

# EARLY CHOLECYSTECTOMY FOR ACUTE CHOLECYSTITIS IN A LOW INCOME SETTING: A MYTH ?

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Submitted in partial fulfillment of the academic requirements for  
the degree of MMed in the Department of Surgery  
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As the candidate's supervisor I have approved this thesis for submission.

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Date: 2018-10-29



## DECLARATION

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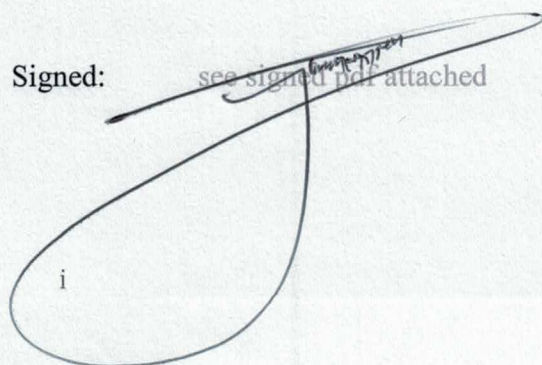
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KEM

King Edward VII Hospital

RAC

Early laparoscopic cholecystectomy

DRX

Delayed laparoscopic cholecystectomy

OC

Open cholecystectomy

YCGU

Yokohama City University School of Medicine



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## **Overview of The Dissertation**

Laparoscopic cholecystectomy is the gold standard surgical management for acute cholecystitis (AC). Controversy exists regarding the optimal timing to perform laparoscopic cholecystectomy in AC. The Tokyo consensus guidelines 2013 (TCG13) are the most widely used and accepted management guidelines in acute cholecystitis. These guidelines advocate early laparoscopic cholecystectomy (ELC) in patients presenting within 72 hours of onset of symptoms of acute cholecystitis. This has several advantages such as sorting the patient's problem during the first admission, decrease in overall hospital costs by avoiding a second admission and averting possible occurrence of gallstone related complications whilst awaiting delayed cholecystectomy. Traditionally a delayed cholecystectomy has been the preferred approach in acute cholecystitis with a theoretical advantage of avoiding a cholecystectomy in acutely inflamed tissues thereby avoiding complications of major ductal or vascular injuries. It has been shown in several studies however that morbidity, mortality and conversion rates are similar in early laparoscopic cholecystectomy and in delayed laparoscopic cholecystectomy.

There are only a handful of studies from the developing world regarding management and the timing of intervention in acute cholecystitis. We therefore studied our profile of patients and compare these to the patient populations commonly cited in literature mostly from first world countries. Late presentation outside the window for early intervention, limited availability of transport to a health care facility with expertise to perform laparoscopic cholecystectomy, limited diagnostic modalities like ultrasound and limited laparoscopic services are amongst the common challenges faced by developing countries. This may potentially exclude a large number of patients for consideration for early laparoscopic cholecystectomy.

This is a retrospective chart review looking at all adult patients who were 18 years and older who presented to King Edward VIII in South Africa between 01 January 2013 and 31 December 2013, who have a confirmed diagnosis of acute cholecystitis and had a cholecystectomy. Data was retrieved from the patients' admission and in-patient files and theatre records. Diagnosis was established using clinical and laboratory criteria and a confirmatory ultrasound, as per the TCG13. We looked at the time of presentation to the health care facility from the initial onset of symptoms of acute cholecystitis, patient demographics, type of operation i.e. laparoscopic or open surgery,



reasons and rate of conversion from laparoscopic to open surgery, time taken from initial presentation to time of operation. All patients meeting the inclusion criteria were included in this study. A total of 176 files were evaluated and 139 of them had complete records for inclusion in the study.

Findings from this study showed that the majority of patients present late i.e. after 72 hours and after 7 days of onset of symptoms when using the two commonest definitions of early presentation. A delayed laparoscopic cholecystectomy was the most commonly performed surgical intervention for acute cholecystitis. It was shown to be a safe option and was associated with low morbidity and mortality. In low income settings DLC still has a significant role in the management of acute cholecystitis despite the current recommendations of ELC in acute cholecystitis. Clinicians in low income settings with limited radiologic and laparoscopic services can use the results of this study in managing patients who present outside the window for ELC.

