RELATIONSHIP BETWEEN ABDOMINAL AORTIC CALCIFICATION WITH 30 DAYS POSTOPERATIVE OUTCOME IN PATIENT UNDERWENT COLORECTAL SURGERY

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DISSERTATION SUBMITTED IN
PARTIAL FULFILMENT OF THE REQUIREMENT FOR
THE DEGREE OF MASTER OF SURGERY
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II. ACKNOWLEDGEMENT

I would like to thank the Almighty ALLAH for the opportunity, time and energy given to me to complete my thesis. Alhamdulillah!

I would like to express my gratitude to my supervisor, Dr Mohd Nizam Md Hashim, who supported me all the way from the beginning. He supported me with ideas, feedback and advices so that I managed to complete my thesis on time.

Next, I would like to thank my co-supervisor, Dr Rosnelifaizur Ramely for his suggestion on the topic and supervised me all the way. He gave me scientific guidance and advice, assisted me in solving problems and encouraged my research progress. Besides, my upmost appreciation to Dr Khairil Amir Sayuti, my co-supervisor and our radiologist who helped me a lot in interpreting CT scan findings.

Thanks to my head of department, Prof Zaidi Zakaria, who always give his views and encouraged us to complete the thesis. I would like to acknowledge the support of my surgical department and university who gave me generous access to the facilities provided.

Thousand thanks to my dearest wife for encouraging me day and night completing the thesis. She was my backbone throughout my 4 years of master programme.

Finally, I sincerely thank my parents who were there to support me during my master programme and obviously they indirectly involved in helping me complete my thesis.

Thank you.

III. TABLE OF CONTENTS

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS

American Society of Anesthesiology	ASA
Computed tomography	CT
Hypertension	HPT
Diabetes Mellitus	DM
Hyperlipidemia	HPL
Ischemic Heart Disease	IHD
Aortic Calcification Score	ACS
Colorectal Cancer	CRC
Clinical Practice Guidelines	CPG
Body Mass Index	BMI
Reactive Oxygen Species	ROS
Reactive Nitrogen Species	RNS

IV. ABSTRAK

Pengenalan: Kebocoran pada penyambungan usus di dalam pembedahan kolorektal merupakan satu komplikasi pembedahan yang sangat merbahaya yang boleh membawa kepada morbiditi dan kematian. Banyak faktor risiko yang telah di kenalpasti seperti American Society of Anaesthesiology (ASA) skor, penyambungan usus besar sebelah kiri dan juga pembedahan kecemasan. Walaubagaimanapun, kadar kejadian masih tinggi. Oleh yang demikian, faktor risiko kebocoran penyambungan usus kolorektal masih belum di fahami secara terbaik dan masih memerlukan penyelidikan yang lebih lanjut. Kajian ini menerangkan mengenai penggunaan skor kalsifikasi salur darah aorta abdomen sebagai salah satu faktor ramalan kepada kebocoran penyambungan usus kolorektal dan morbiditi.

Kaedah: Ini merupakan kajian secara retrospektif dengan menggunakan data pesakit di Hospital Universiti Sains Malaysia mulai Januari 2012 sehingga Jun 2017. Semua pesakit yang menjalani pembedahan kolorektal dengan kaedah penyambungan usus sebelah kiri termasuk penyakit benign dan juga malignan, yang dijalankan secara kecemasan mahupun elektif. Kesemua kes pembedahan samaada secara ‘open’ atau laparoskopik di masukkan ke dalam studi ini. Skor kalsifikasi aorta abdomen ditentukan dengan melihat kepada filem imbasan CT scan dan mencari hubungkaitnya dengan keputusan awal pembedahan (30 hari pertama selepas pembedahan).

Keputusan: Seranai 78 pesakit telah di ambil mengikuti studi ini di mana seramai 42 pesakit (53.5%) merupakan wanita manakala 36 pesakit (46.2%) adalah lelaki. Min umur pesakit adalah 56.47 tahun. Majoriti pesakit menghidap penyakit darah tinggi (42.3%), kencing manis (24.4%), manakala selebihnya di dapati menghidap hiperlipidemia (17.9%) dan penyakit jantung iskemia (11.5%). Tiga puluh dua pesakit (41.0%) adalah ASA 1, 36 orang pesakit (46.2%) mempunyai skor ASA 2 manakala 10 pesakit (12.82%) adalah ASA 3. Bagi skor kalsifikasi aorta abdomen pula, dua puluh empat orang pesakit (30.8%) didapati tiada kasifikasi pada aorta abdomen atau

