การศึกษาปัจจัยเสี่ยงของการเกิดภาวะกล้ามเนื้อหัวใจตาย
ในระหว่างและ หลังจากการให้ยาระงับความรู้สึกในผู้ใหญ่ที่ได้รับการผ่าตัด
ที่ไม่ใช่การผ่าตัดหัวใจ ระหว่าง พ.ศ. 2545 - 2547

นาง ฐิติมา ชินะโชติ

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาการพัฒนาสุขภาพ
คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2547
ISBN 974-53-1128-6

RISK FACTORS OF PERIOPERATIVE MYOCARDIAL INFARCTION IN ADULT NON-CARDIAC OPERATION, 2002-2004; A CASE-CONTROL STUDY

Mrs. Thitima Chinachoti

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Health Development
Faculty of Medicine
Chulalongkorn University
Academic Year 2004

ISBN 947-53-1128-6

Thesis Title	Risk factors of perioperative myocardial infarction in adult non-cardiac operation, 2002 - 2004; a case-control study
By	Thitima Chinachoti
Field of Study	Health Development
Thesis Advisor	Associate Professor Oranuch Kyokong
Thesis Co-advisor	Professor Shusee Visalyaputra

Accepted by the Faculty of Medicine, Chulalongkorn University in Partial Fulfillments of the Requirements for the Master's Degree

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……Thesis Co-advisor
(Professor Shusee Visalyaputra, M.D., M.Sc.)

……Member
(Miss Chulaluk Komoltri, DrPH)

……Member
(Associate Professor Charn Sriatanasathavorn, M.D.)

ฐิติมา ชินะโชติ : การศึกษาปัจจัยเสี่ยงของการเกิดภาวะกล้ามเนื้อหัวใจตายในระหว่างและหลังจากการให้ยาระงับความรู้สึก ในผู้ใหญ่ที่ได้รับการผ่าตัดที่ไม่ใช่การผ่าตัดหัวใจ ระหว่าง พ.ศ. 2545 - 2547 (RISK FACTORS OF PERIOPERATIVE MYOCARDIAL INFARCTION IN ADULT NON-CARDIAC OPERATION, 2002-2004; A CASE-CONTROL STUDY) อาจารย์ที่ปรึกษา: รศ.พ.ญ.อรนุช เกี่ยวข้อง, อาจารย์ที่ปรึกษาร่วม: ศาสตราจารย์แพทย์หญิงชูศรี พิศลยบุตร. 55 หน้า. ISBN 974-53-1128-6

ความเป็นมา : ในปัจจุบันถึงแม้ว่าผู้ป่วยทุกรายจะได้รับการตรวจประเมินภาวะเสี่ยงต่อการเกิดภาวะกล้ามเนื้อหัวใจตายตามมาตรฐานสากล ยังปรากฏว่าผู้ป่วยจำนวน 20 – 30 รายต่อปี มีอาการกล้ามเนื้อหัวใจตายในระหว่างและหลังการผ่าตัด ในโรงพยาบาลศิริราช ผู้วิจัยจึงต้องการค้นหาปัจจัยที่สัมพันธ์กับการเกิดภาวะกล้ามเนื้อหัวใจตาย ที่แก้ไขหรือป้องกันได้

วัตถุประสงค์การวิจัย : เพื่อศึกษาปัจจัยเสี่ยงของการเกิดภาวะกล้ามเนื้อหัวใจตายในระหว่างและ 72 ชั่วโมงหลังจากการให้ยาระงับความรู้สึกในผู้ใหญ่ที่ได้รับการผ่าตัดที่ไม่ใช่การผ่าตัดหัวใจระหว่าง พ.ศ.2545 – 2547 ในโรงพยาบาลศิริราช

รูปแบบการวิจัย : Case-Control study

วิธีการ : ค้นหาผู้ป่วยที่มีภาวะกล้ามเนื้อหัวใจตายในระยะเวลาที่กำหนดจากบันทึกข้อมูลภาวะแทรกซ้อนทางการให้ยาระงับความรู้สึก และผู้ป่วยที่ได้รับการรักษาในหอผู้ป่วยหนักของภาควิชาวิสัญญีวิทยาจำนวนทั้งหมด 74 ราย เลือกกลุ่มควบคุมโดยให้เป็นผู้ป่วยเพศเดียวกับ case ได้รับการผ่าตัดที่มีอัตราเสี่ยงต่อการเกิดภาวะกล้ามเนื้อหัวใจตายเท่ากัน และได้รับการผ่าตัดในปีเดียวกัน จำนวน 222 ราย ทำการวิเคราะห์ปัจจัยเสี่ยงได้แก่ ภาวะโรคทางระบบหัวใจและหลอดเลือด อายุที่มากกว่า 55 ปี ความรีบด่วนของการผ่าตัด ASA – Classification และระยะเวลาที่ใช้ในการผ่าตัด

ผลการวิจัย : ผู้ป่วยที่เกิดภาวะกล้ามเนื้อหัวใจตายในระหว่างและหลังผ่าตัดมีอายุมากกว่า ASA Classification สูงกว่า มีโรคทางระบบหัวใจและหลอดเลือด ได้รับการผ่าตัดเป็นกรณีรีบด่วนมากกว่า และใช้เวลาในการผ่าตัดนานกว่าผู้ป่วยกลุ่มที่ไม่มีภาวะกล้ามเนื้อหัวใจตายอย่างมีนัยสำคัญทางสถิติ ($P < 0.05$) เมื่อศึกษาปัจจัยเสี่ยงโดยอาศัย multiple logistic regression พบว่าระยะเวลาการผ่าตัดที่นานขึ้นเพิ่มอัตราเสี่ยงต่อการเกิดภาวะกล้ามเนื้อหัวใจตาย (Adjusted OR เพิ่มจาก 2.95 เป็น 5.23)

สรุป : จากการศึกษาแสดงว่าระยะเวลาที่ใช้ในการผ่าตัดที่มากขึ้นทุก ๆ 90 นาที มีความเสี่ยงต่อการเกิดภาวะกล้ามเนื้อหัวใจตายในระหว่างและหลังการผ่าตัดเพิ่มขึ้น

สาขาวิชา การพัฒนาสุขภาพ ลายมือชื่อนิสิต.....

ปีการศึกษา 2547 ลายมือชื่ออาจารย์ที่ปรึกษา.....

ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

##467-5006930 : MAJOR HEALTH DEVELOPMENT

KEY WORDS: Anesthesia: audit / Complication/ Cardiovascular/ Myocardial infarction/ Non-cardiac operation/ Perioperative/ Case-control

Thitima Chinachoti: RISK FACTORS OF PERI-OPERATIVE MYOCARDIAL INFARCTION IN ADULT NON-CARDIAC OPERATIONS, 2002-2004; A CASE-CONTROL STUDY. Thesis Advisor: Associate Professor Oranuch Kyokong, Thesis Co-advisor: Professor Shusee Visalyaputra. 55 pp. ISBN 974-53-1128-6

Background: Eventhough an international standard of preoperative risk assessment of cardiac events in perioperative period has been implemented at Siriraj Hospital, there were still reports of peri-operative myocardial infarction, about 20 – 30 cases a year. We would like to identify preventable and modifiable risk factors. *Objective*: To determine the risk factors of peri-operative myocardial infarction in adult non – cardiac operations during 2002 – 2004 at Siriraj Hospital. *Study design*: A Case – control study. *Material and Methods*: Seventy-four cases of peri-operative myocardial infarction were matched with 222 cases of control cases (ratio 1:3) on the basis of same sex, same operational risks and the same year of operation. The underlying cardiovascular disease, age of more than 55 years, emergency operations, ASA-classification and the duration of anesthesia for more than 90 minutes were compared between cases and controls. The crude odds ratio and adjusted odds ratio were analyzed by multiple logistic regressions. *Result*: The patients who developed peri-operative myocardial infarction were older, in a higher ASA-classification, were operated on in emergency situations, had more underlying cardiovascular diseases and were operated on for a longer time. An increasing duration of anesthesia every 90 minutes would progressively increase the risk of peri-operative myocardial infarction (adjusted odds ratio increased from 2.95 to 5.23). *Conclusion*: All parameters of underlying cardiovascular diseases, age, ASA-classification and emergency operations increased the risk of peri-operative myocardial infarction, the same as in other studies. From this study, we demonstrated that increasing the anesthetic duration every 90 minutes also increased the risk of peri-operative myocardial infarction.

Field of study Health Development Student's signature……

Academic year 2004 Advisor's signature……

Co-advisor's signature……

ACKNOWLEDGEMENTS

This course was supported by the Faculty of Medicine, Siriraj Hospital.

I would like to express my gratitude to my advisor and co-advisor, Associate Professor Oranuch Kyokong and Professor Shusee Visalyaputra, for their supervision, instruction and support during the whole process of finishing this thesis and to all staff members of the Thai CERTC Consortium, who were all helpful and responsive during my study period.

