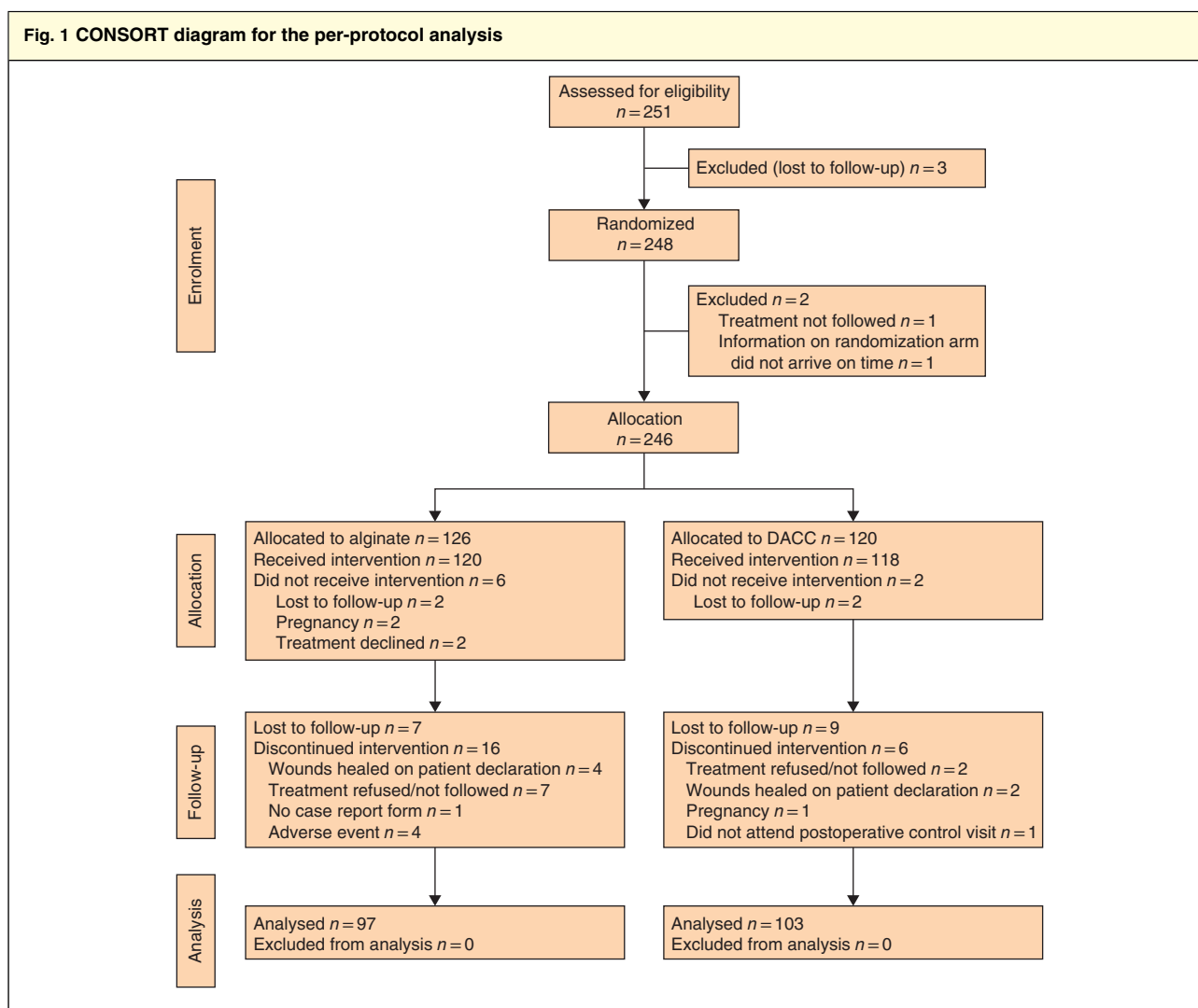
After obtaining informed consent, patients were registered via an online processing system, in which data were stored securely. Every patient received a unique trial code. The randomization list was computer-generated by an investigator with no clinical involvement in the trial. The list used blocks of eight and was stratified by centre. After the surgeon had obtained the patient's consent, they telephoned a contact at the clinical investigation centre of Strasbourg University Hospital who was independent of the recruitment process for allocation consignment. The randomly attributed treatment group was given by phone and also sent by facsimile. The safety monitoring board had access to all data.