memiliki skor 0. Pesakit yang memiliki skor 1 adalah seramai 37 pesakit (47.4%), manakala baki 17 orang pesakit (21.8%) mempunyai skor kalsifikasi aorta 2. Terdapat hubungan statistik yang signifikan di antara darah tinggi dan skor kasifikasi aorta abdomen (ACS) (p = 0.002). Terdapat juga hubungan statistik yang signifikan di antara skor ASA dan skor ACS (p= 0.001). Di dalam kajian ini, majoriti pesakit tidak mendapat morbidity selepas pembedahan (38 pesakit atau 48.7%), 31 pesakit (39.7%) mendapat komplikasi minor (Clavien Dindo gred 1 & 11) dan 9 pesakt (11.6%) mendapat komplikasi major (Clavien Dindo gred 111 sehingga V). Walaubagaimanapun, tiada hubungan statistik yang signifikan di antara skor kalsifikasi aorta abdomen (ACS) dengan morbiditi selepas pembedahan (p=0.921). Kebocoran penyambungan usus didiagnosa pada 10 orang pesakit (12.8%). Terdapat satu kematian selepas pembedahan direkodkan. Walaubagaimanapun, tiada hubungan statistik yang signifikan di antara skor ACS dan kebocoran penyambungan usus (p=0.572)

Kesimpulan: Kajian ini mendapati skor kalsifikasi aorta abdomen tidak berhubung kait dengan morbiti selepas pembedahan juga tidak mempengaruhi kebocoran penyambungan kolorektal. Walaubagaimanapun, satu kajian secara prospektif dan berskala lebih besar lain patut dijalankan di masa hadapan.

ABSTRACT

Background: Anastomotic leakage in colorectal surgery remains a devastating complication with its associated post-operative morbidity and mortality. Various risk factors have been described, such as ASA score, left sided anastomosis or emergency surgery. However, the rate remained high. Thus, risk factor for colorectal anastomotic leakage and associated postoperative morbidities remain incompletely understood and yet to be discovered. This study describes the use of abdominal aortic calcification score as a prognostic factor for colorectal anastomotic leakage and its associated post-operative morbidities.

Methods: This is a retrospective review of patient clinical data at Hospital Universiti Sains Malaysia from January 2012 until June 2017. Cases were all patient who underwent colorectal surgery with left sided anastomosis including benign and malignant disease performed in elective or emergency setting. All cases either open or laparoscopic approach were included in this study. Abdominal aortic calcification score were determined by pre-operative CT scan and its association with early postoperative outcome (30 days) were analysed.

Results: A total of 78 patients were included in this study in which 42 patients (53.8%) were female and 36 patients (46.2%) were male. The mean age of the subject is 56.47 years. Majority had been diagnosed with hypertension (HPT, 42.3 %) and diabetes mellitus (DM, 24.4%), while some others diagnosed with hyperlipidemia (HPL, 17.9%) and ischemic heart disease (IHD, 11.5%). Thirty two patients (41.0%) were ASA 1, 36 patients (46.2%) were ASA 2, while the other 10 patients (12.82%) were ASA 3. As for abdominal aortic calcification score (ACS), twenty-four patients (30.8%) has no aortic calcification (ACS score 0). Patient with a score of 1 were 37 patients (47.4%) while 17 patients (21.8%) had aortic calcification score of 2. There was significant association between hypertension (HPT) and ACS (p-value=0.002). There was also significant association between ASA score and ACS (p-value = 0.001).

In our study, majority of subjects had no post-operative morbidity (48.7%) such as wound infection, atelectasis or even major post-operative morbidity such as sepsis and death. Thirty one patients (39.7%) had minor complications (Clavien Dindo grade 1&11) and 9 patients (11.6%) had major complications (Clavien Dindo grade 111 till V). However, there was no significant correlation between ACS with postoperative morbidity (p=0.921). Postoperative anastomotic leakage was diagnosed in 10 patients (12.8%). There was one postoperative mortality recorded. Otherwise, there was no significant relationship between ACS and anastomotic leakage (p = 0.572)

Conclusion: This study demonstrates that abdominal aortic calcification score does not correlate with post-operative morbidity or influence the colorectal anastomotic leakage. However, future prospective study is suggested with a larger sample size.

1- INTRODUCTION

1-1: INTRODUCTION

Anastomotic leakage is the most fearful complication in colorectal surgery. It has been associated with repeated surgery and with increased duration of hospitalization and cost; the reported postoperative morbidity rate is between 0% and 32 % [2-3].

Several risk factors for colorectal anastomotic leakage have been identified: male gender, pre-operative radiotherapy, low anastomosis (less than 10 cm from anal verge), high BMI, multiple medical comorbidities, advance age, and vascular disease [5]. In oncological surgery, anastomotic leakage has been associated with negative impact on overall, cancer related and disease free survival [6-7].

Despite that, colorectal anastomotic leakage rate remain high, ranging between 2% and 24 % [8]. Thus, risk factor for colorectal anastomotic leakage and associated postoperative morbidities remain incompletely understood at best and yet to be discovered.

Better knowledge of these risk factors would encourage surgeon to improve information given to patient about postoperative morbidity and to adapt surgical strategies. At most, in high risk patient, non -anastomotic management using Hartmann procedure or covering stoma could be proposed.