I appreciate and would like to pay respect to all instructors in the biostatistics section, both internal and external, for their responsible help. I personally would like to say big thanks to Dr. Chulaluk Komoltri for her willingness and extra time in lecturing and statistical consultation.

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CHAPTER 1

INTRODUCTION

RATIONALE AND BACKGROUND

The continuous increase in Thai life expectancy leads to a greater prevalence of cardiovascular disease in non-cardiac surgical patients. Patients with silent or undiagnosed cardiovascular disease are therefore exposed to anesthesia service more often. Even though preoperative cardiac evaluations by cardiologists were routinely performed, many elective and urgent non-cardiac surgical operations were complicated by serious cardiovascular events, such as myocardial infarction, heart failure, cardiac arrest and death. It is very difficult to explain to a patient's family why these serious outcomes still happen in elective non-cardiac surgery.

Since 2002, the guidelines for preoperative cardiovascular evaluation for noncardiac surgery by the American College of Cardiology (ACC) and the American Heart Association (AHA) have been widely used. But the occurrences of unexplained serious cardiovascular events were regularly reported in the Siriraj Anesthesia auditing system. Since 2001, the specific cardiac enzyme essay, Troponin-T, was available at Siriraj Hospital and led to identify causes of hemodynamic unstability in the peri-operative period. We have usually used Troponin-T as an indicator of myocardial infarction. In 2002, from a prospective peri-operative data collection in the auditing system, 25 cases of myocardial ischemia or infarction with 5 deaths from total of 23531 (0.1%) cases in anesthetic service were reported. At the end of each year, a reevaluation of patients who died within 72 hours after anesthesia was performed to complete the anesthesia data base system. Each year we could identify two to three patients who developed acute myocardial infarction 48-72 hours after an operation.

The incidences of peri-operative myocardial infarction in Siriraj Hospital were 0.12 and 0.13% of cases-mixed in 2002 and 2003, respectively. Even though the incidence was much lower than the prediction of the guidelines, some of them were

categorized as unacceptable for quality accreditation, such as two patients who were at low risk by the standard guidelines. Both of them suffered from extensive acute myocardial infarction and died after low risk operations.

With the separation of the peri-operative period into three parts, preoperative, intraoperative and postoperative, the potential risk factors can be grouped and divided into modifiable and non-modifiable. The quality process usually improve the outcomes by modification of the modifiable risk factors. The preoperative period has been most extensively studied for potential historical and diagnostic test predictors of the outcome in patients undergoing non-cardiac surgery. Most of the preoperative predictor risk factors were non-modifiable such as sex, age, underlying disease, etc.

However, the intraoperative factors also appear to affect outcome substantially and are sometime independent of the disease state. During anesthesia, the key success to myocardial protection was to balance myocardial oxygen demand and supply via control of hemodynamic parameters or trying to keep heart rate, blood pressure and cardiac output within a limited acceptable range in each individual patient. Not only anesthetic drugs and techniques but also the intensity of operative procedure affects hemodynamic parameters. Increasing the duration of an operation could easily decrease a patient's body temperature and cause shivering in the peri-operative period which subsequently increases cardiac oxygen demand. Early detection of myocardial ischemia by means of ST segment change, the decision to treat and solved hemodynamic problems and the balance of cardiac oxygen demand and supply as soon as possible were the most importance steps in anesthesia practice because the shorter the duration of ischemic process, the lower the chance of permanent damage or myocardial infarction.

It was not only the patient's condition but also conducting procedure, both anesthesia and operation, that increased the risk of peri-operative myocardial infarction. So we wanted to systematically analyze the risk factors for these adverse events which would lead to a modification of the anesthetic process in the quality improvement process.

Review of literature

Estimated incidence of perioperative cardiac morbidity for non-cardiac surgery is difficult and varies from one study to another (1) because of a variety of study designs and diagnostic criteria of adverse cardiac events (2, 3, and 4). Most quality studies did not report the causes of adverse outcomes. They reported something else such as unstable hemodynamic or arrhythmia. Even though some of them suggested myocardial infarction (4), they still reported some other events that should be considered as associated with myocardial infarction such as heart failure, hypotension or cardiac arrest. This is primarily due to how they count the events or cases. So there needs to be detailed qualitative studies of each suspected case to identify predisposing and attributive causes of peri-operative myocardial ischemia or infarction.

In 1972 Tarhan S, et al (5) reported cases of myocardial infarction after general anesthesia. He was the first who suggested that it would be better to wait for at least 6 months after acute myocardial infarction before performing elective surgery. Even though the incidence rate of reinfarction was unacceptably high, previous myocardial infarction was the major risk of cardiac morbidity. Multiple studies (6, 7, 8, 9, and 10) found other risk factors such as age, previous diagnosis of coronary artery disease, symptoms of ischemia and diagnostic test for coronary artery disease. This came out with the Goldman cardiac risk in 1977 (8).

In 1990, Mangono DT (11) reviewed what was going on to reduce perioperative cardiac morbidity. A special preoperative test which includes exercise stress testing, radionuclear and dipyridamole thallium imaging were recommended for determining cardiac risk. But all tests had a lot of false positives and false negatives together with the increasing cost of medical care.

Not only has the preoperative cardiac risk index contributed to peri-operative cardiac morbidity; the balance between myocardial oxygen demand and supply could easily become unbalanced during anesthesia and stressful operative procedure (1). There were a lot of studies about how to reduce perioperative myocardial infarction in

coronary artery bypass graft (CABG). In addition, more advanced technology such as intraoperative transesophageal echocardiography (TEE) was recommended for early detection of ischemia (1). Because of the need of expertise in evaluating the TEE monitor in Thailand, TEE was still not routinely used in CABG.

During 1990-1998, there were several studies done to demonstrate pattern of myocardial ischemia in patients with coronary artery disease and silent ischemia in relation to type of operation(12, 13, 14), intra-operative hemodynamic changes (15, 16) arrhythmia (17) and anesthetic drugs(18). All studies were prospective cohorts in particular groups of patients who might or might not develop ischemic pattern. And because they were in specially selected groups, all other factors were systematically controlled by the study design. The conclusion was limited to some special conditions such as type of operation and some special anesthetic agents in specific group of patients. In the real situation of anesthetic auditing system (1-4) there were still a lot of patients who had never been diagnosed with coronary artery disease; usually they had non-specific symptoms, non-specific electrocardiography but developed acute myocardial ischemia or infarction in the peri-operative period.

Until 1998, Howell, et al (3) did a case control study of cardiovascular death within 30 days after operation from the Oxford Record Linkage Study (ORLS) which covered 1.9 million people. They identified three risk factors which were myocardial infarction, history of hypertension and renal failure. The other study revealed some relationship of structural heart disease (19), silent myocardial ischemia(20) and emergency surgery(21) to postoperative cardiovascular complication.

In 1996; the American College of Cardiology (ACC) and American Heart Association (AHA) published guidelines and an associated seven steps for preoperative cardiovascular evaluation of patients undergoing non-cardiac surgery (22). This guideline was tested for the ability of prediction (23). They concluded that, by their retrospective study, the predictor score performed extremely well with cardiac outcome and adverse events related more to the medical condition and not the surgical type. But this guideline opens a lot to justification by clinicians such as how long the surgery

should be delayed after introducing cardiac medication to optimize patients' cardiac conditions. Even though the guidelines try to introduce the type of operation to be weighted for the evaluation process, it was too crude to be useful. The guidelines were not based on good research designs; most of them were observational or retrospective studies about the knowledge of cardiovascular management in non-operative setting. The guidelines were subsequently reviewed, more details were added and they were published in 2002 (24).

Intra-operative early detection of myocardial ischemia is the key to success in shortening the duration of ischemia and prevents permanent infarction (25-28). The cardiac Troponin was introduced for intra-operative investigation (29-31) not only for diagnostic tests but also for the prediction of outcomes. These antibody essay studies (cTroponinI and cTroponinT) were confirmed by many trials (25-28) that they were sensitive and more specific to myocardial injury than CK-MB. A qualitative result could be provided within a few minutes with a well-validation bed-side test, making diagnosis in particular settings (i.e., emergency room, operative theaters) possible without involving of the central laboratory and thus allowing for more rapid clinical decisions.

The evaluation of cardiac Troponin level could be quantitative measurement by antibody bioassay within six hours after injury. The initial level of cardiac TroponinT should be more than 5-8 % of the normal range. The level needed to reach 0.1 ng/ml for the confirmation of myocardial infarction.

CHAPTER 2

RESEARCH DESIGN

Research Questions

Primary research question: Is there an association between peri-operative myocardial infarction and underlying cardiovascular disease, type of anesthesia, emergency situation, ASA physical status, age, and duration of anesthesia during non-cardiac operations at Siriraj Hospital.

Secondary research question: What is the in-hospital mortality rate of peri-operative myocardial infarction during non-cardiac operations at Siriraj Hospital.

Objectives

Primary objective

To evaluate the association between the factors(underlying cardiovascular disease, type of anesthesia, emergency situation, ASA physical status, age and duration of anesthesia) and peri-operative myocardial infarction during non-cardiac operations at Siriraj Hospital.