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## Part 1: Literature Review

Acute cholecystitis (AC) is inflammation of the gallbladder. In 90% to 95% of cases it is secondary to gallstones. Few cases (<1%) are due to tumour obstructing the cystic duct. Obstruction of the cystic duct is the initiating event leading to gallbladder distention, inflammation and gallbladder wall oedema. Secondary bacterial contamination of bile is present in 30-50% of patients undergoing cholecystectomy for acute cholecystitis. <sup>[1]</sup> See figure 1.



Fig 1. Ultrasound picture of calculous cholecystitis

Acute cholecystitis begins as an attack of non-remitting, non-subsiding biliary colic that may persist for several days. It usually presents as right upper quadrant pain with a positive Murphy's sign (an inspiratory pause on palpation of the right upper quadrant). A positive Murphy sign is extremely sensitive (97 %) and predictive (PPV 93 %) for acute cholecystitis. <sup>[2]</sup> The pain is often associated with nausea and vomiting, patients may have fever and are systemically unwell. Patients may be febrile, have a raised white cell count usually 12-000 to 15-000 cells/mm<sup>3</sup> and a raised C – reactive protein level. Liver function tests are usually normal, however there may be a mild elevation of serum bilirubin, alkaline phosphatase and transaminases. Ultrasonography is the most useful radiologic investigation in diagnosing acute cholecystitis, with a sensitivity and specificity



of 95%.<sup>[3]</sup> Biliary scintigraphy (HIDA scan) may be utilised in atypical cases when diagnosis remains in doubt after ultrasound. It is highly sensitive and specific for acute cholecystitis.<sup>[4]</sup> CT scan is not routinely used in diagnosing acute cholecystitis.

Complications of untreated acute cholecystitis include gangrenous cholecystitis, gallbladder perforation and cholecysto-enteric fistulas. Management for acute cholecystitis involves giving intravenous fluids, keeping patients nil per mouth, adequate analgesia, intravenous antibiotics, treatment for related complications and ultimately definitive surgery. Laparoscopic cholecystectomy is the gold standard surgical management for AC.<sup>[5,6]</sup>

There is an on-going debate regarding optimal timing of cholecystectomy in AC. Definitive surgery can either be early or delayed. Early cholecystectomy is variably defined as operation within 24 hours, 72 hours or within 7 days of onset of symptoms whilst interval cholecystectomy is defined as surgery 6 to 12 weeks from the initial onset of symptoms. The timing of surgery depends on the time the patient presents to a health care facility with the expertise and resources to optimally manage acute cholecystitis. The most widely used guidelines are the Tokyo 2013 consensus guidelines (TCG13).<sup>[7]</sup> According to these guidelines, laparoscopic cholecystectomy should be done within 72 hours of symptom onset. In mild acute cholecystitis, early laparoscopic cholecystectomy is advocated and only if this is not possible should the patient be offered a delayed or interval laparoscopic cholecystectomy 6 weeks following success of supportive medical treatment. For disease of moderate severity early laparoscopic cholecystectomy is advised if advanced laparoscopic skills are available or else a delayed laparoscopic cholecystectomy should be done. If the patient with moderate disease cannot be offered an ELC and does not settle on conservative medical management, an urgent open cholecystectomy is advised. For severe acute cholecystitis which is characterized by organ dysfunction, percutaneous gallbladder drainage as an initial measure is advocated followed by DLC in 6 to 12 weeks.

Open and laparoscopic cholecystectomy have been found to be comparable procedures in terms of morbidity and mortality.<sup>[8]</sup> Many studies have shown that there is a slightly higher incidence of bile duct injuries in laparoscopic cholecystectomy compared to open cholecystectomy.<sup>[9]</sup> The rate of bile duct injuries tends to be higher during the early part of a surgeon's career and has been attributed to the learning curve effect.<sup>[10]</sup> Laparoscopic cholecystectomy has proven beneficial in reducing analgesic requirements, hospital costs, length of time away from work and no increased



risk of complications compared to interval cholecystectomy. <sup>[11,12]</sup> A population-based analysis involving 4 113 patients with acute cholecystitis showed the benefits of doing cholecystectomy in the acute presentation within the first 24 to 72 hours of onset of symptoms. The early procedure offered the convenience of sorting the patient's problem during a single admission. <sup>[13]</sup> Some studies have looked at the outcomes of offering laparoscopic cholecystectomy in a resource-constrained setting and found no greater morbidity or mortality encountered with the procedure in resource-limited countries where laparoscopic services are extremely limited. <sup>[14]</sup>

### **Problem statement**

Added to the challenges of limited radiologic and laparoscopic services is the reality that the majority of patients present late outside of the recommended period for early laparoscopic cholecystectomy. At what cost should we then continue to offer delayed laparoscopic cholecystectomy to this group of patients?