Procedures

The same surgical technique was used for all patients. All surgeons were experienced in the management of the condition. Antibiotic prophylaxis with imidazole (single 1-g dose) was given within 30 min of surgery. Surgical excision was performed, with the patient in the prone jack-knife position, under either general or spinal anaesthesia. Povidone was used for skin antiseptic preparation, or chlorhexidine gluconate in patients with povidone allergy. After probing the fistula with a blunt needle, methylene blue was injected to define the exact borders of the sinus. An elliptical incision was made in the skin around the pilonidal sinus. Surgical diathermy was used for complete excision of the sinus, if required, down to the presacral fascia. After excision, the length, width and depth of the wound were recorded. Once haemostasis had been achieved, the DACC-coated or alginate dressing, according to the randomization, was placed in the wound cavity. After surgery, all patients were advised to take paracetamol regularly (1000 mg 4 times a day), with an additional non-steroidal anti-inflammatory drug as required. No antibiotic was prescribed.

Follow-up

Follow-up consisted of a predetermined schedule for all patients at the outpatient clinic. Patients were visited at home by a nurse, who dressed wounds once a day with a dressing according to the randomization arm. Each patient returned to the hospital a mean(s.d.) of every



DACC, dialkylcarbamoyl chloride.

15(3) days. Inspection of the wound was performed by a surgeon together with a wound care nurse. Wound size (length, width and depth) was recorded at each hospital visit. Follow-up ended a mean(s.d.) of 120(3) days after surgery.

Outcomes

The primary endpoint was wound healing after 75 days. The trial steering committee decided before the trial that a 20 per cent improvement in the number of wounds healed at 75 days with DACC-coated dressings would be considered clinically valuable. Complete healing was defined as a wound that had healed totally, with no cavity.

Secondary endpoints were evaluated at the hospital visits, every 15 days after surgery. These included the status of

the local wound (wound area, presence of necrosis, fibrin, granulation, epidermalization, exudate and local infection) and patient assessment of the qualities of the dressing (dressing comfort during the day, pain during dressing removal and presence of leakage). Pain score was evaluated using a visual analogue scale (VAS) (score 0, no pain; 10, maximum pain), during dressing and during the day. The day on which the patient returned to usual activities was recorded. Self-assessment of patient mobility during the day was recorded at each hospital consultation.

Statistical analysis

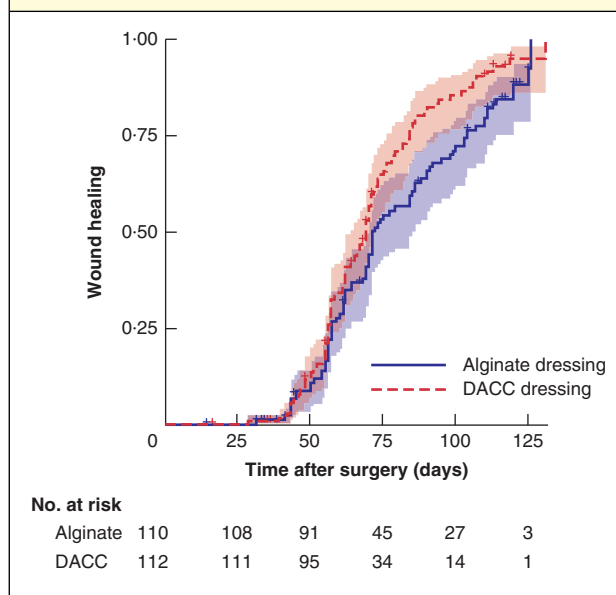
Using the Casagrande and Pike method, it was determined that a sample of 222 (rounded up to 250 patients to compensate for potential missing data and loss to

Table 1 Demographics		
	Alginate (n = 120)	DACC (n = 118)
Age (years)*	26.1(6.8)	25.6(8.2)
Sex ratio (F : M)	39 : 81	36 : 82
BMI (kg/m²)*	26.0(4.7)	26.0(5.0)
Socio-occupational category		
Skilled worker	12	4
Unemployed	17	16
Higher managerial and professional occupation	5	5
Supervisory, clerical and junior managerial, administrative and professional role	29	35
Student	20	23
Unskilled manual worker	19	19
Intermediate managerial, administrative and professional role	14	7
Retired	0	1
Missing	4	8
Risk factors associated with pilonidal sinus		
Poor hygiene	2	2
Associated immunopathology	1	2
Anaemia	1	0
Hypertension	1	0
Other medical co-morbidity	16	12
Smoker	66	56
No physical activity	23	20
History of pilonidal sinus		
Previous abscess with incision and drainage	68	64
Previous pilonidal excision	4	11