Healing of bowel anastomotic site largely depend on blood supply. Without adequate blood supply or ischemia, anastomosis will fail and leakage will result. Atherosclerosis is a known cause of tissue ischemia [9] and is suggested to have detrimental effect on anastomotic healing [9]. An atherosclerotic plaque is made up of fat, cholesterol and calcium, causing hardening and narrowing of the arteries and lead to ischemia. The calcium burden of atherosclerotic plaque is readily detectable on CT scan [10].

Agatson et al identified coronary artery calcium scoring, using a method of non-invasive CT scans to detect and quantify coronary artery calcification, as a predictor of coronary artery disease [10].

Thus, study on aortic calcification in association with colorectal anastomotic leakage and associated postoperative morbidity is possible.

1.2: LITERATURE REVIEW

Anastomotic leakage is a serious complication encountered after intestinal surgery, yet we often do not know why leakage occur in any particular patient or circumstance. Despite advances in surgical technique, anastomotic leak rates remain a significant problem with associated postoperative morbidities. The aetiology of anastomotic leakage remain incompletely understood at best and yet to be discovered.

Sufficient tissue perfusion is the core factor of anastomotic healing. A link between ischemia and anastomotic fistula was emphasized by Vignali et al. They measured the transmural colonic blood flow using laser-Doppler flowmetry before and after anastomosis, and concluded that a decrease in arterial flow was predictive of the anastomotic leakage. This finding was the rationale for this study, proposing a hypothesis linking between Aortic Calcification Score and anastomotic leakage and postoperative morbidities.

Harbaugh et al analysed 1180 patients from Michigan Surgical Quality Collaborative (MSQC) database who underwent elective major general or vascular surgery between 2006 and 2009 and who underwent CT abdomen as pre-operative planning. Abdominal aortic calcification was measured using novel analytic morphomic technique and was reported as percentage of the total wall area containing calcification. Multivariate logistic regression confirmed that Abdominal Aortic calcification for patient with no clinical cardiovascular risk was a significant predictor of morbidity.

N. Komen et al proposed a calcium score; a new predictive scoring system for colorectal anastomotic leakage. They measured calcium score on CT scan using computer software. From the study, it is clear that patient with higher calcium score have an increased risk of leakage. However, the proposed scoring system using software has disadvantages of being difficult to use

in daily clinical practice, especially for non-radiologist physician, non-reproducible in term of using sophisticated computer software, particularly in the context of emergencies where quick decision needed, whether to perform an anastomosis, Hartmann procedure or covering stoma.

C. Eveno et al proposed an Aortic Calcification Scoring (ACS) system, used to assess abdominal aortic calcification on pre-operative, non-contrasted CT scan in colorectal patient. They conclude that ACS is correlated with surgical outcomes, particularly anastomotic leakage after colorectal surgery. ACS system is very practical to be used in daily clinical practice as it can provide a rapid, reproducible, easily accessible method for non-radiologist physician to assist in surgical decision, particularly in the context of emergencies. Furthermore, the scoring system does not require additional reviews, which could delay surgical procedures in cases of emergency. In addition to that, CT scans are always obtained in emergency situation and always available pre-operatively for elective colorectal surgery. In our study, we proposed to use Aortic Calcification Score (ACS) to find correlation of the outcome of colorectal surgery with abdominal aortic calcification.

1-3: RATIONALE OF STUDY

Colorectal anastomotic leakage is associated with significant morbidity or even mortality. Since the exact cause of anastomotic leakage is yet to be discovered, we considered abdominal aortic calcification might play an important role to predict early surgical outcome. We plan to analyse the 30 days postoperative outcome patient who underwent elective or emergency colorectal resection for benign or malignant disease at Hospital Universiti Sains Malaysia (HUSM). Then, we will correlate these variables to the degree of abdominal aortic calcifications on preoperative CT scan. Abdominal aortic calcification score (C.Eveno et al, 2016) used in this study could be a useful tool for adapting surgical strategies by delaying anastomosis particularly in high risk patient. There was no similar study performed before in HUSM or Malaysia thus this study aim to find such correlation in the local setting.

2- STUDY PROTOCOL

DOCUMENT SUBMITTED FOR ETHICAL APPROVAL

Jabatan Surgeri

Department of Surgery

Pusat Pengajian Sains Perubatan,

Kampus Kesihatan

Universiti Sains Malaysia

16150,Kubang Kerian,

Kelantan,Malaysia.

Tarikh: 26 Disember 2017

Chairperson,

Human Research Ethics Committee USM (HREC)

Health Campus,USM,

Kubang Kerian,Kelantan.

Protocol Title: RELATIONSHIP BETWEEN ABDOMINAL AORTIC CALCIFICATION AND 30 DAYS POSTOPERATIVE OUTCOME IN PATIENT UNDERWENT COLORECTAL SURGERY

Principal Investigator: Dr. Ahmad Adham bin Ali

Dear Prof,

Thank you for considering my thesis proposal.