### **Research question**

Is early laparoscopic cholecystectomy for acute cholecystitis feasible in a low income setting?

### **Gaps in the literature**

More studies are needed to get a better perspective on the feasibility of early laparoscopic cholecystectomy in a low income setting where late presentation is the norm. Further studies are needed to interrogate reasons why patients present late following onset of symptoms for acute cholecystitis.

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## **Part 2: A Submission Ready Manuscript**

**Title:** Early Cholecystectomy Operations for Acute Cholecystitis in A Low Income Setting: A Myth?

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**Conflict of Interest:** none



## **Abstract**

### **Introduction**

Current literature advocates early laparoscopic cholecystectomy (LC) for acute cholecystitis (AC) given the advantages of resolving the pathology in one sitting, decreasing hospital costs with no increase in morbidity and mortality and the safety of the procedure. This study reviewed the patient population in a low income setting where the majority present late to services with limited laparoscopic services resulting in the majority of patients presenting outside the window for early intervention.

### **Methods**

Adult patients admitted to surgical wards in regional state hospital with a diagnosis of AC were included in the study. The admission, operation and discharge records were used to collect data. The severity of the cholecystitis, the time taken to present to the referral facility the time taken to present to our regional hospital, time to operation, type of operation, conversion rates and complications were evaluated.

### **Results**

A total of 139 patients met the inclusion criteria. The mean age was  $47 \pm 13.4$  years (range 19 – 74) and were mostly females (86.3%). Early presentation was in 14.4 % of patients when using the 72 hour definition of early presentation and 49.6 % when using the 7 day definition. A median of 64 days from admission time to operative intervention was noted. All patients were considered for LC; there was a conversion rate of 25.6%. No major or minor complications were documented.

### **Conclusion**

Interval laparoscopic cholecystectomy is a safe and a consistently reliable option. It should be considered in developing countries with low income with similar patient cohorts as ours.

**Keywords:** Acute cholecystitis, early cholecystectomy, interval cholecystectomy, delayed cholecystectomy, developing world



## **Introduction**

The management of acute cholecystitis currently is guided by the latest Tokyo consensus guidelines 2018. Early laparoscopic cholecystectomy (ELC) (within 72 hours of onset of symptoms) is regarded as the standard of care for patients presenting with acute cholecystitis (AC) since it has better outcomes when compared to delayed or interval laparoscopic cholecystectomies (DLC). However, this “standard of care” is mostly drawn from results from higher income countries where patients present early to institutions that are equipped to make a diagnosis of AC and manage the patients timeously.

In low income countries like South Africa early presentation is difficult due to financial constraints, lack of infrastructure and poor access to appropriate health services. Furthermore, only a few regional and central hospitals offer laparoscopic cholecystectomy (LC). Often patients must first be attended to at local clinics, community health centres and local district hospitals before being transferred to the larger centres where the operation can be offered. Delay in diagnosis of AC due to a lack of ultrasound facility at these referral facilities further delays the appropriate referral and serve to highlight some of the challenges pertaining to ELC in this setting.

This study reviews these challenges and reports the incidence of delayed presentation of AC and its management strategy in comparison to that advocated in the literature.

## **Methods**

A chart review was conducted over a 12 month period between January to December 2013 at King Edward VIII Hospital (KEH), Durban, KwaZulu-Natal (KZN). All adult patients aged 18 years and older admitted with a diagnosis of AC were included. Diagnosis was made on clinical, laboratory findings and was supported by sonographic evidence of AC.

The admission notes, operative details and discharge notes of all patients with confirmed diagnosis of AC were reviewed to document the patients’ demographic details, the time of onset of symptoms, severity of cholecystitis and date of first presentation to referral facility.



The date of presentation, distance from referral centre to KEH, reason for delayed presentation, proposed operation type (laparoscopic or open), timing of operation from time of presentation, time duration of operation in minutes, conversion from laparoscopic to open procedure, and major and minor complications, were also documented.

For all patients the severity of AC was graded according to the 2013 Tokyo consensus guidelines, as follows.

