CHAPTER III

RESEARCH DESIGN AND METHODOLOGY

3.1 Research Questions

3.1.1. Primary Research Question:

Does laparoscopic cholecystectomy using abdominal wall lifting technique give the success rate within 10% difference when compare to laparoscopic cholecystectomy using tension pneumoperitoneum?

3.1.2. Secondary research questions

3.1.2.1. How often does the cardiac arrhythmia occur in each group?

3.1.2.2. What are the complications of routine laparoscopic cholecystectomy and laparoscopic cholecystectomy using abdominal wall lifting technique?

3.1.2.3. Are postoperative pain scores by visual analog scale different, when compare between the two groups?

3.1.2.4. Can post-operative shoulder pain be prevented by abdominal wall lifting technique?

3.1.2.5. What is the cost per successful case of routine laparoscopic cholecystectomy and laparoscopic cholecystectomy using abdominal wall lifting technique?

3.2 Research objectives:

The objectives of the study were comparing:

1. the success rate of laparoscopic cholecystectomy using abdominal wall lifting technique and tension pneumoperitoneum.
2. rate of cardiac arrhythmia in each group.
3. the complication rate in each group.
4. postoperative pain at 6, and 24 hours after the operation by visual analog scale in both groups.
5. rate of shoulder pain in each group.
6. cost per successful case in each group.

3.3 Conceptual framework:

The success of the laparoscopic cholecystectomy depends on:

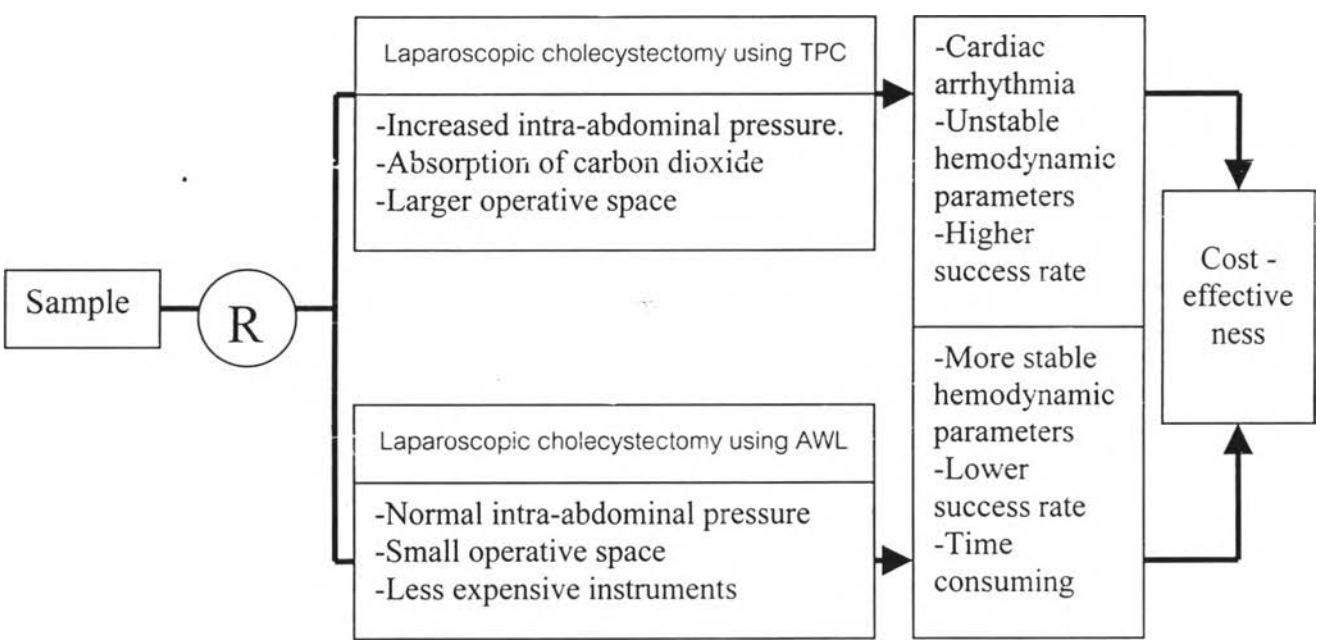
1. gallbladder status : mark adhesion, unclear anatomy at Calot's triangle, thick or friable gallbladder wall may lead to failure of the operation.