DISSERTATION PROPOSAL

MASTER OF GENERAL SURGERY

RELATIONSHIP BETWEEN ABDOMINAL AORTIC CALCIFICATION WITH 30 DAYS POSTOPERATIVE OUTCOME IN PATIENT UNDERWENT COLORECTAL SURGERY

BY:

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TABLE OF CONTENTS

1-TITLE:

1-a- Relationship between Abdominal Aortic Calcification and 30 days Postoperative Outcome in Patient underwent Colorectal Surgery

1-b-This is a cross sectional study to see the relationship between abdominal aortic calcification and 30 days postoperative outcome in patient underwent colorectal surgery. It involves all patients who are diagnosed with colorectal disease either malignant or benign condition who required colorectal resection and anastomosis at Hospital Universiti Sains Malaysia from January 2012 until June 2017. Patient clinical notes, operative notes and preoperative CT scan will be reviewed. The postoperative outcome that will be included in this study include colorectal anastomotic leakage as defined by International Study Group Rectal Cancer[15] and also postoperative morbidity according to Clavien-Dindo grading system[14]. Then, preoperative CT scan will be assessed to look for abdominal aortic calcification and classify it based on aortic calcification score (ACS). Relationship between abdominal aortic calcification and 30 days postoperative outcome will then be analyzed to find whether or not it fit the expected outcome of this study. The patients involve are screened with our inclusion and exclusion criteria. The medical records will be reviewed and data will be entered into data collection form. The data will then be analyzed. The literature review of studies done before relating to this topic have produced similar results. However in Malaysia we do not have such study available yet.

2-a-Introduction

Anastomotic leakage is the most fearful complication in colorectal surgery. It has been associated with repeated surgery and with increased duration of hospitalization and cost; the reported postoperative morbidity rate is between 0% and 32 % [2-3].

Several risk factors for colorectal anastomotic leakage have been identified: male gender, pre-operative radiotherapy, low anastomosis (less than 10 cm from anal verge), high BMI, multiple medical comorbidities, advance age, and vascular disease [5]. In oncological surgery, anastomotic leakage has been associated with negative impact on overall, cancer related and disease free survival [6-7].

Despite that, colorectal anastomotic leakage rate remain high, ranging between 2% and 24 % [8]. Thus, risk factor for colorectal anastomotic leakage and

associated postoperative morbidities remain incompletely understood at best and yet to be discovered.

Better knowledge of these risk factors would encourage surgeon to improve information given to patient about postoperative morbidity and to adapt surgical strategies. At most, in high risk patient, non -anastomotic management using Hartmann procedure or covering stoma could be proposed.

Healing of bowel anastomotic site largely depend on blood supply. Without adequate blood supply or ischemia, anastomosis will fail and leakage will result. Atherosclerosis is a known cause of tissue ischemia [9] and is suggested to have detrimental effect on anastomotic healing [9]. An atherosclerotic plaque is made up of fat, cholesterol and calcium, causing hardening and narrowing of the arteries and lead to ischemia. The calcium burden of atherosclerotic plaque is readily detectable on CT scan [10].

Agatson et al identified coronary artery calcium scoring, using a method of non-invasive CT scans to detect and quantify coronary artery calcification, as a predictor of coronary artery disease [10].

Thus, study on aortic calcification in association with colorectal anastomotic leakage and associated postoperative morbidity is possible.

2-b-Literature review

Anastomotic leakage a serious complication encountered after intestinal surgery, yet we often do not know why leakage occur in any particular patient or circumstance. Despite advances in surgical technique, anastomotic leak rates remain a significant problem with associated postoperative morbidities. The aetiology of anastomotic leakage remain incompletely understood at best and yet to be discovered.

Sufficient tissue perfusion is the core factor of anastomotic healing. A link between ischemia and anastomotic fistula was emphasized by Vignali et al [11]. They measured the transmural colonic blood flow using laser-Doppler flowmetry before and after anastomosis, and concluded that a decrease in arterial flow was predictive

of the anastomotic leakage. This finding was the rationale for this study, proposing a hypothesis linking between Aortic Calcification Score and anastomotic leakage and postoperative morbidities.

Harbaugh et al [12] analysed 1180 patients from Michigan Surgical Quality Collaborative (MSQC) database who underwent elective major general or vascular surgery between 2006 and 2009 and who underwent CT abdomen as pre-operative planning. Abdominal aortic calcification was measured using novel analytic morphomic technique and was reported as percentage of the total wall area containing calcification. Multivariate logistic regression confirmed that Abdominal Aortic calcification for patient with no clinical cardiovascular risk was a significant predictor of morbidity.

N. Komen et al proposed a calcium score; a new predictive scoring system for colorectal anastomotic leakage. They measured calcium score on CT scan using computer software. From the study, it is clear that patient with higher calcium score have an increased risk of leakage [13]. However, the proposed scoring system using software has disadvantages of being difficult to use in daily clinical practice, especially for non-radiologist physician, non-reproducible in term of using sophisticated computer software, particularly in the context of emergencies where quick decision needed, whether to perform an anastomosis, Hartmann procedure or covering stoma.

