# CHAPTER II

# RESEARCH METHODOLOGY

## 2.1 Research Questions

### 2.1.1 Primary research question

- Is there any clinically significant difference in the pain score in postoperative period between fistulotomy alone (F) and fistulotomy with marsupialization (FM) in the treatment of fistula in ano?

### 2.1.2 Secondary research question

- Is there any difference in the postoperative pain after first defecation?
- Are there any differences in total amount of pethidine and paracetamol usage?
- Are there any differences in postoperative complications?

## 2.2 Research Objectives

To compare the following items between two techniques of simple fistula surgery, F and FM:

5. Pain score in the postoperative period.
6. Pain score after the first defecation.
7. Amount of pethidine and paracetamol usage.
8. Complication.

## 2.3 Hypothesis

### 2.3.1 Research hypothesis

There is a significant difference in the pain score in postoperative period between F and FM for the treatment of fistula in ano.

### 2.3.2 Statistical hypothesis

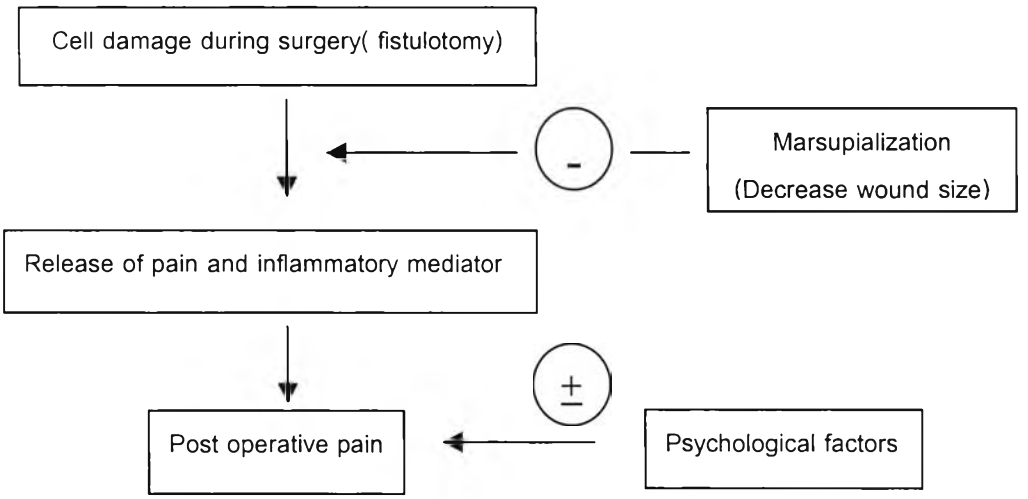
Null hypothesis

There is no statistical significant difference in the pain score in postoperative period between F and FM for the treatment of fistula in ano.

Alternative hypothesis

There is a statistical significant difference in the pain score in postoperative period between F and FM for the treatment of fistula in ano.

## 2.4 Proposed conceptual framework (figure 3)




## 2.5 Assumption

- The visual analogue pain score is reliable and sufficient to assess the pain level of the patients with fistulotomy.
- The surgeons have the equal skill and same technique in fistulotomy and marsupialization for fistula in ano.

## 2.6 Operational definition

**Simple fistula in ano** is defined as intersphincteric and low transsphincteric type of fistula in ano.

**Low transsphincteric type** is defined as part of fistula tract across some part of superficial external anal sphincter

**Fistulotomy** is a technique of lay open of fistula tract.

**Marsupialization** is defines as a technique of suturing wound edge to the fistula tract after fistulotomy.

**Incontinence** is defined as an impairment of anal sphincter to formed stool, liquid stool, or flatus [30].

**Visual analogue pain scale** is the pain measurement that represents the continuum of the pain symptom to be rate. It is a self-rated score which is a 100 mm line that is marked at the end to indicate the range of pain being considered. The independent evaluator informed the patients that "0" score is "no pain" and "100" score is "worst pain" or the most severe pain that they had ever experienced. The patients were informed to mark the maximal pain in each day of the post operative day 1, 3, 5, 7, 14 and mark the maximal pain after the first defecation.

0 _____ 100

(no pain) (worst pain ever)

## 2.7 Research design

Prospective randomized controlled trial. The randomized process ensured that the allocation of the treatment is independent of characteristics of the patients.

## 2.8 Research methodology

### 2.8.1 Population and sample

Target population

Patients with simple fistula in ano.

Sample population

Patients who are in eligible criteria and scheduled for surgery as an inpatient service in King Chulalongkorn Memorial Hospital.