- A severe grade was the presence of organ failure
- A moderate grade was the presence of a WCC > 18 000, a palpable tender right upper quadrant mass, duration of symptoms > 72 hours or marked local inflammation such as gangrenous or emphysematous cholecystitis.
- A mild grade was the absence of organ failure and presence only of mild inflammation.

All patients with missing data were excluded. All data was entered into an Excel spreadsheet.

IBM SPSS version 24 was used to analyse the data. A p value <0.05 was considered as statistically significant. Continuous variables which were not normally distributed were compared using Spearman's correlation analysis and relationships displayed graphically using scatterplots. Comparisons between not normally distributed paired variables were done using non-parametric Wilcoxon signed ranks tests. Factors were entered into the model one at a time and assessed for significance using the Wald statistic. Odds ratios and 95% confidence intervals were reported.

Full ethical approval was obtained from the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (ref no. BE347/14) and permission to conduct research obtained from the KZN Department of Health's Research Unit and the KEH Management.



## Results

One hundred and thirty nine patients were studied. One hundred and twenty patients were female (86,3%) and 19 patients were male (13,7%). The mean age was  $47 \pm 13.4$  years with a range from 19 to 74 years. The average symptom duration (from initial onset) before presentation to a nearest health care facility was 16,6 days, the average symptom duration (onset of symptoms) before presentation to KEH was 20 days. The average distance from referral centres, where patients initially presented, to KEH, was 31,62 km with a range from 1,8 km to 197 km. When using the 72 hour definition for late presentation, 85,6% of patients qualified as late presentations to KEH and when using the 7 day period to define late presentation, 50.3% patients qualified as late presentations. The majority of reasons for late presentations were not documented; transport issues from rural areas, no guardians for children that will be left behind at home and affordability for travel and delay in diagnosis at referral centres were amongst the documented reasons for late presentations. Ninety four percent of patients presented with mild cholecystitis and the remaining 6% had moderate disease severity. There were no patients presenting with severe cholecystitis. The majority of patients had one admission before operation (80.6%). The readmission rate whilst awaiting DLC was 19.4%. There were 21 patients who had a total of 2 admissions and 3 patients had 3 admissions, 1 of whom was a defaulter. (table1)

All but one patient underwent interval cholecystectomies even those presenting within 72 hours to a week reason being the lack of availability of an emergency theatre at King Edward (see discussion). The average number of days from admission to operation was 62 days. Of the 139 patients, 117 patients were booked upfront for LC; the remaining 22 were booked upfront for open cholecystectomies (OC) indication being previous open abdominal surgery and not for reasons related to timing of presentation. Of the 117 LC's undertaken, 87 (74,36%) were completed laparoscopically and 30 (25,6%) were converted to OC. Documented reasons for conversion were dense adhesions, unclear anatomy, inability to achieve Strasberg's critical view of safety, gallbladder perforation with gross stone spillage, empyema and excessive bleeding from liver bed. The average time for LC was 80,2 minutes (range 25 to 180min). The average time taken for the 22 OC was 80 minutes (range 30 to 150min). The average hospital stay time post interval cholecystectomy was 48 hours. There were no major or minor complications. (table 2)



Age		N %
<20 years		1 (0.7)
20 – 40		46 (33)
41 – 60		63 (45.3)
>60 years		29 (21)
Gender		
Male		19 (13.7)
Female		120 (86.3)
Referring Institute		
Self		32 (23)
Clinic		61 (44)
District hospital		46 (33)
Duration of symptoms		
0– 3 days		20 (14.4)
3– 7 days		49 (35.3)
>7 days		70 (50.3)
Distance from KEH		
<5 km		16 (11.5)
5 – 10 km		60 (43.2)
11 – 15 km		12 (8.6)
16 – 20 km		30 (21.6)
>20 km		21 (15.1)
Admissions Before operation		
1		112 (80.6)
2		24 (17.3)
3		3 (2.1)
>3		0 (0)

Table 1. Demographic and Clinical Data of patients diagnosed with AC



<b>Timing of Surgery</b>		<b>N (%)</b>
Early		1 (0.72)
Interval		138 (99.28)
<b>Disease Severity</b>		
Mild		131 (94)
Moderate		08 (06)
Severe		0 (0)
<b>Surgical option</b>		
laparoscopic		117 (84.2)
open		22 (15.8)
<b>Conversions to Open Surgery</b>		30 (25.6)
<b>Length of hospital stay</b>		
1– 3 days		114 (82)
4– 7 days		21 (15)
>7 days		04 (03)
<b>Operative time</b>		
Laparoscopic		80.2 ± 30.5 minutes
Open		80 ± 31 minutes

Table 2. Surgical procedures and outcomes

## Discussion

The gold standard of management of acute cholecystitis is a laparoscopic cholecystectomy.<sup>[1]</sup> The timing of this operation however depends largely on 2 variables, namely time of presentation and the severity of the cholecystitis.