C. Eveno et al proposed an Aortic Calcification Scoring (ACS) system, used to assess abdominal aortic calcification on pre-operative, non-contrasted CT scan in colorectal patient [1]. They conclude that ACS is correlated with surgical outcomes, particularly anastomotic leakage after colorectal surgery [1]. ACS system is very practical to be used in daily clinical practice as it can provide a rapid, reproducible, easily accessible method for non-radiologist physician to assist in surgical decision, particularly in the context of emergencies. Furthermore, the scoring system does not

require additional reviews, which could delay surgical procedures in cases of emergency. In addition to that, CT scans are always obtained in emergency situation and always available pre-operatively for elective colorectal surgery.

In our study, we proposed to use Aortic Calcification Score (ACS) to find correlation of the outcome of colorectal surgery with abdominal aortic calcification.

2-c-Problem statement &rationale of studies.

Colorectal anastomotic leakage is associated with significant morbidity or even mortality. Since the exact cause of anastomotic leakage is yet to be discovered, we considered abdominal aortic calcification might play an important role to predict early surgical outcome. We plan to analyse the 30 days postoperative outcome patient who underwent elective or emergency colorectal resection for benign or malignant disease at Hospital Universiti Sains Malaysia (HUSM). Then, we will correlate these variables to the degree of abdominal aortic calcifications on preoperative CT scan. Abdominal aortic calcification score[1] used in this study could be a useful tool for adapting surgical strategies by delaying anastomosis particularly in high risk patient.

2-d-Objectives

Primary objective

To study relationship between abdominal aortic calcification with 30 days postoperative outcome of patient who underwent colorectal resection and anastomosis.

Specific objectives:

1. To determine prevalence of anastomotic leakage in patient underwent colorectal surgery in HUSM
2. To determine prevalence of postoperative morbidity according to Clavien-Dindo classification in patient underwent colorectal surgery in HUSM
3. To study relationship between abdominal aortic calcification with 30 days postoperative outcome in patient underwent colorectal resection and anastomosis.

HYPOTHESIS

Null hypothesis

- There is no association between short term outcome of colorectal surgery with abdominal aortic calcification

Alternative hypothesis

- There is association between short term outcome of colorectal surgery with abdominal aortic calcification

3- RESEARCH METHODOLOGY

Study Design

Cross sectional study

* Estimated left colonic or rectal resection and anastomosis at HUSM is between 14- 22 cases per year.

Study area

- Hospital University Science of Malaysia (HUSM)

4-STUDY POPULATION

Reference population

- All colorectal patient operated at HUSM from January 2012 until June 2017

Source population

- All patients underwent colorectal surgery in HUSM from January 2012 until June 2017

Inclusion criteria:

I. All colorectal patient with left colonic or rectal resection and primary anastomosis including both elective and emergency surgery.
II. Including both benign and malignant colorectal diseases
III. Including both open and laparoscopic surgery
IV. Pre-operative CT scan performed

Exclusion criteria:

I. Small bowel or Right sided colon anastomosis
II. Incomplete data >30 %
III. No pre-operative CT scan available

Study sample:

All colorectal patients who fulfilled the study criteria will be included in this study.

5- SAMPLE SIZE

Sample size was calculated based on study objective as below

Based on objective 1: One proportion formula

Sample size, $n = (z/\Delta)^2 \times (p(1-p))$

$Z = 1.96$

$\Delta = 0.1$

$p = 0.19$ (prevalence of anastomotic leakage following colorectal surgery as reported by Platell et al [2])

Total sample size, $n = (1.96 / 0.1)^2 \times (0.19 (1-0.19)) = 60$

$= 59 + 10\%$ dropout $= 66$

Based on objective 2: One proportion formula

Sample size, $n = (z/\Delta)^2 \times (p(1-p))$

$Z = 1.96$

$\Delta = 0.1$

$p = 0.25$ (prevalence of postoperative morbidities following colorectal surgery as reported by Kingham et al, 2009)[4])