### 2.8.2 Eligibility criteria

Inclusion criteria

Simple uncomplicated fistula in ano with first diagnosis

Inpatient surgery, operation was performed under spinal anesthesia

Can follow up as outpatient visit at least 3 months

Agree to participate and sign the informed consent

Exclusion criteria

Complex fistula in ano

Multiple opening, multiple tract, horseshoe type, suprasphincteric type, extrasphincteric type, recurrence fistula, cannot find internal opening

Prior incontinence

Immunocompromised patient

Bleeding tendency

2.8.3 Sample size calculation

The primary outcome of the study is the pain score recorded at postoperative day 1, 3, 5, 7, and 14 as a visual analogue pain score that will be compared using mean and SD in repeated measurement.

Therefore mean and SD of the duration of postoperative pain were used for sample size estimation as the following formula

$$\text{N/group} = \frac{2SD^2(Z_{\alpha/2}+Z_{\beta})^2}{d^2}$$

$Z_{\alpha/2}$ is the value of the standard normal distribution cutting off probability $\alpha/2$ in each tail = 1.96 for $\alpha$ = 0.05

$Z_{\beta}$ is the value of the standard normal distribution cutting off probability $\beta$ in the upper tail = 1.28 for 90 % power

SD* is the standard deviation of pain score = 22

d* is the clinical difference of pain score between both group = 20 points ( estimate from 50 % reduction of pain score in fistulotomy alone group)

The sample size estimation calculated from this formula is 25.

( * SD and d were drawn from pilot study)

2.8.4 Randomization and allocation concealment

The patients who meet the eligible criteria will be randomized in a 1:1 ratio to one of two treatment groups;

- Fistulotomy alone group
- Fistulotomy with marsupialization group

The randomization list will be computer-generated random sequence.

The allocation will be concealed and blinded to patients and evaluator.

2.8.5 Intervention

This study will be conducted during 2 weeks period and 2 visits are planned: first visit as an inpatient for surgical intervention and end-point visit as an outpatient for follow up at colorectal clinic.

Inpatient visit:

After complete evaluation, all patients will be performed fistulotomy under spinal anesthesia with 0.5% hyperbaric bupivacaine 1.5-2 cc. If all criteria are met, patients will be randomized into fistulotomy alone (F) group or fistulotomy with marsupialization (FM) group. The procedure will stop if the patient was allocated into F group and marsupialization of wound edge will be performed if the patient was allocated into FM group.

Postoperative care is the same in all patients. Paracetamol tablet (500 mg) four time a day are prescribed for pain relief, and pethidine 50 mg. injection intramuscularly will be added every 4 hours on patient's demand in case of intolerated pain. Self-wound care by tab water is introduced and patients are allowed to have soft diet after the operation was finished. Bulk forming agent (mucilin®) is also added in the postoperative period. Most of the patients will be discharged on the first postoperative day and they will be informed to self-record the maximal pain in postoperative day 1, 3, 5, 7 and 14. Pain score after first defecation, number of paracetamol usage in 7 days after discharge, post operative continence status and complication are also informed to record at home.

Data recorded in the inpatient visit are age, sex, underlying disease, fistula type, fistula length, number of pethidine injection, time to first pethidine injection and complication.

Outpatient visit:

All patients are scheduled for follow up in 2 weeks.

Data retrieved from the patient's self-record form is a pain score in postoperative day 1, 3, 5, 7, and 14. Pain score after first defecation, number of paracetamol usage, post operative continence status, and complication are also retrieved from the self-record form. Wound condition will be evaluated by independent evaluator in the follow up day.

2.8.6 Outcome assessment

Patient population

The patient population was defined as all patients who were in eligible criteria and were randomized into either F or FM group.

Primary outcome variable

For the primary outcome, pain score was recorded at postoperative day 1, 3, 5, 7, and 14. The pain score of each group was compared using mean and SD in repeated measurement. The small number of postoperative pain score was referred to the better technique.

Secondary outcome variable

The secondary outcomes were pain score after the first defecation, the amount of pethidine and paracetamol usage and complications.

1. For the pain score of first after the first defecation, the lower pain score was referred to the better technique.
2. For the total amount of pethidine and paracetamol usage, the less amount of usage was the better technique.
3. For the complications, the lower was the better.

2.8.7 Data collection

The following data were recorded

1. Demographic data, baseline characteristics

These following data were recorded by the surgeons who operated the patients

- Age (yrs)
- Sex (Male: Female)
- Underlying disease, such as DM, hypertension (HT), heart disease (HD), etc
- Fistula type ( intersphincteric, low transsphincteric)
- Length of fistula tract

Table 1 Data collection of demographic data and baseline characteristics

| | | |
|---|---|---|
| Age | ____ yrs | |
| Sex | [ ] Male | [ ] Female |
| Underlying disease | | |
| - *DM* | [ ] Yes | [ ] No |
| - *HT* | [ ] Yes | [ ] No |
| - *HD* | [ ] Yes | [ ] No |
| Fistula type | | |
| | [ ] Intersphincteric | [ ] Low transsphincteric |
| Fistula length | ____ cm | |

2. Outcomes

These following data were obtained from the evaluator in the admission visit and the patients at the follow up visit.