Secondary objective

To study the in-hospital mortality among patients with peri-operative myocardial infarction during non-cardiac operations at Siriraj Hospital.

Research Hypothesis

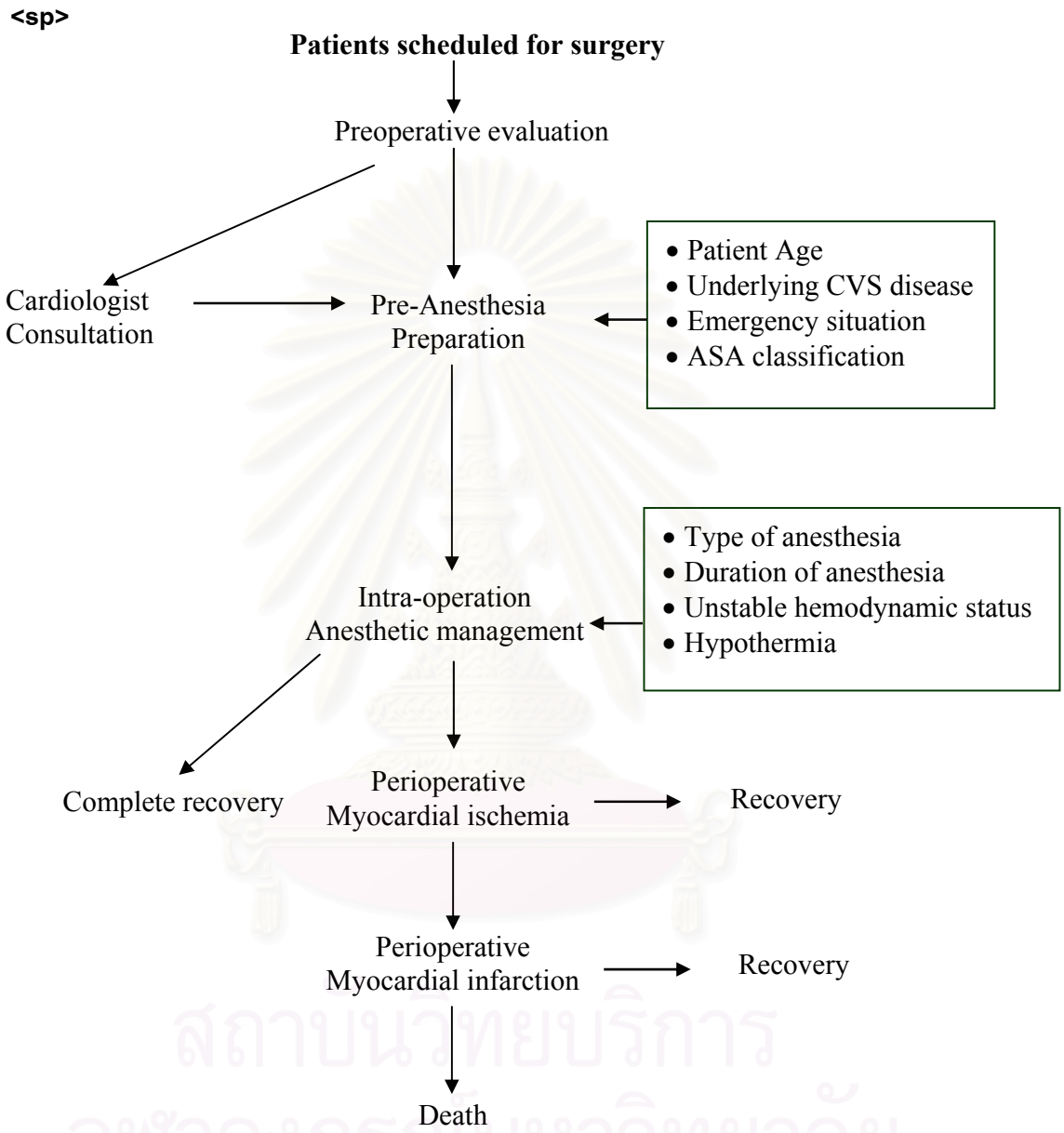
Research hypothesis

Potential risk factors (underlying cardiovascular disease, type of anesthesia, emergency situation, ASA physical status, age, and duration of anesthesia) are associated with the occurrence of per-ioperative myocardial infarction.

Statistical hypothesis

Patients with factors such as underlying cardiovascular disease, emergency situation, higher ASA physical status, old age, and longer duration of anesthesia have a higher chance of developing peri-operative myocardial infarction.

Figure 2.1 Conceptual framework



Operational definition

Perioperative period

The peri-operative period is the period of time from the beginning of anesthesia until 72 hours after the end of the operation.

Duration of anesthesia

Duration of anesthesia is the period of time from the beginning of anesthesia service until the patient is transferred from the operating theater to the recovery room or ICU.

Beginning of anesthesia is the time when the first hemodynamic data were recorded in the anesthetic record form.

End of anesthesia is the time when the last hemodynamic data were recorded in the anesthetic record form.

"Unstable hemodynamic parameters" is the anesthetic record that displayed one of these two situations

1. The decrease of systolic blood pressure lower than 30% of the baseline before anesthesia for more than 15 minutes.
2. The decrease of systolic blood pressure lower than 20% of the control for more than 10 minutes and after specific treatment, such as vasoconstrictor, when the response was not sustainable. The blood pressure was reduced to the level of less than 20% of control again.

CHAPTER 3

RESEARCH METHODOLOGY

Research design

This study has been carried out as a case-control study.

Research methodology

Study population

Patients aged more than 35 years who had non-cardiac operations during 2002-2004 at Siriraj Hospital.

Sample

Case: All patients who met the criteria of new myocardial infarction from the anesthetic audit chart system.

Control: "Controls" were non- myocardial infarction patients of the same sex, year and group of operation according to ACC-AHA guidelines as cases. For each case, three controls were selected from the hospital database. The entire medical records of these control patients were then reviewed by inclusion and exclusion criteria of "control". The first three controls that fulfilled these criteria were included as controls.

Inclusion and Exclusion Criteria

Case*:* Patients who developed new myocardial infarction during an operation or within 72 hours after an operation. "***New infarction****"* was diagnosed if patients satisfied two of the four criteria:

1. ST segment elevation at least 3 mm or ST segment depression at least 2 mm for more than one minute.
2. Serum Troponin-T elevation or more than 0.1 ng /ml.
3. New Q wave.

4. Unstable hemodynamic parameters which could not be explained by other causes such as massive blood loss, sepsis and a high level of central blockage

Control: The patients who underwent the same group of operations in the same year and did not have any suspected evidence of myocardial infarction including

No report of intra and postoperative ST-T change.

No unstable hemodynamic parameters

No evidence of unplanned ICU admission.

No evidence of intravenous nitroglycerine before, during and after the operation.

No report of suspected myocardial ischemia.

Sample size estimation

Since several factors were associated with the development of myocardial infarction, a multivariate analysis, i.e., multiple logistic regression analysis, was used to assess the effect of each factor, adjusting for other factors. According to the rule of thumb for multiple logistic regressions, the number of cases should be roughly 5 to 10 times the number of predictors in the multiple logistic models, with the expected number of significant predictors for myocardial infarction of 6 variables and 7 factors (the ASA classification was divided into three groups, so two dummy variables were needed in the logistic model and one factor was added in the sample size calculation):

1. Presence of cardiovascular disease diagnosed before the operation (yes, no)
2. Type of anesthesia (regional, general).
3. Emergency (yes, no).
4. ASA classification (1 - 2, 3, > 3)
5. Patient age (35 to 55, > 55 year)
6. Duration of anesthesia ($\leq$ 1.5 hrs. > 1.5 hrs.)

The number of myocardial infarction cases was about 35-70 which is (5-10)* 7.

Since the ratio of cases to controls in this study was 1:3, a sample of 70 myocardial infarction cases and 210 non-myocardial infarction controls were recruited.

Data collection

Cases

1. Medical records of all cases in the anesthesia audit system, reporting myocardial infarction, myocardial ischemia, unstable hemodynamic, death and unplanned ICU admission, were reviewed for specific causes of those events and outcomes.

2. If the case met the criteria for operational definition. The Troponin-T level was the strongest to confirm criteria for myocardial infarction.

3. Every case that was admitted to the surgical ICU for more than 2 days from 2002 to 2004 was reviewed.

4. Two cardiologists who were the investigator team reviewed all medical records independently to confirm the events of myocardial infarction. If any disagreement happened, an open discussion took place in a group with others. Only those cases with consensus were collected as “case” in this study.

Controls

1. The data from the hospital data system were extracted for every patient who underwent an operation at Siriraj Hospital during three years of the study period and 40,000 cases were obtained each year. Data for each case included patient’s name and identification number, patient’s demographic data, date of operation, surgical unit, operation and ICD-CM code, status of discharge and date of admission and discharge.

2. The data were sorted by surgical unit. Only data from surgical units with previously selected cases of perioperative myocardial infarction were selected. The operation included general surgery, orthopedics, urology, neuro surgery and head and neck operation.