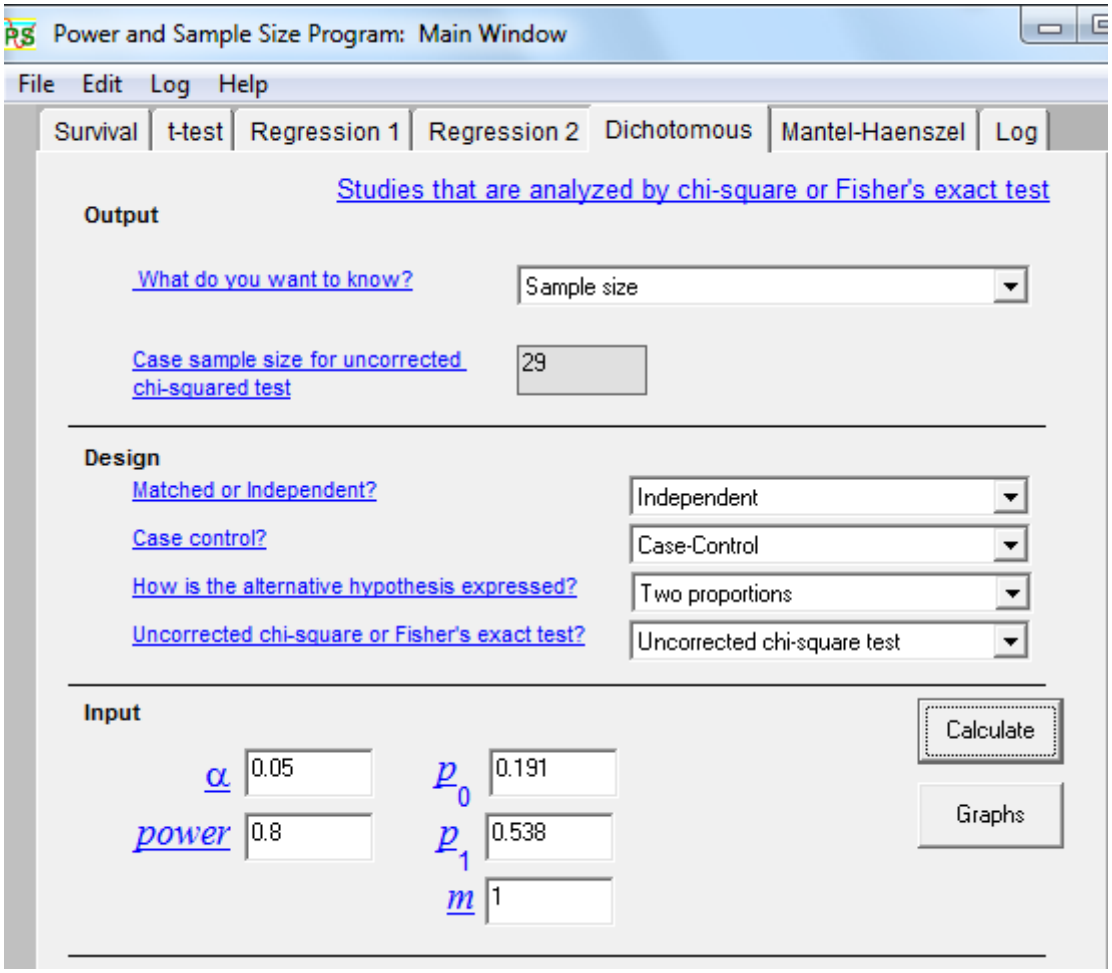
Total sample size, $n = (1.96 / 0.1)^2 \times (0.25 (1-0.25)) = 72$

$= 72 + 10\%$ dropout $= 79$

Objective 3

Sample size calculation was done using PS software. Parameters used are $\alpha = 0.05$, power = 0.8; $P_0 = 0.191$ (as per report by C.Eveno et al[1]) and P1= 0.538 (based on

expert opinion), m=1. Total sample size obtained n= 29 x2 = 58. After adding 10 % dropout, sample size needed are 64.



As a conclusion, the largest sample size which need to accomplish the objectives of the study obtained from the calculation in objective 2 which was 79 samples.

6- Research Tool

Research Proforma will be used to collect all related data for this study purpose.

NUMBER: _____

AGE: _____ SEX: MALE / FEMALE

CO-MORBIDITIES: DM HPL CKD STAGE_____

HPT IHD

DIAGNOSIS: _____

PREOPERATIVE CT SCAN: YES/NO DATE: _____

AORTIC CALCIFICATION SCORE: GRADE 0:_____

GRADE 1:_____

GRADE 2:_____

OPERATION: _____ ASA: 1/2/3/4/5

DATE: _____ TOTAL LENGTH OF STAY: _____DAYS

NATURE: OPEN/ LAPAROSCOPIC/ HAND ASSISTED / OTHERS: _____

BOWEL RESECTED: _____

ANASTOMOSIS PERFORMED: _____

TYPE: HANDSEWN / STAPLER / OTHERS_____

COVERING STOMA: YES/NO TYPE: _____

TYPE: EMERGENCY / ELECTIVE LENGTH: _____ MIN

ICU ADMISSION POST OP: YES/ NO LENGTH: _____ DAYS

POSTOPERATIVE MORBIDITIES:

CLAVIEN DINDO: MINOR (1-11): _____

MAJOR (111-V): _____

ANASTOMOTIC LEAKAGE: YES/ NO GRADING: A/B/C

MODALITIES OF TREATMENT:

REOPERATION: YES/NO OP: _____

MORTALITY: YES/ NO DATE: _____ POST OP DAY: _____

CAUSE OF DEATH: _____

The related study research tools are explained as follows:

Aortic Classification Score (C.Eveno et al[1])

Stage 0	No abdominal aortic calcification
Stage 1	Abdominal aortic calcification on less than 50% of the circumference
Stage 2	Abdominal aortic calcification on more than 50 % of circumference

Abdominal aortic calcification

The degree of circumference of abdominal aortic calcification will be analysed on pre-operative CT scan and interpreted based on aortic calcification score by Eveno et al [1]. The level of aorta that will be analysed is between the origin of celiac trunk till the level of bifurcation of aorta. The degree of calcification of aortic calcification will be classified into 3 stage; stage 0, no abdominal calcification; stage 1, aortic calcification of less than 50 %; and stage 2, aortic calcification of more than 50 %.

