Efficacy of flap repair for anal fistula: study protocol for a systematic review of randomized controlled trial

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Abstract

Background: Clinical trials have reported that flap repair (FR) can treat anal fistula (AF) effectively. However, no study systematically investigated its efficacy and safety for patients with AF. This study will systematically assess its efficacy and safety of AF.

Methods: We will retrieve MEDLINE, EMBASE, Cochrane Library, Elsevier, Springer, Web of Science, Scopus, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, VIP Information, and Wanfang Data from their inceptions to May 1, 2019 without any language limitations. The primary outcome is fistula cure rate. The secondary outcomes consist of fistula recurrence rate, fecal continence, quality of life, and complications. RevMan 5.3 software will be used for methodological quality assessment, data synthesis, subgroup analysis and sensitivity analysis.

Results: The results of this study will summarize a high-quality synthesis of current evidence for the treatment of FR for patients with AF.

Conclusion: The findings of this proposed study will provide evidence for judging whether FR is an effective and safety intervention for AF or not.

PROSPERO registration number: PROSPERO CRD42019135507.

Abbreviations: AF = anal fistula, FR = flap repair, RCTs = randomized controlled trials.

Keywords: anal fistulas, efficacy, flap repair, randomized controlled trial, safety

1. Introduction

Anal fistula (AF) is a very common anal disorder, which is the main etiology of perianal abscesses and suppurations.[1,2] It mainly manifests as a variety of symptoms, such as pain, fecal incontinence, impaired quality of life and work incapacity.[3–6] It has been estimated that more than 1:10,000 individuals can affect such disorder.[7] Its prevalence rate in men to women is 1.23: 0.56 per 1000 population with an average age of 40 years.[8–10]

Several managements are responsible for the treatment of AF.[11–20] Of them, flap repair (FR) is reported for treating AF.[11,17] However, no study has been systematically assessed the efficacy and safety of FR for the treatment of AF. Thus, in this

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study, we will evaluate the efficacy and safety of FR for patients with AF.[11,17]

2. Methods and materials

2.1. Inclusion and exclusion criteria for study selection

2.1.1. Types of studies. Only randomized controlled trials (RCTs) regarding the efficacy and safety of FR for patients with AF will be included. Non-clinical studies, non-controlled trials, and non-RCTs will be excluded.

2.1.2. Types of participants. All patients of clinically diagnosed with AF will be included without any restrictions of gender and age.

2.1.3. Types of interventions. The patients in the experimental group receive FR. The patients in the control group receive any treatments, except FR.

2.1.4. Types of outcomes. The primary outcome is Fistula cure rate. The cure was defined as complete wound healing with absence of symptoms.

The secondary outcomes consist of fistula recurrence rate; fecal continence, as measured by Rockwood Fecal Incontinence Severity Index or other relevant scales; quality of life, as measured by Global Quality of Life Scale or other associated scales; and complications.

2.2. Literature search strategy

Relevant RCTs of FR for patients with AF from the databases including the MEDLINE, EMBASE, Cochrane Library, Elsevier,

Table 1

Search strategy for MEDLINE.

Number	Search terms
1	rectal
2	anal
3	fistula
4	fistulas
5	Or 1–4
6	surgical flaps
7	flap repair
8	flap
9	wound healing
10	wound repair
11	Or 6–10
12	randomized controlled trial
13	controlled clinical trial
14	placebo
15	randomly
16	randomized
17	trial
18	study
19	Or 12–18
20	5, 11, and 19

Springer, Web of Science, Scopus, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, VIP Information, and Wanfang Data from their inceptions to May 1, 2019 without any language limitations. The strategy for searching MEDLINE is presented as an example in Table 1. The similar modified strategy will be used to other electronic databases.

In addition, we will also search grey literatures, including conference proceedings, dissertations, and reference lists of all eligible RCTs to avoid missing any potential studies.

2.3. Data collection
2.3.1. Study selection. Two reviewers will independently read all the titles and abstracts of all searched literature. Then, all duplicated and irrelevant studies will be excluded based on the eligibility criteria. After that, the full text of remaining literatures will be read to judge whether those studies meet the final eligible criteria. A third reviewer will be invited to solve any disagreements, raised between two reviewers regarding any issues of study selection. The whole process of study selection will be presented in the flowchart of Preferred Reporting Items for Systematic Reviews and Meta-Analyses with specific reason for each excluded study at different stages.

2.3.2. Data extraction and management. Two reviewers will independently extract data from all eligible literatures through prediluted data extraction sheet. Any divergences will be settled down by discussion with a third reviewer invited. The extracted information comprises of

1) General information: title, first author, year of publication, inclusion and exclusion criteria, etc;
2) Methods: sample size, randomization, concealment, blinding, etc;
3) Treatments: name of different interventions, control, dosage, frequency, etc;
4) Outcomes: Primary, secondary, and safety outcomes, etc.

2.3.3. Missing data dealing with. If any insufficient information or missing data will occur, we will contact primary authors to obtain those data. If we cannot receive that information, we will only analyze the available data, and will discuss the potential impacts of missing information.

2.3.4. Methodological quality assessment for eligible studies. Cochrane Risk of Bias Tool will be utilized for assessing the methodological quality of all eligible studies. It consists of 7 domains, and each aspect is further divided into 3 degrees: low, unclear, and high risk of bias. Two reviewers will independently assess the methodological quality for each eligible study. Any disagreements regarding the methodological quality assessment between two reviewers will be solved by a third reviewer through discussion.

2.4. Statistical analysis
2.4.1. Treatment effect measurements. Measurement data will be expressed as mean difference or standardized mean difference with 95% confidence intervals. Enumeration data will be expressed as relative risk or odds ratio with 95% confidence intervals.

2.4.2. Heterogeneity identification. The I^2 test is used for identified heterogeneity among eligible studies. $I^2 \leq 50\%$ means low heterogeneity among included studies, while $I^2 > 50\%$ means significant heterogeneity. Then, subgroup analysis or sensitivity analysis will be carried out to identify the source of heterogeneity.

2.4.3. Data synthesis. RevMan 5.3 software will be used for meta-analysis performance. If there is small heterogeneity, a fixed-effects model will be utilized for analysis. If there is substantial heterogeneity among eligible studies, a random-effects model will be applied, and subgroup analysis will be carried out. If substantial heterogeneity is still identified after subgroup analysis, we will not pool data, and will report outcome results as narrative descriptions instead of meta-analysis performance.

2.4.4. Subgroup analysis. Subgroup analysis will be employed in according to the different study characteristics, treatments, controls, and outcome measurements.

2.4.5. Sensitivity analysis. Sensitivity analysis will be carried out to check robustness of pooled data by removing low quality studies.

2.4.6. Publication bias. In this study, we will perform funnel plot,[21] and Egger regression[22] to identify any reporting bias if more than 10 studies are included.

3. Discussion

To the best of our knowledge, this is the first study to focus on assessing the efficacy and safety of FR for the treatment of patients with AF. The results of this study will determine if FR is a superior modality for patients with AF. Moreover, we also believe that this study may provide helpful evidence for clinical recommendations, which may benefit for either patients or clinical practice, as well as help clinicians to make the best choice for such patients.

Author contributions

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