2. exposure : TPC expands the abdominal wall in every directions, presses the bowel loops downward and gives good visualization . On the other hand, abdominal wall lifting technique provides smaller space and surgeons have to

use a retractor to press the bowel loops to improve the exposure of Calot's triangle. Gallbladder shape, mesentery of a gallbladder and retractability of the liver also play important role for the exposure during the laparoscopic procedure.

3. surgeon's experience and team : understanding of anatomy of the biliary system, good handling of the tissue, direction of traction of the gallbladder , all are important issues which may affect the success rate.

Fig.1. Conceptual Framework.



Tension pneumoperitoneum produces 2 major effects on a patient.[38, 39]

1. mechanical : compression of intraabdominal and intrathoracic contents ;
2. absorption of carbon dioxide

Increased intraabdominal pressure reduces venous return to heart and produces hypotention. Head up position as use in laparoscopic cholecystectomy also reduce cardiac output and cause hypotention. [42] Carbon dioxide is used as insufflating gas

for TPC procedure, because of its high solubility and non-combustion. Cardiac arrhythmia has been reported in relation to laparoscopy. Hypercarbia has been shown to produce tachycardia and premature ventricular contractions (PVC).[67, 68] There changes are usually benign unless arterial CO_2 is more than 60 mm.Hg. A patient is usually monitored with end tidal CO_2 ($ETCO_2$) during the operation. Mullet CE. [69] reported CO_2 elimination in laparoscopic surgery, carbon dioxide excretion and $ETCO_2$ increased in parallel from the eighth to the tenth minute after the start of CO_2 insufflation, and reached a plateau 10 minutes later. Thus beyond the first 15 minutes of CO_2 insufflation, the rate of CO_2 diffusion into the body is no longer related to the duration of intraperitoneal insufflation. Ten minutes after the cessation of CO_2 insufflation, $ETCO_2$ returns to normal values. In normal patients, $ETCO_2$ will represent CO_2 level in the arterial blood (Pa CO_2).

Abdominal wall lifting technique can reduce the potential hazards of increased intra-abdominal pressure and cardiovascular changes due to the absorption of CO_2. It can also eliminate fatal complication, such as gas embolism. However the abdominal wall lifting technique creates smaller space for surgeon to operate and does not suppress bowel loops from floating up. Smaller operative space causes poorer exposure of the Calot's triangle and affects the success rate. For patients' benefits, surgeons usually consider and attempt the other type of laparoscopic cholecystectomy before convert to open surgery.

Usually surgeons use 4 surgical ports in laparoscopic cholecystectomy, using TPC technique. Abdominal wall lifting technique does not require an airtighted system. Used or damaged ports can be used in the AWL cases and this reduces cost of the operations.

3.4 Research Hypothesis

Laparoscopic cholecystectomy using AWL technique is theoretically less harmful especially in the cardiovascular complication. If it provides the same or within 10 per cent difference in success rate as of TPC technique, we should use AWL in laparoscopic cholecystectomy.

For the null hypothesis :

Null hypothesis: $p_{(AWL)} = p_{(TPC)}$

There is no significant difference in success rate between the two groups.

Alternative hypothesis: $p_{(AWL)} \neq p_{(TPC)}$

There is a significant difference in success rate between the two groups.

3.5 Operational definitions :

1. Successful operation meant ability to perform laparoscopic cholecystectomy without conversion to the other procedure or open surgery and without injury to the CBD.
2. Cardiac arrhythmia. Premature ventricular contraction, (PVC) during the time of operation was counted as having cardiac arrhythmia.
3. Complications. All adverse effects at postoperative and follow-up period were counted as complications and were recorded.
4. Severity of postoperative pain was measured by visual analog scale. The independent evaluator informed the patients that "zero" score is "no pain" and "100" score is unbearable pain or the most severe pain she or he had ever experienced. And let the patient marked the score of current pain on the line with 10 cms. long.
5. Shoulder pain was dull pain around the patient's shoulder and occurred in some patients at the postoperative period. Usually, it was not severe and was be recorded as Yes or No.
6. Cost effectiveness analysis was analyzed in patient's and provider's perspective. In patient's perspective; direct and indirect costs were measured and compared to successful operation. Capital, labor and material costs were measured and compared for the cost-effective analysis in the provider's perspective.