3. Patients below 35 years were excluded.

4. Five records with the same operation, sex and year of operation in each case were selected as controls. All medical records were retrieved from the center of medical records.

5. Each medical record was reviewed for inclusion and exclusion criteria of controls. The first three records that matched with each case were chosen as controls.

6. If the matching operation was impossible, the groups of operation codings by guidelines were used instead of the same operation.

All data of cases and controls were transcribed in case record forms and reference numbers were used instead of name and hospital number. Entire medical records of all cases and controls were reviewed for the events, management and outcomes including after discharge from the hospital follow up.

Measurement

All of the measured variables were recorded in the case record form (Appendix) including;

Demographic data, baseline characteristics:

- Age (years)
- Gender
- Weight (kg)
- Height (cm)
- Baseline heart rate and blood pressure
- Type of operation
- Operation

Preoperative data

- ASA classification
- Emergency or urgency or elective operation
- Underlying diseases or conditions at risk
    - Diabetic mellitus and level of control
    - Obesity level according to body mass index
- Underlying cardiovascular disease
    - Hypertension

- Ischemic heart disease
- Valvular heart disease
- Congestive heart failure

- Preoperative medication
- Preoperative physical condition
  - Normal activity (Met-level)
  - Functional fitness
- Preoperative investigation
  - 12 lead EKG
  - Electrolyte
  - BUN, creatinine
  - Liver function test
  - Hemoglobin, Hematocrit
  - Preoperative ischemic pattern
  - History or diagnosis of myocardial infarction and duration before this procedure.
  - Exercise-tolerance
  - Preoperative coronary angiography
  - Preoperative coronary bypass graft
  - Arrhythmia

Intra-operative data

- Type of anesthesia
- Duration of anesthesia (min)
- Hemodynamic parameters

  EKG signal change

  Drugs used for myocardial protection: nitroglycerine, beta-blocker, dopamine, dobutamine and other vasopressor.

ICU admission

Planned or unplanned

Duration of ICU admission

Troponin-T level and serial follow up.

Drugs used for myocardial protection.

Specific treatment for myocardial injury.

Outcome measurement

Primary outcome

- Perioperative myocardial infarction.

Secondary outcomes

- Underlying cardiovascular disease
- Type of anesthesia (general, regional)
- Emergency or elective procedure
- Age
- ASA-classification.
- Duration of anesthesia
- Days in intensive care and in hospital.
- Final case discharge status as full recovery, permanent damage or death.

Data analysis

General consideration

The statistical analysis focused on the detection of significant differences between the peri-operative myocardial infarction and the non-myocardial infarction groups with respect to age, ASA-classification, underlying cardiovascular condition or disease, emergency situation, type of anesthesia and duration of anesthesia.

Data analysis

Data from case record forms were stored and examined for errors and inconsistencies.

For univariable analysis, the unpaired t-test was employed for comparison of quantitative variables that were normally distributed, such as duration of anesthesia, age, between patients with and without myocardial infarction. For data that did not satisfy the normality assumptions, the non-parametric method (i.e., Mann-Whitney U test) was performed.

Chi-square test was used to compare qualitative variables, e.g., ASA-classification and emergency situation between cases and controls. The crude odds ratio and its 95% CI were reported.

For multivariable analysis, a multiple logistic regression was employed to determine the effect of each risk factor on myocardial infarction after having been simultaneously adjusted for other risk factors in the model. The adjusted odds ratio, along with its 95%CI and p-value, were reported.

All data analyses were performed using SPSS version 11.5

Ethical consideration

This study was a retrospective medical records reviewed. There was no need to make any direct contact between the investigative team and the patients. But the name and personal detail of both cases and controls were exposed to some member of the investigative team. So we tried to limit the degree of exposure to assure confidentiality. Both the director of the Anesthesiology department and the Siriraj Ethical Committee reviewed and approved this study.

Limitations

This study was retrospective study even the process of cases collection were routine regularly report follow the department policy. There were some variables that could not retrieved in standard medical record system such as patients' body temperature intra-

operation and immediate postoperative. Not every patient was evaluated by cardiologist and the activity evaluation was not available. The problem was solved by using physical fitness evaluation that were regularly perform and recorded in anesthetic record.

There were so many factors related to peri-operative myocardial infarction and the incidence was very low. The total number of the patients was critical for reliability of the multiple logistic models. Limitation of studied variables was thoughtful before and this was the reason while sex of the patient was used in matching process and this factor could not be proved in this study.

The study started matching by using three match factors (sex, operative year and operation group). The same year of operation between case and control was used to limit environment of medical care which include residents, process of hospital accreditation and person involved in hospital setting. At the beginning, we started by using operation group code by AHA and found that the range of intermediated risk was wide. Appendectomy was in the same group of colectomy and all orthopedics operations were categorized in the same risk. So we modified matching technique by searched control by the same operation of cases as much as possible and if it was not possible after retrieved more than 20 of medical records, the group of operation was used in stead.

Implications

If preventable or modifiable risk factors could be identified, the improvement of service would be done by minimizing those specific risk factors. For example, the possibility to reduce anesthetic time would be carried out by an allocation of more qualified teams both in anesthesia and surgery.

CHAPTER 4

RESULT OF THE STUDY

Selection of cases and controls

During 2002 to 2004 at Siriraj Hospital, a total of 87 cases were identified for perioperative myocardial infarction by at least two out of four criteria for cases. Ten cases were excluded since the operation involved aorta i.e., root, ascending, descending and abdominal aorta. The other three cases were excluded due to disagreement in diagnosis of myocardial infarction. Only 74 cases of perioperative myocardial infarction (MI-group) were then eligible for further analysis and matching process.

To select controls, 5 controls were chosen for each case using hospital database. These 5 controls were matched to case by year of operation, gender and ICD code for procedure. Since only 3 controls were needed for each case, the first three controls that had exactly the same operation as case were recruited as non-MI controls. However, some cases did not had the exactly the same operation as case. Thus, for MI cases that had no controls with the same operation. Controls with the same group of operation were selected instead. Among 222 records which were chosen as “control or non myocardial infarction group”; only 152 (68.5%) controls that matched by the same operation as the cases and the others were matched by the same group of operation risk.

Myocardial infarction patients

Demographic and patient characteristics

During 2002-2004, 74 patients developed peri-operative myocardial infarction at Siriraj Hospital. Forty three (58.1%) of them were male. Age varied from 36 to 92 years with mean value and standard deviation of 65.27 $\pm$ 12.0 years. Fifty seven (77%) of them were older than 55 years. Forty cases (54.1%) were operated in the surgical unit of general surgery, 16(21.6%) orthopedics, 7(9.5%) ENT and 11(24.8%) others. The two most common operations were open cholecystectomy and total hip replacement (Table 6.1).

The details of demographic data and clinical characteristics of perioperative myocardial infarction patients were displayed in Tables 6.1 and 6.4. Only 10 patients were classified in ASA classification of I while the others were suffered from at least one disease or medical condition. Thirty two (43.2%) were classified in ASA classification of 3 or they had at least one organ failure or uncontrolled medical condition. Seven patients (9.5%) were classified in ASA classification of 4 with more than one organ failure. About one third of per-ioperative myocardial infarction patients were operated in emergency surgical conditions.

The two most common underlying diseases were hypertension (56.8%) and diabetes mellitus (40.5%). Among 42 hypertensive patients or only 47.6% had a good control of their blood pressure (Table 6.1). Twenty one (28.4%) patients had underlying diagnosis of ischemic heart disease before operation and among them 10 (47.6%) had a well medical control and most of them also had hypertension. Only three patients had unstable angina whereas five patients had old myocardial infarction prior to operation. The total number of patients with underlying cardiovascular disease was 45 (60.8 %). Only 31 (41.9%) patients had normal functional activity whereas the others had limited activity of class 2 and 3.

Clinical courses

The episodes of myocardial infarction happened during intraoperative period in 35 (47.3%) patients in which 11(31.4%) started immediately after induction of anesthesia (Table 6.2). Twenty-two (29.7%) patients had myocardial infarction within two hours after operation and the patients were under close monitoring at recovery room or intensive care unit. The last group included 17 (23.0%) patients in which the process of myocardial infarction started during 2 to 72 hours after operation. Anesthetic technique or anesthetic decisions were responsible for or associated with the episodes of myocardial infarction in 38 (51.4%) patients.

The three most common physiological reactions which were caused by anesthesia and could lead to myocardial infarction were hypoxia, unstable hemodynamic response to anesthetic overdose during induction period and sympathetic reaction to reintubation process. The decision to extubation at the end of operation was recorded as improper decision making if the reintubation was performed within two hours after extubation.