Clavien DIndo Classification of Surgical Complications – used to assess postoperative morbidities

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
	Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications
	Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

*Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks.
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

Postoperative complications

Early postoperative morbidity is defined as complications that happened within 30 days of surgery and will be grade according to Clavien-Dindo grading system [14]. Grade 0 indicate no complication. Grade I complications require no or minor interventions. Grade II required moderate interventions such as intravenous medication and Grade III complications required surgical, endoscopic or radiological intervention. Grade IV complications indicate life threatening complication requiring intensive care management. Grade V indicated complications causing death. As per C. Eveno et al[1], Grade I and II will be combined into 'minor complications' and Grade 111 to V will be considered as 'major complications'.

Minor Complications	Grade I & II will be combined into minor complications where no surgical or radiological intervention required
Major Complications	Grade 111 till Grade V will be combined as major complications whereby active surgical, endoscopic or radiological intervention required, occurance of life threatening complications or death

Grading of Anastomotic Leakage based on International study group of rectal cancer (2010) [15]

Grade A	No Active therapy required
Grade B	Active intervention but not relaparotomy
Grade C	Relaparotomy

Anastomotic leakage is defined as anastomotic dehiscence with communication between endoluminal and extraluminal compartments. It is divided in 3 grades according to International study group of rectal cancer [15]. Grade A requiring no active intervention, Grade B requiring intervention but manageable without

relaparotomy (fasting, antibiotic), percutaneous or transanal drainage. Grade C requiring relaparotomy with lavage and/or stoma; where patient exhibits sign of peritonitis and sepsis.

7- Data collection

Data collection will be recorded in a data collection form as presented in study proforma.

8-Proposed data analysis

SPSS version 22 will be used for data used for data analysis.

Objective 1: frequency and percentage will be used to determine the prevalence of anastomotic leakage following colorectal surgery in HUSM

Objective 2: frequency and percentage will be used to determine the prevalence of postoperative morbidity following colorectal surgery in HUSM

Objective 3: Pearson Chi Square test will be used to determine association between abdominal aortic calcification with 30 days postoperative outcomes in patient underwent colorectal surgery. If assumption of Chi Square is not met, Fisher exact test will be used.

9- ETHICAL ISSUE

9.1 Declaration of Conflict of Interest

I hereby declare there is no conflict of interest

9.2 Handling Privacy and Confidentiality Issues

This study was conducted after ethical approval had been obtained from Human Research Ethical Committee (HREC) of USM and National Medical Research Register (NMRR). Patients' personal information were kept confidential using anonymous technique and only researcher is allowed to assess the particular of the subjects. The data would be presented collectively without exposing any singularity.

9.3 Publications And Presentation

The data and results would be presented either in poster format or published in any upcoming conference without revealing any subject's private information.

9.4 Community Benefits

We hope that the study results will help the clinician to identify high risk patient underwent colorectal surgery at risk of anastomotic leakage and postoperative morbidities. Then, postoperative strategies such as delayed anastomosis or covering stoma can be used in this group of patient.