3.6 Research Design

This study was a randomized controlled trial, in which the patients were randomly allocated into one of the two groups (TPC or AWL) by block randomization.

3.7 Population and Sample

3.7.1 .Target population: The target populations in this study were patients who had symptomatic gallstones and required surgical treatment.

3.7.2 Study population : The study population were people who passed the eligibility criteria :

1. Inclusion criteria
   - Patients with gall stones who admitted at King Chulalongkorn Memorial Hospital
   - No major associated diseases
   - Agreed and signed informed consent.
2. Exclusion criteria. Patients with the following conditions were excluded from the study.
   - acute cholecystitis.
   - common bile duct stone (s).
   - serologic evidences of HIV infections.
   - pre-operative cardiac arrhythmia

3.7.3 Sample: Because of the limitation of number of patients and time, all the study population was used as the samples in this study.

3.7.4 Allocation: Block of 4 randomization was used in the study. A research nurse kept the code of block randomization and determined the type of laparoscopic operation when the patient entered the operative room. Surgeons could not select a type of laparoscopic procedures.

3.8 Sample size estimation

The sample size for primary research question was calculated by using Pocock's formula . The success rate of the control group (TPC) was 0.94 (derived from our previous study [10] The effect size of 10 percent was estimated by expert's opinion. The value of α error was 0.05 and was used as two tailed. The AWL technique provided smaller operative space, which caused more difficulty for the surgeons to operate. Success rate in AWL group should be lower than in the TPC group, however, AWL technique provided higher success rate in the previous study [66] .

Sample size: The sample size was calculated by using Pocock's formula:

$$N \text{ (per group)} = \frac{[P1\ (1-P1) + P2\ (1-P2)]}{(P1 - P2)^2}\ (Z\alpha + Z\beta)^2$$