Timing of cholecystectomies can be undertaken either early (early cholecystectomy) following symptom onset and presentation or can be delayed (also called interval cholecystectomy) i.e. after the acute episode has settled and the patient has been discharged to return for an elective LC.

In current literature there is no standard definition of what constitutes an early cholecystectomy. Early cholecystectomy has been variably referred to a cholecystectomy undertaken anywhere within 24 hours to within 10 days of onset of symptoms, but never more than 10 days. The most widely quoted time intervals within this range is 24 hours, 72 hours and 7 days from onset of symptoms.

Definitions for delayed or interval cholecystectomy generally refer to intervention anytime between 10 days and 45 days, but may be as long as 12 weeks after initial symptom onset.<sup>[2]</sup> However cholecystectomies within this time (10 days and 45 days) should be avoided, as the adhesions from inflammation is most dense, resulting in higher morbidity and prolonged hospital stays (5 days longer) when compared to both early cholecystectomies (less than 10 days) and interval cholecystectomies (more than 45days).<sup>[3]</sup> The conversion rates however are comparable. The debate thus surrounds early cholecystectomy (within 10 days of onset of symptoms) and delayed cholecystectomy (after 45 days of initial symptom onset).

ELC was initially contraindicated in acute cholecystitis, in contrast to patients with uncomplicated gallstone disease without cholecystitis.<sup>[4]</sup> Reasoning was justifiable with studies revealing early cholecystectomies being associated with a much more challenging surgical operation during the acute inflammatory process and consequently longer operative times and a trend towards more bile duct injuries, the most feared complication in laparoscopic cholecystectomy.<sup>[5]</sup> This however has not been universally accepted and several studies have refuted these assertions.<sup>[6]</sup>

In 2013, the Tokyo consensus and numerous other internationally well recognized studies advocated that ELC be the standard of care for patients presenting early with acute cholecystitis. A meta-analysis of 5 out of 6 randomised control trials showed similar complication and conversion rates when comparing early vs interval cholecystectomies, with a shorter hospital stay by 4 days in the early group.<sup>[7]</sup> A separate trial (not included in this meta-analysis ) showed similar results.<sup>[8]</sup> Of these early cholecystectomies (performed within 10 days), one study showed that the



earlier the operation, the shorter the hospital stay.<sup>[9]</sup> Another large database including 95000 patients showed the earlier the operation within this time period (10 days), the fewer the complications.<sup>[10]</sup> Similar results were revealed in a population based analysis involving 4 113 patients with acute cholecystitis which showed the benefits of doing cholecystectomy in the acute presentation within the first 24 hours of onset of symptoms.<sup>[11]</sup>

The early procedure offers the convenience of resolving the patient's pathology during a single admission. This approach has proven beneficial in reducing hospital costs, low conversion rates, reducing length of time away from work and does not increase the risk of complications compared to delayed intervention.

Despite evidence pointing to a better overall outcome with early cholecystectomy, a recently published local study in a nearby regional hospital concluded that most patients (88,2%) had presented late (>72hours) and thus had DLC, however complications were similar to other reports.<sup>[12]</sup> The findings in our study reveal very similar results with 85,61% of patients presenting late (>72hours), all of whom underwent delayed cholecystectomies. With a post op average hospital stay of 48hours and no major or minor complications, a conversion rate of 25,6% and an average laparoscopic cholecystectomy time of 80,2 min these are comparable to values quoted in early cholecystectomies.