The episodes of acute myocardial infarction were started as early as during induction of anesthesia and mostly were related to anesthesia. Two cases had severe hypotension and bradycardia occurred during upper airway procedure under which local anesthetic agents were used and anesthesia team were not involved at the beginning of these cases. Three patients with ischemic heart disease had severe hypotension after induction and intubation and the operation were therefore cancelled due to myocardial injury. Three cases were suffered from unexpectedly difficult intubation with pulmonary aspiration in one case. All of them had EKG change after successful intubation. The last three cases had severe hypotensive response to regional block (2 spinal, 1 epidural). A 92-year-old man was scheduled for dynamic hip screw under continuous epidural block. He rapidly developed severe hypotension after administration of 15 ml of 2% Xylocaine via the epidural catheter. The resuscitation was performed unsuccessfully and the patient died without operation.

During two hours after operation, twenty two patients developed acute myocardial infarction which occurred either in the recovery room or intensive care unit. These were related to hypoxia and hypoventilation. Severe hypotension with ST-T change suddenly happened after specific airway manipulation, especially reintubation. Only four patients complained about severe chest pain without respiratory events.

Seventeen patients developed acute myocardial infarction during 2-72 hours after operation. Eleven patients were admitted at ordinary ward. Three patients who had (30.8%) inguinal hernia repair or trans-urethral resection of prostrate gland (TURP) died within 2 hour after the episode of acute myocardial infarction. These two operations have been categorized in low surgical risk according to AHA guidelines. Most of the patients in this group, the myocardial infarction occurred spontaneously without specific stimulated conditions.

Tachycardia, anemia, hypoxia, acidosis, pain and hypothermia were the six most common precipitating factors occurred before the episode of myocardial infarction (Table 6.2). Only 17 cases (23.0%) that myocardial infarction occurred spontaneously with proper all medical care. Others were related to anesthesia, surgery and general nursing care.

Outcomes of myocardial infarction

Four patients in this series were sent for emergency coronary angiography within one hour after diagnosis of myocardial infarction and two of them were treated successfully by coronary dilatation. The others were sent for emergency coronary by pass graft and one case was successful but the last died seven days after operation.

Nineteen patients (25.7%) died and 17 of them primarily due to myocardial infarction which included 4 sudden deaths (died within 2 hours after episode). The causes of deaths for the other 2 cases were severe infection and septicemia. Eight patients who still alive, suffered from secondary effect including complete cord transactions (3 cases) and brain death (5 cases).

There were eleven patients that developed acute myocardial infarction at ordinary ward and four of them died (Table 6.2). If the outcomes divided into full recovery and serious complication (permanent damage and death from acute myocardial infarction) and stratified by medical service areas (Table 6.3). The full recovery rate was lowest when acute myocardial infarction occurred at an ordinary ward. Even though many patients developed myocardial infarction in operating theater and recovery room area and half of them were related to anesthesia, their final outcomes were better than those who occurred at ward.

Case-control study

Demographic and patient characteristics

All controls or non MI patients were matched to cases by gender, year of operation and group of operation (68.5% were in the same operative procedure as cases). For both cases and controls, 41.9% were female. Controls were about five years younger than cases (mean $\pm$ SD of 59.1 $\pm$ 9.67 vs. 65.27 $\pm$ 12.01, $p<0.001$). Sixty two percent of non MI patients and seventy seven percent of MI group were older than fifty five year (Table 6.4). Only height, weight and body mass index of both group were comparable. MI-group had more underlying diseases i.e., hypertension, diabetes mellitus, and ischemic heart diseases than non MI-group and higher pre-anesthetic systolic and diastolic blood pressures. MI-group had the operation under general anesthesia more frequently than non MI-group (78.4% vs. 62.2%). The technique of

combined general anesthesia with continuous epidural block was used more often in the non-MI group (12.6% vs. 8.1%). The anesthetic techniques were then categorized into 3 groups ie, general, regional anesthesia and combined general and regional anesthesia.

Seven patients in MI-group were classified by ASA classification of class 4 compared to none in non-MI group (Table 6.1). Prior categorization of ASA classification into 3 groups of (1,2), 3 and >3 was changed to 2 groups of (1,2) and >2 due to a small number of patients in ASA class 4.

The duration of anesthesia between the two groups was both clinically and statistically significant difference. Only 10.8% of patients in MI-group that their operations were finished within 90 minutes compared to as high as 24.3% for the non-MI group (Table 6.4). Most patients were operated within the duration of 91 to 180 minutes. By stratifying the duration of anesthesia into less than 90 minutes, 91-180minutes and more than 180 minutes, the duration of anesthesia became statistically significant when compared between the MI and non MI groups.

Factors associated with perioperative myocardial infarction

When each variable was considered alone as in a univariable analysis (Table 6.4), it was found that ASA classification of more than 2, underlying diabetes mellitus and emergency situation were strongly associated with peri-operative myocardial infarction with the crude odds ratios of greater than 5. The crude odds ratios for ASA classification more than 2 and emergency situation were 7.13(3.93, 12.95) and 6.93(3.49, 13.74) respectively. The MI group had more underlying diabetes mellitus (40.1%) than non-MI group (9.9%), with crude odds ratio for DM of 6.20(3.27, 11.75). Similar finding was found for underlying cardiovascular disease with odds ratio of 3.16(1.83, 5.45).

Regarding patient's age, it was found that patients aged >55 years had 2 times higher chance of developing peri-operative myocardial infarction compared to those aged $\leq$ 55 years (OR= 2.04, 90%CI = 1.11, 3.74).For type of anesthesia, use of both RA and GA increased the risk of peri-operative myocardial infarction to 1.20(0.40, 3.64) compared to RA whereas for GA alone was as high as 2.35(1.10, 4.90).

Increased duration of anesthesia from 90 to 180 and more than 180 minutes were associated with significantly increased risk of myocardial infarction. The crude

odds ratio was step up from 2.33(1.02, 5.36) to 3.21(1.35, 7.62) for duration of anesthesia of 91-180 and >180 minutes respectively.

Multiple logistic regressions

According to the plan for statistical data analysis mentioned in the proposal, six variables would be included in a multiple logistic model i.e., age (≤55, >55 years), ASA classification (1-2, 3, >3), underlying cardiovascular disease (no, yes), emergency surgery (no, yes), type of anesthesia (RA, GA) and duration of surgery (≤ 90, >90 minutes). However, after data collection it appeared that some categories of these variables had fewer subjects whereas some had more subjects than expected. Thus, some changes were made. That is, ASA classification would have only two groups (1-2, >2), type of anesthesia with 3 groups (RA alone, GA alone, combined RA and GA), and duration of surgery with 3 groups (≤90, 91-180, >180 minutes). Furthermore, one more predictor was added i.e., underlying DM. In summary, a new multiple logistic regression model would have 7 predictors or 9 independent (dummy) variables compared to only 6 predictors or 7 independent variables as planned in the proposal. Therefore, the calculated sample size of 70 MI cases (7*number of dummy variables in a logistic model) would not be enough for a new multiple logistic model. This resulted in a wide 95% confidence interval of adjusted odds ratio from a new logistic model.

Taking into account all predictors simultaneously as in a multiple logistic regression analysis revealed that the adjusted odds ratios for all predictors were in good agreement with the crude odds ratio, but with wider 95% confidence interval due to insufficient number of subjects.

Patients aged more than 55 years old had 2.55 times risk of developing perioperative MI (95% CI = 1.13, 5.79) compared to those aged less than 55. Having underlying CVS, DM increased the risk of MI to 3.40 (95% CI = 1.67, 6.94) and 4.58 (95% CI = 2.09, 10.01) respectively. Patients with ASA classification of class 3 or higher had 4.49 (95% CI = 2.15, 9.37) times risk of developing perioperative MI compared to those with ASA class of 1, 2. Emergency surgery was the strongest predictor for perioperative MI with adjusted OR of 9.78 (95% CI = 3.64, 26.27).

Regarding type of anesthesia, use of both RA and GA did not increase risk of having perioperative MI compared to RA alone with the adjusted OR of 0.60 (95% CI = 0.16, 2.24). Similarly, use of GA alone was not statistically associated with MI development with the adjusted OR of 1.39 (95% CI = 0.53, 3.65). Duration of surgery

played an important role in perioperative MI development. That is, risk of MI increased statistically significant as duration of surgery increased. Patients undergoing surgery for 91-180 and longer than 180 minutes had 3.16 (95% CI = 1.12, 8.94) and 5.37 (95% CI = 1.75, 16.51) times risk of MI compared to those having surgery within 90 minutes.