P1 = proportion of success rate in controlled group = 0.94

P2 = proportion of success rate in study group = 0.84

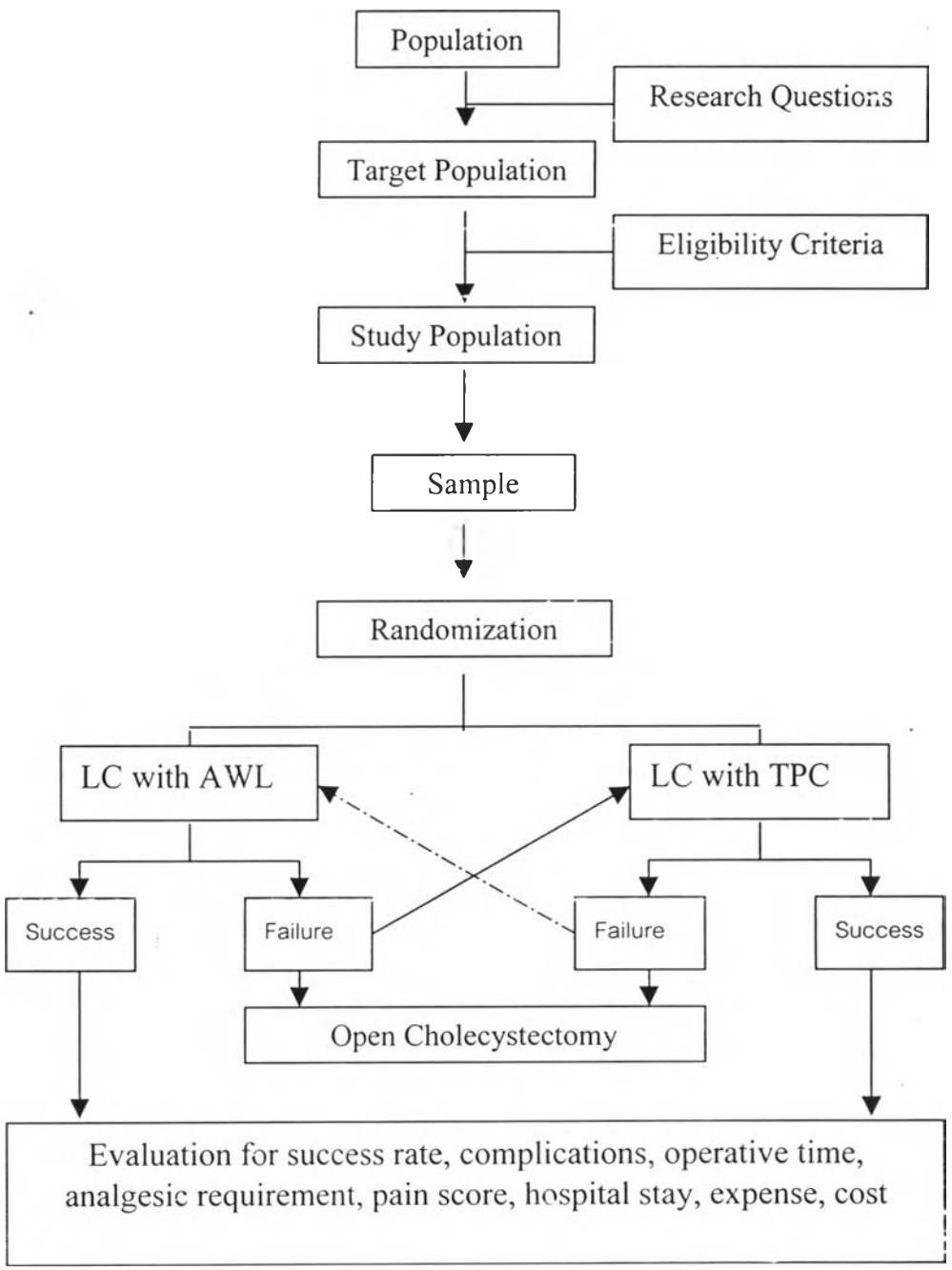
α = 0.05 (two tailed) ; β = 0.2

$$n = \frac{[0.94\ (0.06) + 0.84(0.16)]}{(0.1)^2} \times (1.96+0.84)^2$$

$$n = \frac{0.1908 \times 7.84}{0.01} = 149.6$$

Estimated sample size (rounded up) = 300 patients to detect the 10 per cent difference.

3.9 Research Framework



3.10 Methods

The operations were performed under general anesthesia with electrocardiography, blood pressure, heart rate and end tidal carbon dioxide monitoring. Nasogastric tube and urinary catheter were placed during the operation. Under aseptic technique, a Veress needle was introduced into the abdominal cavity through a subumbilical incision and CO_2 gas was insufflated into the abdominal cavity. The first trochar was punctured at the subumbilical region when the intraabdominal pressure was 10-12 mm.Hg. Laparoscopic examination was performed through the first trochar. The 2nd, 3rd, and 4th trochar were punctured into the cavity under laparoscopic view.

In AWL group, the procedure was the same, but the 2nd trochar was punctured at right subcostal region, above gallbladder area. It was then pulled off and changed into an expandable retractor. The CO_2 gas was deflated and the retractor was connected to the "Laparolift" hydraulic machine (Origin Company) to lift the abdominal wall up. The operative space was created and the 3rd, 4th and 5th trochar were introduced into the abdominal cavity under laparoscopic view.

The dissection technique in the 2 groups was the same. First, a surgeon identified cystic duct and cystic artery then divided them between clips, separately. The gallbladder was dissected out of its bed and was removed through either the epigastric port or subumbilical port. After careful hemostasis, the punctured sites were closed. The wounds were covered with a large bandage to blind the evaluator

and also the patient about type of operations. The patient was observed vital signs in the recovery room for 1-2 hours, and then was sent back to the patient's ward.

3.11 Prevention of biases

As many clinical experimental studies, there were many steps which biases might occur. This study was designed to avoid biases in many steps as described below.

1. Selection bias. Using block randomization prevented selection bias and a research nurse determined type of the operation when the patient entered operative room. Surgeons could not select type of operation by themselves.

2. Measurement bias. Measurement bias was prevented by blinding the evaluator about type of operation by cover the entire operative field with one large sheet of bandage. The patients were educated about the analog pain scoring a day before the operation. The research nurse who did not know the type of operation evaluated the pain score of each patient.

3.12 Criteria for conversion

The surgeons made their best effort to finish the assigned operation. In case that it might be harmful to the patients they convert to the other or open cholecystectomy. The criteria for conversion were

1. active bleeding, which could not be controlled by laparoscopic means.
2. unclear anatomy around Calot's triangle, no progression in dissection after attempting for at least 20 minutes.
3. injury of bile duct or visceral organ, which required open surgery to repair.