Despite a high re admission rate of 19,4%, in a community where late presentation is the not uncommon, the cost of this high re admission rate can arguably be offset with the cost of prolonged hospital stay if attempting same admission cholecystectomies on these late presentations. This was reported in a study comparing same admission verses delayed cholecystectomy for delayed presentation patients. They concluded that DLC provide lower conversion rates and shorter length of stay in acute cholecystitis patients presenting beyond 7 days of symptoms and that this group of patients should be offered DLC. <sup>[13]</sup>

Furthermore in low income settings such as ours, the hospital at all times has a single emergency operating room run by 2 emergency nursing teams and a single anaesthetist. This single emergency operating room covers all general surgery emergencies, trauma emergencies, gynaecological emergencies, ENT emergencies, urological emergencies and orthopaedic emergencies. Thus cases



like gunshot abdomens, acute appendicitis and ectopic pregnancies take precedence over patients presenting with mild to moderate cholecystitis. For these reasons early cholecystectomy is not feasible even for the few patients that do present early and from the favourable results revealed in this review of our delayed cholecystectomies, this type of approach is safe in low income setting.

## **Conclusion**

In many developing countries complex technology is not readily available and laparoscopic services are extremely limited. <sup>[14]</sup> Our practice is contrary to the recommendation that ELC be the procedure of choice in AC since the majority of our patients present late. Notwithstanding this, this review demonstrates that DLC in our resource constrained developing country is still feasible and safe despite most first world countries demonstrating ELC to be superior. Pursuing guidelines proposed by first world countries to developing world populations may not always be feasible and may be dangerous to overall patient outcome. DLC still remains the most widely used option in most developing world countries despite the benefits associated with ELC. This is also true for most surgeons throughout the world surprisingly. <sup>[15]</sup> DLC is a safe and a consistently reliable operative intervention with acceptable conversion rates and low morbidity and should be considered in developing world countries with similar patient cohorts as ours.



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## **APPENDICES**

### **APPENDIX 1: THE FINAL STUDY PROTOCOL**

## **RESEARCH PROTOCOL FOR**

**DR G. M. MAKITINI**

**Dept: GENERAL SURGERY**

**Student No.: 963071082**

**Supervisor: Mr S. MEWA KINOO**

**Co- supervisor: Prof B. SINGH**

**2014 first semester**



## **1. TITLE**

"A Retrospective Chart Review of Early cholecystectomy in acute cholecystitis in the Third World: A MYTH

## **2. AIM**

The aim of this study is to determine the prevalence of early cholecystectomy operations performed for acute cholecystitis in King Edward VIII, a tertiary hospital in KwaZulu-Natal.

## **3. Specific Objectives**

- To describe the demographic profile of patients presenting to KEH VIII diagnosed with acute cholecystitis
- To describe and compare time to presentation, onset of symptoms and time of cholecystectomy
- To identify any factors contributing to the late presentation, e.g. transport delays or delay from referral institution to KEH VIII
- To ascertain the number of repeat admissions while waiting for interval cholecystectomy

## **4. Literature Review**

Acute cholecystitis is inflammation of the gallbladder. In 90% to 95% of cases it is secondary to gallstones. Few cases (<1%) are due to tumour obstructing the cystic duct. Obstruction of the cystic duct is the initiating event leading to gallbladder distention, inflammation and gallbladder wall oedema. Secondary bacterial contamination of bile is present in 30-50% of patients undergoing cholecystectomy for acute cholecystitis<sup>1</sup>.

Acute cholecystitis begins as an attack of non-remitting, non subsiding biliary colic that may persist for several days. It usually presents as right upper quadrant pain with a positive Murphy's sign. Patients may be febrile, have a raised white cell count usually 12,000-15,000 cells/mm. Liver function tests are usually normal, however there may be a mild elevation of serum bilirubin, alkaline phosphatase and transaminases. In complicated cases there are many more abnormalities depending on the cause. Ultrasonography is the most useful radiologic investigation in diagnosing acute cholecystitis, with a sensitivity and specificity of 95%<sup>1</sup>. HIDA scan may be



utilised in atypical cases as it can exclude acute cholecystitis. It is highly sensitive and specific for acute cholecystitis<sup>1</sup>. CT scan is not routinely used in diagnosing acute cholecystitis as it is less sensitive than ultrasonography and may not be readily available in all centres.

Standard management is intravenous fluids, adequate analgesia, intravenous antibiotics, treatment for related complications and definitive surgery. Definitive surgery can either be early or delayed. Traditionally, early intervention refers to definitive cholecystectomy within 72 hours of onset of symptoms, whereas delayed or interval cholecystectomy refers to intervention 6 to 10 weeks after initial onset of symptoms. The surgery is either done laparoscopically or by the open approach.