Table 6.1 Characteristics and underlying conditions of 74 patients with perioperative myocardial infarction

Characteristics	Number (%)	Remark
Unit of service		
General surgery	40 (54.1%)	14 cases of open Cholecystectomy
Orthopedics	16 (21.6%)	7 cases of total hip replacement
ENT	7 (9.5%)	
Urology	5 (6.6%)	
Neurology	3 (4.1%)	3 cases of spine operation
Other	3 (4.1%)	
Gender		
Male	43 (58.1%)	
Female	31 (41.9%)	
ASA classification		
1	10 (13.5%)	
2	25 (33.8%)	
3	32 (43.2%)	
4	7 (9.5%)	
Emergency : Yes	27 (36.5%)	
Underlying DM : Yes	30 (40.5%)	
Well control	21 (70%)	
Moderate control	8 (26.7%)	
Poor control	1 (3.3%)	
Underlying CVS : Yes	45 (60.8%)	
Underlying Hypertension : Yes	42 (56.8%)	
Well control	20 (47.6%)	
Moderate control	16 (38.1%)	
Poor control	6 (14.3%)	
Ischemic heart disease: Yes	21 (28.4%)	
Well control	10 (47.6%)	
Moderate control	8 (38.1%)	
Poor control	3 (14.3%)	
Ischemic symptom: Yes	12 (16.2%)	
≤once a month	11 (91.7%)	
> once a month	1 (8.3%)	
Post myocardial infarction :Yes	5 (6.8%)	
Only by EKG	4 (80%)	
EKG plus symptom	1 (20%)	
Functional activity classification		
1	31 (41.9%)	
2	33 (44.6%)	
3	10 (13.5%)	

Table 6.2 Clinical courses and outcomes of 74 patients with perioperative myocardial infarction

	Number (%)	Remark
First episode of infarction		
Intraoperation	35 (47.3%)	
Induction	11	Overdose of induction agents 3 cases Difficult airway/aspiration 3 cases Local anesthetic overdose 3 cases
Maintenance	24	Problem with airway equipment 3 cases Under replacement 4 cases Light anesthesia 3 cases Prolonged hypotension 2 cases Immediate reintubation after extubation due to rapid conscious change 2 cases
Within 2 hours post operation	22 (29.7%)	
At recovery room	13	Reintubation from hypoventilation 4 cases Reintubation from hypotension, acidosis and hypoxia 3 cases Drug overdose 1 case
At ICU	9	Reintubation from hypoventilation 2 cases
72 hours post operation	17 (23%)	
At ward	11	Death 4 cases
At ICU	6	
Confirmed diagnostic of MI		
Chest pain	34 (45.9%)	
EKG change	72 (97.3%)	
Hypotension	58 (78.4%)	
Troponin T (ng/ml) :		
$\geq$ 0.1	61 (82.4%)	
> 0.01 - < 0.1	13 (17.6%)	
Final outcome		
Full recovery	47 (63.5%)	Emergency cardiac intervention 4 cases
Permanent damage	8 (10.8%)	
Death from MI	17 (23.0%)	Sudden death 4 cases
Death from other	2 (2.7%)	
Anesthetic involved	38 (52.7%)	
Hypoxia	19	
Reintubation	12	
Drug overdose	7	
Precipitating factors		
Tachycardia	29 (39.2%)	
Anemia (Hct<28%)	21 (28.4%)	
Hypoxia	19 (25.7%)	
Acidosis	17 (22.9%)	
Pain	15 (20.3%)	
Shivering	9 (12.2%)	

Table 6.3 Final outcomes of perioperative myocardial infarction patients related to medical treatment areas

Place	Number (%)		Total
	Full recovery	Serious complication	
Recovery room	10 (83.3%)	2 (16.7%)	12
Intensive care unit	11 (73.3%)	4 (26.7%)	15
Operative theater	21 (61.8%)	13 (38.2%)	34
Ordinary ward	5 (45.5%)	6 (55.5%)	11
Total	47(65.3%)	25 (34.7%)	72

* Two cases were excluded because their death were not related to myocardial infarction

Table 6.4 Characteristics of controls (non-MI) and cases (MI)

Characteristics	Number(%) or Mean ± SD (Median)		Crude OR (95% CI)	P-value
	Controls (n=222)	Cases (n=74)		
Age(yrs):	59.1± 9.7	65.3 ± 12.0		<0.001
≤ 55	84 (37.8%)	17 (23%)	1	0.023
> 55	138 (62.2%)	57 (77%)	2.04(1.11,3.74)	
Height (cm)	162.2 ± 7.7	161.9 ± 8.8		0.658
Weight(kg)	61.9 ± 7.3	60.0 ± 12.3		0.110
Body mass index(kg/m^2)	23.3 ± 3.2	22.9 ± 4.6		0.469
Gender:				
Male	129 (58.1%)	43 (58.1%)		
Female	93 (41.9%)	31 (41.9%)		
Baseline pressure (mmHg)				
Systolic blood pressure	130.3(14.4%)	140.8(24.7%)		<0.001
Diastolic blood pressure	63.1(8.4%)	79.6(17%)		<0.001
ASA-classification				
1, 2	192 (86.5%)	35 (47.3%)	1	<0.001
>2	30 (13.5%)	39 (52.7%)	7.13 (3.93,12.95)	
Diabetes : Yes	22 (9.9%)	30 (40.1%)	6.20 (3.27,11.75)	<0.001
Hypertension : Yes	43 (19.4%)	42 (56.8%)		<0.001
Ischemic heart disease: Yes	6 (2.7%)	21(28.4%)		<0.001
Underlying CVS : Yes	76 (31.2%)	46 (62.2%)	3.16 (1.83,5.45)	<0.001
Emergency surgery: Yes	17 (7.7%)	27 (36.5%)	6.93 (3.49,13.74)	<0.001
Type of anesthesia:				
RA	56 (25.2%)	10 (13.5%)	1	0.014
RA and GA	28 (12.6%)	6 (8.1%)	1.20 (0.40,3.64)	
GA	138 (62.2%)	58 (78.4%)	2.35 (1.10,4.90)	
Duration of anesthesia (min):	147.3 ± 67.7 (135)	211.6 ± 123.3 (165)		<0.001
≤ 90	54 (24.3%)	8 (10.8%)	1	0.025
91-180	107 (48.2%)	37 (50.0%)	2.33 (1.02,5.36)	
> 180	61 (27.5%)	29 (39.2%)	3.21 (1.35,7.62)	

RA = Spinal or epidural anesthesia, RA and GA = Combined general anesthesia with spinal or epidural blockage, GA = general anesthesia

Table 6.5 Results of multiple logistic regression analysis in comparison with crude analysis

		Univariable analysis	Multivariable analysis	P-value
		Crude OR	Adjusted OR (95% CI)	
Age (yrs): ≥ 55		2.04	2.55 (1.13,5.79)	0.025
Underlying CVS disease : Yes		3.16	3.40 (1.67,6.94)	0.000
Diabetes mellitus : Yes		6.20	4.58 (2.09,10.01)	0.000
ASA > 2		7.13	4.49 (2.15,9.37)	0.000
Emergency : Yes		6.93	9.78 (3.64,26.27)	0.000
Type of anesthesia: RA + GA		1.20	0.60 (0.16,2.24)	0.450
	GA	2.35	1.39 (0.53,3.65)	0.505
Duration (min)	91-180	2.33	3.16 (1.12,8.94)	0.029
	>180	3.21	5.37 (1.75,16.51)	0.003

CHAPTER 5

DISCUSSION

Even the incidence of perioperative myocardial infarction in non-cardiac operation at Siriraj Hospital was not high (0.12 % of case-mixed). But the mortality rate was surprisingly high. In this study we reported 17(23%) deaths caused directly by myocardial infarction which included 4 sudden deaths (occurred within 2 hours after first episode). All sudden deaths were operated in low or intermediate operative risk index according to ACC/AHA 2002 guidelines (24). This study was extended from anesthetic auditing system to identify modifiable risk factors for anesthetic quality improvement.

Duration of anesthesia

This study was the first to show that duration of anesthesia do influences the probability of perioperative myocardial infarction. Increasing duration of anesthesia was a statistically significant independent predictor of perioperative myocardial infraction. Every 90 minutes of increasing duration risk of perioperative myocardial infarction increased accordingly. This result should be emphasized because it has been previously assumed that increasing duration of anesthesia has little effect on anesthetic adverse outcome. Extensive review of perioperative cardiac morbidity by Mangano (1) in 1990 from at least six studies could not concluded that only duration of anesthesia and surgery were independent effect on perioperative cardiac events but the incidence of cardiac events was increased associated with the duration more than three hour(8, 9). In large data base from many countries (2, 3, 4) they could demonstrated the relationship between severe cardiac events with preoperative factors such as patients' age, sex, ASA classification and underlying diseases. But the duration of anesthesia and surgery were not independent predictor for cardiac events compared to special surgical type.

All survey studies identified "major vascular procedures" was an independent risk factor for peri-operative myocardial infarction. The following studies in vascular surgery confirmed that the duration of surgery of more than three hours increased risk of peri-operative cardiac events. But the studies in same operation such as elective hip

arthroplasty (13) and transurethral surgery (14) confirmed the association of preoperative coronary disease and serious adverse cardiac outcome of OR of 3.5(1.3, 9.2) but could not related to duration of anesthesia.