*Values are mean(s.d.). DACC, dialkylcarbamoyle chloride.

follow-up) would provide the trial with 90 per cent power to detect a difference of 20 per cent (50 versus 70 per cent) in the number of wounds completely healed after 75 days. The significance level was set at 0.05. χ^2 or Fisher's exact test was used, as appropriate, to determine the association between the categorical variables. Odds ratios (ORs) were calculated and presented with 95 per cent confidence intervals. The normality of the continuous distribution was evaluated graphically with the Shapiro–Wilk test. Student's *t* test or the Wilcoxon rank sum test was used to evaluate differences in the means of continuous variables. Likert scales were analysed with the Wilcoxon rank sum test. The Kaplan–Meier method was used to analyse wound healing between the two groups, and compared with the log rank test. The primary outcome was studied using per-protocol analysis. Maximum bias analysis was used to manage incomplete data by imputing missing data in the control group to success, and imputing missing data in the experimental group to failure. All statistical calculations

Fig. 2 Kaplan–Meier analysis of cumulative incidence of wound healing after excision of pilonidal sinus, per-protocol analysis



DACC, dialkylcarbamoyle chloride. $P = 0.038$ (log rank test).

were performed using R 3.4.3 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Between December 2013 and September 2017, 251 patients with a symptomatic pilonidal sinus were enrolled in the study (Fig. 1). Three patients were not randomized because they were lost to follow-up and did not have surgery. Two individuals were excluded after randomization as the protocol was not followed. Some 126 patients were allocated to the alginate arm and 120 to the DACC arm. Seven patients were lost to follow-up in the alginate arm and nine in the DACC arm. Patients with data missing for the primary outcome are detailed in Fig. 1. There were four adverse events in the alginate arm: severe pain (1), hyperglycaemia (1), pregnancy (1) and hyperalgetic inflammatory granulation needing surgical excision (1).

Baseline characteristics were similar in the two groups (Table 1). Two-thirds of the patients were men; the mean age was 25.9 years and mean BMI was 26.1 kg/m². In all centres, the surgical technique was performed in accordance with the protocol. After pilonidal sinus excision, mean(s.d.) wound length was 5.9(2.2) cm, width was 2.9(1.1) cm and depth was 2.9(1.1) cm. There were no differences between the two groups.

Primary endpoint: number of wounds healed after 75 days

In the per-protocol analysis, 58 of 97 patients (60 (95 per cent c.i. 51 to 71) per cent) in the alginate group and 78 of 103 (75.7 (67.8 to 85.0) per cent) in the DACC group had completely healed wounds at 75 days (OR 2.55, 95 per cent c.i. 1.12 to 5.92; $P = 0.023$). The difference in the proportion of wounds healed between the two groups was 16.0 (2.38 to 29.96) per cent in per-protocol analysis. In per-protocol analysis, Kaplan–Meier analysis showed a significant difference in wound evolution for DACC-coated compared with alginate dressings ($P = 0.038$) (Fig. 2).

In the intention-to-treat analysis with maximum bias, 86 of 126 patients (68.3 per cent) in the alginate group and 78 of 120 (65.0 per cent) in the DACC group had a healed wound after 75 days (OR 0.84, 95 per cent c.i. 0.49 to 1.52; $P = 0.592$).

Secondary endpoints

Wound characteristics

During follow-up, wounds with alginate dressings had more fibrin than those with DACC-coated dressings, but the difference was not significant ($P = 0.079$) (Fig. S1a, supporting information). There was no difference in wound characteristics between the two groups with regard to epidermalization, granulation, exudate or local infection (Fig. S1b–e, supporting information). The median time for complete wound healing was 69 (95 per cent c.i. 62 to 72) days in the DACC group and 71 (69 to 85) days in the alginate group.

Patient assessment of the dressing

There was no difference in patients' assessment of the dressings between the two arms during follow-up with regard to comfort, leakage or mobility. There was slightly more leakage with DACC dressings during the first 30 days, but the difference was not significant. Pain during the day was low, and there was no difference between the dressings: the VAS score was less than 2 of 10 at 15 days and less than 1 of 10 thereafter. After 15 days, the VAS score was lower than 1 of 10 for the entire follow-up period (data not shown).

Return to usual activities

The cumulative incidence of patients returning to their usual activities *versus* that in patients who were still prevented from returning was studied. Return to usual activities did not depend on the type of dressing used ($P = 0.733$). At 100 days, for example, 83 and 88 per cent of patients had returned to usual activities in the DACC and alginate groups respectively.