10-Expected Result

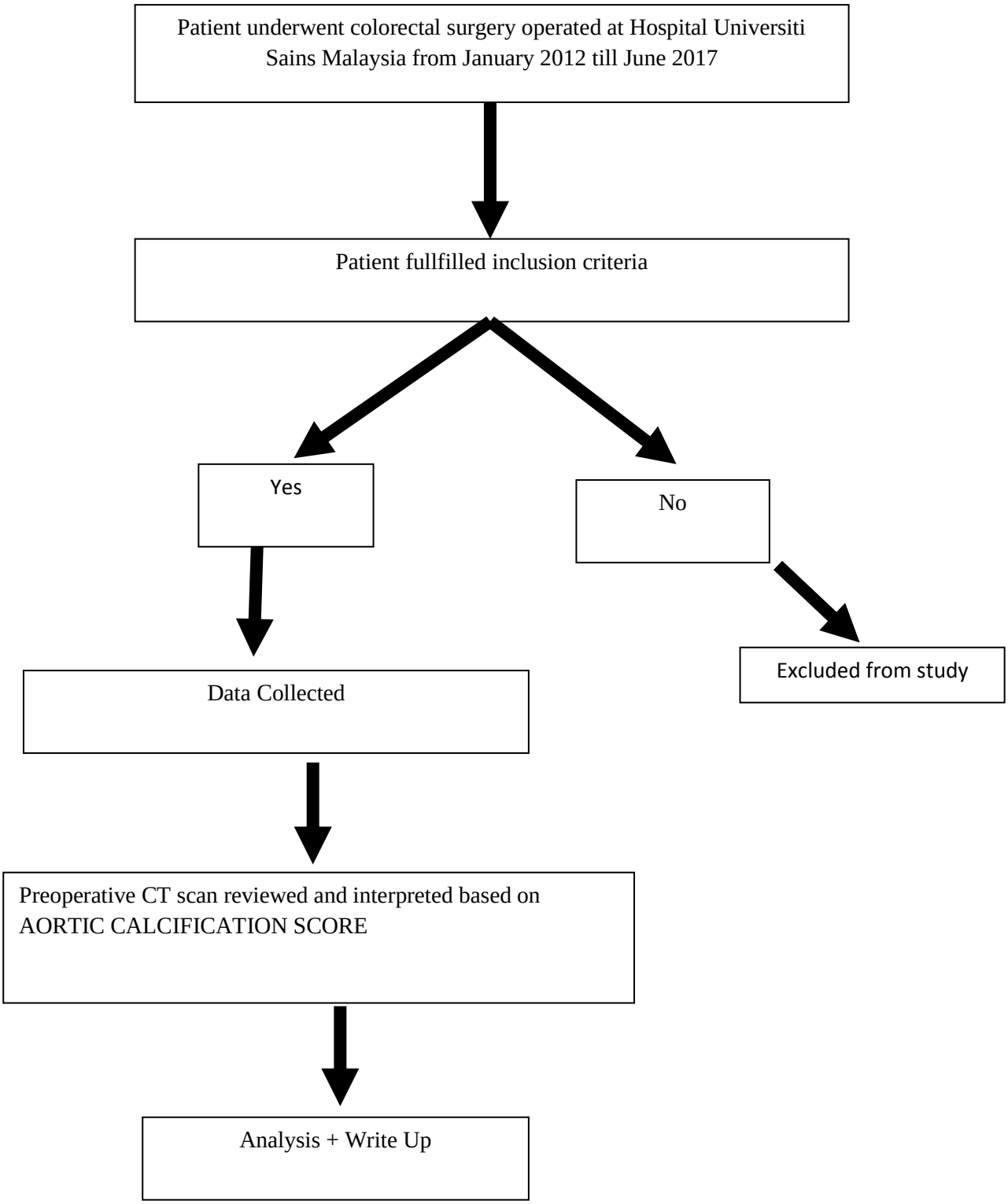
Research outcome

Our research outcome suggests that patient with abdominal aortic calcification who underwent colorectal surgery are at risk for anastomotic leakage and associated postoperative morbidities.

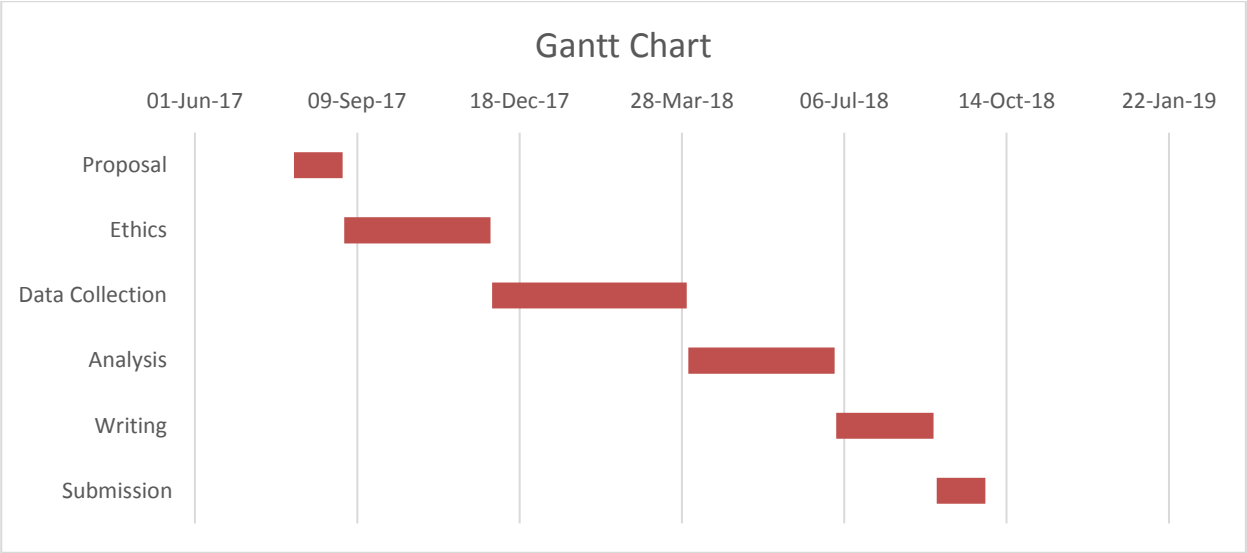
Conclusion

This study will find relationship between abdominal aortic calcification with early postoperative outcomes specifically anastomotic leakage and associated postoperative morbidities. This will help us to identify high risk patient and postoperative strategies such as delayed anastomosis can be implied.

11- FLOW CHART



12- GANTT CHART



MILESTONES

March 2018: Completion of data collection

July 2018: Completion of Data Analysis

Aug 2018: Completion of report writing

September 2018: Completion of submission