In this study we excluded all major vascular surgery and limited the variability of duration between the surgical procedures by selected “controls” in the same operative procedure and if it was not possible, we used the same group of operative risk. The duration of anesthesia and surgery were variable that not limit to only the effect of type of procedure but they were interfered by other management processes. Like other university hospital that clinical together with practical teaching and training of all specialty which include anesthesia, surgery and nurses in every level were going on together with surgical procedures. Teaching, learning and training process almost always increases operative and anesthetic time both directly and indirectly. Prolong exposure of surgical field and breathing of dry gas from anesthetic breathing system caused rapid decreasing of patients’ core temperature and hypothermia may be the origin of myocardial ischemic process. From this study we could not demonstrated the effect of hypothermia directly because lack of regular record of patient’s body temperature during anesthesia. But at least nine of thirteen or 69.2% of patients who developed first episode of myocardial infarction in recovery room were precipitating by moderate or severe shivering. We suggested that intraoperative temperature monitoring, warming technique and limited duration of anesthesia were valuable and could reduced risks of peri-operative myocardial infarction.

Emergency surgery and ASA classification

In 1998, Pedersen and Johansen (10) concluded that the incidences of overall postoperative complications after anesthesia and surgery were not different between elective and emergency situation. But emergency situation had higher incidence of serious outcomes (myocardial infarction, brain damage and death) in the ratio of 0.16% versus 0.04% in elective situation. In this case-control study “emergency surgery” was a significant predictor (adjusted OR of 9.78 and 95%CI 3.64, 26.27) for peri-operative myocardial infarction. Emergency patients in this series were classified in the higher ASA classification than non-emergency patients. Fifty percent of the patients in the emergency group were suffering from severe infection mostly from acute cholecystitis or empyema gall bladder. These two factors (ASA classification , emergency surgery) were related to one another and could not be used separately.

Even the adjusted OR for ASA>2 was lower than crude OR (from 7.13 to 4.49) while it was increased in the factor of emergency surgery. But the range of 95% CI for OR of ASA>2 was narrower than emergency surgery (Table 6.5). This could be concluded that factor of ASA>2 was more precise than factor of emergency surgery.

The study confirmed the anesthetic evaluation process by ASA classification is still useful and reliable to predict anesthetic outcomes. Mostly in university hospital, emergency surgeries were operated during non-official hours and nearly all medical personals were less experience than during official hours. These situations should be closed monitor by closed supervision, internal auditing systems, feedbacks and intra- and inter-department conferences. Internal and external consultation and allocation of more experienced personals in more complex patients could reduced the incidence of adverse events.

Historical factors: Age, underlying cardiovascular disease and diabetes mellitus

The incidence of coronary artery disease increased with age. Many cardiac risk index suggested that age of more than 65 years was one of the risk estimation (10, 13, 27) and was recommend to evaluate before seven stepwise of AHA. This study, the age differenced between the two groups was statistically significant at 55 years. Even adjusted OR of age>55 years was increased from 2.04 of crude OR to 2.55 (1.13, 5.79), it was the lowest positive adjusted OR in this study. This meant that only the factor of age > 55 year alone was not strongly associated to peri-operative myocardial infarction.

We confirmed the association of underlying cardiovascular disease and peri-operative myocardial infarction with in the same range of adjusted OR (3.4 compared to 2.5-4) as Howell (3). But our study also could demonstrate the association between underlying diabetes mellitus and peri-operative myocardial infarction. This could be explained by the disturbances of autonomic nervous system, abnormal response to stress and under diagnosis of coronary artery disease in diabetic patients.

Anesthetic techniques

Multiple clinical randomized control trials were done to prove the difference of anesthetic techniques (general or regional anesthesia) in patients with cardiac disease on the incidence of peri-operative myocardial infarction, dysrhythmia and congestive

heart failure. But the results were not conclusive. In 1978 Goldman et al found that spinal anesthesia was not associated with new or worsen heart failure (32). In 1983 Rao et al reported the incidence of reinfarction was higher after regional anesthesia (1.8% v s 2.7%). Other studies (1) could not demonstrated association between type of anesthesia and peri-operative myocardial infarction. In our study, types of anesthesia between the two groups were statistically different (Table 6.3). But crude OR and adjusted OR were quite low. We concluded that types of anesthesia were not associated with peri-operative myocardial infarction. Our conclusion was limited by small numbers of patients in each subgroup of regional, combined regional and general and general anesthesia. Many patients both from “cases” and “controls” were operated under combined technique. Their outcomes were difference from the other two groups. This was very interesting factors and needed more control clinical trials to prove their effectiveness in decreasing the incidence of cardiac events.

Anesthetic related to occurrence of peri-operative myocardial infarction

Surprisingly that anesthesia attributed to myocardial infarction for 38 cases or 51.4 % in this series. The problems of airway and respiratory management happened in 31 cases and were the most common problems. The others of 7 cases suffered from drug overdose. In the review article of Mangano (1) in 1990, he separated preoperative predictors into historical (age, disease, ASA etc.) and diagnostic testing (EKG, Chest X-ray, exercise stress test etc.) and intraoperative predictor into classical predictors (choice of anesthesia, site of surgery, emergency and duration) and dynamic predictors (hyper or hypotension, tachycardia, myocardial ischemia, ventricular dysfunction and dysrhythmias). All his dynamic predictors were hemodynamic and ventricular function which could be commonly caused by hypoxia, hypercarbia and inappropriate level of anesthesia. Patients with peri-operative myocardial infarction were less tolerate to tachycardia and unstable hemodynamic situation.

Can we avoid all the problems of airway management and respiratory care? In this series, 25 from 31 cases, the problems were preventable by common practical guidelines which included proper preparation for unexpected difficult intubations, careful monitor of tube position during thyroid and laryngeal operation and careful decision to extubation in special group of patients such as septicemic patients, patient with compromised airway and unhealthy patients.

The respiratory adverse events and the problems of airway care were also the most common complication during anesthesia. Pulse oxymeter monitoring warned of hypoxia and makes a change for early detection and manipulation to solve the causes of desaturation and leave no permanent damage to our ordinary patients. But the patients with underlying casdiovascular disease or diabetes mellitus were less tolerated to hypoxia, hypercarbia and their effects. If hypoxia was happened together with hypercarbia as in the situation of post-operative hypoventilation, they strong stimulated sympathetic activities. In this situation, patient with underlying diseases were easier to be in the unbalance situation between myocardial oxygen demand and supply. Myocardial ischemia and myocardial infarction could easily occur after a short period of hypoxia, hypercarbia and tachycardia.

These situations of hypoxia, hypercarbia and tachycardia happened consequently and hardly to avoid during anesthesia and operation. All efforts should be done to protect myocardial injury. In 1998, Wallace A, et al (34) study revealed that prophylactic beta blocker could reduce postoperative myocardial ischemia and the severity of myocardial injury. But the implementation of preoperative administration of beta blocker was not widely acceptable (35) especially by anesthesiologist. The more extensive study of this drug as a routine use should be performed and this may reduce the tragedy from myocardial adverse events.

Conclusion and recommendation

Even this data came from only one university hospital, their outcome reflects both patient demographic, risk and medical care system. Preoperative cardiac evaluation is not limit to the implementation of ACC/AHA guideline but more cooperation, data collection and study are needed to build up care path both for elderly patients and patients with underlying cardiovascular disease. Limit duration of anesthesia by appropriated teaching and training activities, more experienced personals for more complex patients and surgeries, closely monitor of patients' body temperature, continuous record keeper and regular feedback in anesthesia and surgical department were the key to reduce incidence of cardiac events. The study in the effect of combined anesthetic technique and prevention cardiac events by beta blocker were recommended.

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Appendix

APPENDIX A
Case record form

H.N.							

Month			
Date			
Code case			
Code control			

Patient record form of

Perioperative myocardial infarction

Part 1 Patient information

1.1 Service unit ( ) General ( ) Urology ( ) Head*neck
( ) Trauma ( ) ENT
( ) Plastic ( ) Neuro ( ) Ortho
( ) Eye ( ) Ob-gyn

1.2 Age _____(Years)

1.3 Sex ( ) Male ( ) Female

1.4 Height _____ centrimeter

1.5 Weight _____ kgs.

1.6 ASA Physical Status ( ) 1 ( ) 2 ( ) 3 ( ) 4 ( ) 5 ( ) 6

1.7 Emergency ( ) No ( ) Yes

Personal History

2.1 Smoking ( ) Cannot determine ( ) No ( ) Yes**...**pack-year.....

2.2 Drinking ( ) Cannot determine ( ) No ( ) Yes sometime
( ) yes frequency ( ) yes alcoholic

2.3 Drug abuse ( ) Cannot determine ( ) No ( ) yes...specific.....

Patient Medical History and Underlying Disease Status

3.1 **Hypertension** ( ) No ( ) Yes Treatment ( ) None
( ) Medical Treatment Specify
_____
_____

Control of BP ( ) Uncontrolled (no treatment or no response to treatment)
( ) Moderate Control (responded to treatment but target BP not attained)
( ) Good Control (normal BP with treatment)

3.**2 Diabetes** ( ) No ( ) Yes Insulin dependent ? ( ) No ( ) Yes
Level of diabetic control ( ) Within normal range
( ) In acceptable range
( ) Poor control (blood glucose>180 mg%,HbA1C>8)

3.3 **Coronary Artery Disease** ( ) None
( ) Yes with management
( ) No drug but control other risk factors such as body weight, smoking, hypertension, diabetes.
( ) Medication spicify.....
( ) Post PTCA at.....
( ) Post CABG at.....