Discussion

This multicentre RCT compared DACC-coated and alginate dressings after pilonidal sinus excision, with prior agreement that a 20 per cent improvement in wound healing at 75 days would be clinically significant. In per-protocol analysis, there was 60 per cent wound healing in the alginate arm *versus* 75.7 per cent in the DACC arm, a 16.0 per cent difference that was not considered clinically valuable.

All open wounds are contaminated, and wound infection is a major factor in delayed healing. The wounds after pilonidal sinus excision could be a good model for studying clean acute wound healing. The location of this type of wound could explain the potentially high rate of microorganism colonization. The precise mechanisms by which microorganisms cause infection are controversial⁷. The microbial expression of toxins and enzymes destroys tissue cells, which can delay healing. The expression of polynuclear leucocyte enzymes could also lyse healthy tissue cells. *In vitro* and *in vivo* studies have demonstrated that a range of wound dressings, including alginates, hydrocolloids and hydrofibres, promote a reduction in the wound surface bioburden without a chemically active agent⁸. Alginates have been found to retain bacteria within the dressing matrix⁹. The mechanism of action for DACC dressings is based on the hydrophobic interaction between the hydrophobic coating on the dressing and the microbes whose surfaces contain water-repellent molecules¹⁰. Microbes, including fungi, are irreversibly bound through hydrophobic interactions to the DACC coating on the dressing surface. Recent *in vitro* evidence indicates that DACC enhances binding of methicillin-resistant *Staphylococcus aureus*¹¹ and biofilms¹².

The binding and removal of pathogenic microorganisms may not be the only mechanism resulting in enhanced wound healing. A pilot study by Falk and Ivarsson¹³ investigated the effects of a DACC-coated dressing on cultured fibroblasts. They showed that cultured fibroblasts had an increased proliferation rate in the presence of the DACC-coated dressing compared with control cells, cultured with the medium alone. In the present study, wounds dressed with alginate had more fibrin during follow-up than those with DACC-coated dressing. This difference was not significant, but the high amount of fibrin could have decreased the wound healing rate in the alginate arm. Further studies are necessary to understand and analyse the impact of each dressing on the different mechanisms involved in wound healing.

Few RCTs have been conducted in patients with pilonidal sinus disease to investigate the effectiveness of different dressings^{14,15}. Biter *et al.*¹ showed the feasibility of using

negative-pressure wound therapy (NPWT) after pilonidal sinus excision. In their study, complete wound healing was achieved after a median of 84 days in the vacuum therapy group *versus* 93 days in controls ($P = 0.44$). Thus, NPWT did not significantly increase the complete wound healing time compared with conventional care, although the wound size ratio was significantly lower in the vacuum therapy group for the first 15 days. Furthermore, a systematic review by Ubbink and colleagues¹⁶ (including 13 RCTs evaluating NPTW in both chronic and acute wounds, as well as split skin grafts) showed that NPWT did not result in faster wound healing compared with that in control patients. Thus, DACC-coated dressings could be a good alternative (either in conjunction with NPTW or alone) to increase the healing process of acute wounds.

This study has some potential limitations. Blinding to both patients and doctors was not possible, and the number of patients lost to follow-up or with a discontinued intervention was fairly high. Estimation of the wound healing rate differed according to whether the data were analysed as binary data (wound completely healed at 75 days or not) or as survival to complete healing. On the one hand, statistical analysis of only complete data (at 75 days) could be biased with regard to the estimation of wound healing rate in each group. On the other hand, in the case of survival analysis, patients who left the study before, or had no principal endpoint at, 75 days were included in the analysis. In this case, the wound healing rate was lower but more accurate, because all available data were included. A better follow-up process would be desirable, although pilonidal sinus disease affects a young population that is often less compliant with restrictive research protocols. Other means of wound assessment such as telemedicine, for example, could be used.

Collaborators

Other members of the SORKYSA group: N. Chilintseva, T. Knepler, S. Manfredelli, B. Simeu, B. Tréchet, E. Triki and E. Valero (Department of Digestive Surgery, Strasbourg University Hospital); M. Di Liberatore, S. Gergeanu, R. Ionescu and G. Mihaescu (Department of Digestive Surgery, Hôpital Sainte Catherine, Saverne); M. Nicolae, D. Patrice and I. Zeca (Department of Digestive Surgery, Hôpital Pasteur, Colmar); P. Barsotti and S. Dan (Department of Digestive Surgery, Hôpital Emile Muller, Mulhouse).

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Disclosure: The authors declare no conflict of interest.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.