From the evaluator

- Number of patient need pethidine injection (persons)
- Time to first pethidine injection (hrs)
- Complications: urinary retention, bleeding, others
- Wound condition

From the patients

- Visual analogue pain score (VAS) in post operative day 1, 3, 5, 7, and 14 (mm)
- Visual analogue pain score after the first defecation (mm)
- Total amount of paracetamol use in 7 days after discharge(tablet)
- Continence status ( incontinence to flatus, liquid stool, formed stool, none)

**Table 2 Data collection of outcomes**

| | | |
|---|---|---|
| Number of patient need pethidine injection | | ____ persons |
| Time to first pethidine injection | | ____ hrs |
| Complications | | |
| - *urinary retention* | [ ] Yes | [ ] No |
| - *bleeding* | [ ] Yes | [ ] No |
| - *others*..... | [ ] Yes | [ ] No |
| Wound condition | [ ] no inflammation | [ ] inflammation |
| VAS in post operative day 1 | | ____ mm |
| VAS in post operative day 3 | | ____ mm |
| VAS in post operative day 5 | | ____ mm |
| VAS in post operative day 7 | | ____ mm |
| VAS in post operative day 14 | | ____ mm |
| VAS after the first defecation | | ____ mm |
| Total amount of paracetamol use in 7 days | | ____ tablets |
| Continence status | | |
| - *incontinence to* : | [ ] flatus | [ ] liquid stool |
| | [ ] formed stool | [ ] none |

2.8.8 Data analysis

The demographic and baseline quantitative data was presented as mean (SD), ratio and frequency as appropriate.

For the primary outcome:

Pain score was assessed by visual analogue pain score (VAS) which is a 100 mm line starting from 0 (no pain) to 100 (worst pain ever).

0 _____ 100

(no pain) (worst pain ever)

Descriptive Statistics of VAS on postoperative day 1, 3, 5, 7, and 14 was presented as mean (SD) and analyzed by repeated measure ANOVA, as well as 95% CI.

For the secondary outcomes:

The pain score after the first defecation, time to first pethidine injection and total amount of paracetamol usage were presented as mean (SD) or median (min - max) as appropriate, and the data was analyzed by unpaired t-test or Mann-Whitney U test, which was based on the assumption of parameter.

The number of patient that needed pethidine injection, wound condition, and complication were presented as frequency or ratio as appropriate. The data was analyzed by Pearson $\chi^2$ test (continuity correction) or Fisher's exact test which was based on the appropriateness of parameter.

All statistical analysis will be calculated using SPSS/PC Version 11.5. A two-sided significance level of 0.05 was used for all analysis.

Table 3 Data analysis

| | |
|---|---|
| **Demographic data and baseline characteristics** | |
| Age | mean (SD) |
| Sex | frequency (ratio) |
| Underlying disease | frequency |
| Fistula type | frequency (ratio) |
| Fistula length | mean (SD) |
| **The primary outcome** | |
| VAS in postoperative day 1, 3, 5, 7, 14 | repeated measure ANOVA |
| **The secondary outcomes** | |
| VAS on the first defecation | unpaired t-test |
| Number of patient need pethidine injection | Pearson $\chi^2$ test |
| Time to first pethidine injection | unpaired t-test |
| Total amount of paracetamol use in 7 days | Mann-Whitney U test |
| Wound condition | Fisher's exact test |
| Complications | Fisher's exact test |

2.8.9 Ethical consideration

The researchers submitted the documents required by the regulations according to Ethics Committee and obtained their opinion in writing. Patients were included after the approval of the Ethics Committee had been received.

The trial was conducted in accordance with ICH guidelines for Good Clinical Practice. All eligible patients received detail of the study protocol and research assistants explained the protocol thoroughly to the patients. All patients had to give written informed consent before enrollment. The patient's right to confidentiality was maintained during data collection and processing.

Technique of fistulotomy with marsupialization was published in many literatures. It is accepted as one of standard treatment for fistula in ano.

### 2.8.10 Limitation

Visual analogue pain score is self- rated score. There are some confounding factors such as background psychological factor that may affect the patient's perception. However, this technique provides simple, efficient and minimally intrusive measure of pain intensity which has been used widely in clinical and research setting where a quick index of pain is required and to which a numerical value can assigned.

### 2.8.11 Implication

The results obtained from this study would provide the information for the selection of the appropriate technique for the treatment of simple fistula in ano.