3.4 **Previous Myocardial infarction** ( ) No
( ) Yes Date (most recent).....

Detail of MI
( ) Only from EKG of Q wave
( ) Specific symptom with EKG change
( ) Admission due to MI
( ) Heart failure due to MI
( ) Diagnostic by echocardiography

3.5 Ischemic symptom ( ) Never
( ) Not more than once a month
( ) With in 2-3 days before operation
( ) Unstable angina

3.6 Cerebrovascular Disease ( ) No ( ) Yes
Carotid Endarterectomy ( ) No ( ) Yes
Previous CVA/Stroke ( ) No ( ) Yes
TIA ( ) No ( ) Yes

3.7 Specify any other significant medical history:

_____
_____
_____
_____
_____

3.8 Current medications (list):

- _____
- _____
- _____
- _____
- _____

3.9 Previous surgeries: Time Operation

_____
_____
_____
_____
_____
_____

4.Functional status

4.1 Control blood pressure.....mmHg
4.2 Heart rate.....beat/min
4.3 Hematocrit.....% Hemoglobin.....gm%
4.4 Metabolic level
4.5 Functional activity

5 Preoperative investigation

5.1 12 lead EKG

_____
_____
_____
_____
_____

5.2 Blood chemistry
BUN_____ Creatinine_____ __Blood glucose_____
Na_____ K_____ Ca_____ Cl_____ Mg_____
5.3 Preoperative cardiologist consultation ( ) No ( ) Yes
Comment_____
_____
5.4 Preoperative anesthesiologist consultation ( ) No ( ) Yes
Comment_____
_____

5.3 Preoperative other consultation ( ) No ( ) Yes
Comment__
_____

Part 2 Surgery and anesthesia

Operation

1 Preoperative diagnosis_____
_____
_____
2. Operative plan_____
3. Operative in detail_____
_____
_____
4.Operative site ( ) Intrathoracic
( ) Intraabdomen
( ) Head and neck and extremities
5.Time Anesthetic start time……Anesthetic end time……..
Total time…… ( ) < 1.5 hour ( ) > 1.5 hour
6. Intraoperative airway management ( ) none
( ) Endotrachial tube
( ) Laryngeal mask
( ) Mask
( ) Tracheostomy tube
7. Primary anesthetic technique
( ) General anesthesia
( ) Combined general plus regional specify……..
( ) Regional anesthesia specify……..
( ) MAC with sedation
( ) other……..
8. Intraoperative mornitor (check all)
( ) NIBP ( ) EKG ( ) Pulse oximeter ( ) Capnograph
( ) A-line ( ) CVP ( ) PA pressure ( ) Temperature
( ) Nerve stimulator ( )
Other……
9. Surgical position
( ) Supine ( ) Lateral ( ) Lithotomy ( ) Prone
( ) Other……..
10. Incesional line……

Anesthesia

1. Premedication: ( ) No ( ) Yes
Specify all medications active or administered prior to induction of anesthesia.
Time of Rate & Duration
Drug Name Dose Administration if Infusion
_____ _____ _____ _____
_____ _____ _____ _____
_____ _____ _____ _____

2 Anesthesia Agents
2.1 Induction Agents, Dose, Route of Administration:
_____ _____ _____ _____
_____ _____ _____ _____
_____ _____ _____ _____
2.2 Nitrous oxide ( ) yes ( ) No

2.3 Inhalation ( ) Halothane ( ) Isoflurane ( ) Sevoflurane
2.4 Opioids ( ) Morphine ( ) Pethidine ( ) Fentanyl
( ) other.....
2.5 Benzodiazepine ( ) No ( ) Yes Domicum.....mg
Valium.....mg
2.6 Other drugs

2.7 Regional Anesthesia Technique ( ) None (skip to section)
( ) Thoracic epidural ( ) Lumbar epidural ( ) Spinal
( ) Other specify _____
2.8 Regional Anesthesia Agents, Doses:
Agent: _____Test dose: _____
Definitive dose:_____ or Infusion rate: _____
2.9 List ALL fluids administered during maintenance of anesthesia
Time of Rate & Duration
Fluid Name Dose Administration if Infusion
_____ _____ _____ _____
_____ _____ _____ _____
_____ _____ _____ _____
Total volume of IV fluids (crystalloids, colloids): _____ cc

Part 3 Intraoperative clinical course

1 Was controlled hypotension used? ( ) No (Skip to section)
( ) Yes
Technique: ( ) Deep inhalation anesthesia ( ) Hypotensive drug (specify)_____
Target blood pressure:.....mean _____systolic _____mmHg.

2 Intraoperative blood pressure
Preoperative blood pressure (baseline) _____ mean _____mmHg
Lowest intraoperative systolic blood pressure _____mmHg
Highest intraoperative systolic blood pressure_____mmHg
Duration of highest blood pressure _____minutes
Lowest intraoperative mean blood pressure _____mmHg
Duration of lowest blood pressure _____ minutes
Did mean or systolic blood pressure drop:
20% below baseline? No _ Yes_____ total duration (minutes)
40% below baseline? No _ Yes_____ total duration (minutes)
50% below baseline? No _ Yes_____ total duration (minutes)
> 50% below baseline? No _ Yes ___ ___ total duration (minutes)

3. Intraoperative Heart rate
Preoperative heart rate (baseline) _____ beat/min
Lowest intraoperative heart rate _____ beat/min
Duration of lowest heart rate_____ minutes
Highest intraoperative heart rate_____beat/min
Duration of highest heart rate _____ minutes
Did heart rate change to:
More than 100/min No _ Yes_____ total duration (minutes)
More than 120/ min No _ Yes_____ total duration (minutes)
More than 140/min No _ Yes_____ total duration (minutes)
Lower than 50/min No _ Yes _____ total duration (minutes)

4 Blood and Fluid Loss
Estimated blood loss _____cc.
Lowest recorded Hct/Hgb (intraoperative) _____ time _____

Did Hgb drop below 8.0g/dl? _ No _ Yes Duration _____ minutes
Blood products administered intraoperatively:
Whole blood _____ cc
Packed cells _____ cc
Other blood products (specify type and volume) _____ cc
Total intraoperative urine output: _____ cc

5 Intraoperative Body Temperature

Did temperature drop below 35 c ( ) No ( ) Yes ( ) Do not know
Lowest intraoperative temperature _____ c
Duration of temperature below 35c _____ minutes
Did immediate postoperative body temperature lower than 35 C
( ) No ( ) Yes ( ) Do not know

6 Adverse Intraoperative Events

Cardiac arrest ( ) No ( ) Yes duration _____ minutes
Cardiogenic shock ( ) No ( ) Yes duration _____ minutes
Hypoxia ( ) No ( ) Yes duration _____ minutes
Hypercarbia ( ) No ( ) Yes duration _____ minutes
Other relevant events:
_____
_____

Brief Summary of Events:

_____
_____
_____

Conclusion detail of myocardial infarction

1. Time of first diagnostic of MI ( ) Intraoperative ( ) Recovery room
( ) With in 24 hour after operation
( ) More than 24 hour after operation

2. Status of patient at first diagnostic
( ) Intraoperative ( ) Recovery room
( ) ICU ( ) Ward

3. Primary symptom of MI
- Chest pain or discomfort ( ) Yes ( ) No
- EKG change ( ) Yes ( ) No
- Unstable hemodynamic ( ) Yes ( ) No
- Other.....

4. Precipitating factors
- Pain ( ) Yes ( ) No
- Tachycardia ( ) Yes ( ) No
- Hypertension ( ) Yes ( ) No
- Hypoxemia ( ) Yes ( ) No
- Hypercarbia ( ) Yes ( ) No
- Light anesthesia ( ) Yes ( ) No
- Unstable hemodynamic ( ) Yes ( ) No
- Severe infection ( ) Yes ( ) No
- Other.....

5.Initial management

1._____
2._____
3._____

6.Troponin T

Date Time Troponin-T level

_____
_____

7. Final outcome

1.Duration of ICU admission……days

2.Duration of hospital stay after infarction……days

3.Does infarction cause

Unstable hemodynamic ( ) No ( ) Mild ( ) Moderate ( ) Severe

Cardiogenic shock ( ) No ( ) Yes

Prolong ventilatory support ( ) No ( ) Yes:

Renal impairment ( ) No ( ) Yes

4.Final outcome

( ) Full recovery ( ) Need specific management

( ) Death from myocardial failure

( ) Death from other ……

……

……

VITAE

Mrs. Thitima Chinachoti was born on the 19th of October,1952 in Siriraj Hospital, Bangkok, Thailand. In 1978, she graduated with M.D. degree from the Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand. In 1982, she received Thai Board in Anesthesiology from Medical Council of Thailand. Her present position is Associate Professor in the Department of Anesthesiology, Siriraj hospital, Mahidol University, Thailand.