Acute cholecystectomy is the definitive treatment for acute cholecystitis<sup>2,3</sup>. According to the Tokyo consensus guidelines and numerous other internationally well recognized studies it is now widely accepted that early cholecystectomy be the standard of care for patients diagnosed with acute cholecystitis i.e. intervention within the first 72 hours of onset of symptoms<sup>2</sup>. This approach has proven beneficial in reducing hospital costs, reducing length of time away from work for patients, and has no increased risk of complications compared to delayed intervention<sup>5</sup>. A population based analysis involving 4 113 patient with acute cholecystitis was conducted which clearly showed the benefits of doing cholecystectomy in the acute presentation within the first 24 to 72 hours of onset of symptoms. Results of this study confirm similar conclusions as in the Tokyo guidelines. The early procedure offers the convenience of sorting the patient's problem during a single admission<sup>3</sup>.

Central to advocating early cholecystectomy is the time duration of presentation, from the onset of symptoms, to the health care facility with resources to offer cholecystectomy. In Third world countries like South Africa, only a few regional and central hospitals offer cholecystectomies. This often means that patients must first be attended to at local clinics, Community Health Centres and local hospitals before being transferred to the larger centres where the services of general surgeons and gastroenterologists are offered. What further compounds the delay in diagnosis is the fact that even basic investigations required to make the diagnosis of acute cholecystitis such as abdominal ultrasonography, are often not available. Even in those facilities where ultrasound is available, there is no 24 hour radiological service. Further, many of the patients using our facility rely solely on public transport and state ambulance services. This has a direct impact on the clinical management decision regarding timing of definitive surgery. All these factors make it more difficult to pursue a policy of early cholecystectomy in acute cholecystitis in the Third World. Most of the studies on this subject do not consider any of the above factors and most of the studies are done in First world countries. Considering the above factors, clearly, early cholecystectomy cannot be the only option in our part of the world.

Currently, in our setting, interval cholecystectomy is the procedure most commonly performed for acute cholecystitis. It is primarily performed laparoscopically or by the open approach. This study aims to show that in a third world setting like ours, interval



cholecystectomy cannot be ruled out as most of our patients do not present within the window period when early cholecystectomy can be performed.

## **KEY REFERENCES**

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## **STUDY DESIGN**

A simple descriptive study

## **STUDY POPULATION**

All adult patients admitted with a diagnosis of acute cholecystitis at all the Surgical wards at King Edward VIII hospital during the period 2013 (January 1<sup>st</sup> to 2013 December 31<sup>st</sup>).

## **SAMPLING STRATEGY**

-All patients admitted with diagnosis of acute cholecystitis who meet the inclusion criteria during the study period will be included

## **STATISTICAL PLANNING (variables/confounders)**

1. Age, gender, race and employment status of all patients in the study



2. Time from onset of symptoms to presentation to hospital (in hours and days)
3. Estimate of time to confirmation of diagnosis to transfer to KEH VIII
4. Transport mode used to get to health care facility, either private, public or state ambulance service
5. Operation performed i.e. early vs interval cholecystectomy
6. Referral pattern

### **SAMPLE SIZE**

-all patients admitted with a diagnosis of acute cholecystitis during the study period who meet the inclusion criteria (approximately 50 patients)

### **INCLUSION CRITERIA**

Adults between 16 years of age and older

Diagnosis of cholecystitis confirmed by sound clinical assessment and radiologic findings

Patients admitted within the study period i.e. 2013 January 1<sup>st</sup> to 2013 December 31<sup>st</sup>.

### **EXCLUSION CRITERIA**

Situations where diagnosis is ambiguous/diagnostic dilemma

### **DATA COLLECTION METHOD AND TOOLS**

-admission books in all the surgical wards will be used to get patient file numbers, files will then be collected from the KEH VIII filing department to access the relevant information

-a data collection sheet will be used to collect the information required



## **DATA ANALYSIS TECHNIQUES**

Data will be analysed using Statistical Package for Social Sciences (SPSS) version 21.

## **STATISTICAL ANALYSIS**

Continuous variables will be summarized using mean, standard deviation and range (minimum-maximum). Categorical data will be represented using frequency distribution tables.

## **7. STUDY LOCATION**

King Edward VIII hospital, Department of Surgery

## **8. STUDY PERIOD**

2013 January 01 to 2013 December 31

## **9. LIMITATIONS TO THE STUDY**

Lack of comparison group

Data collection often incomplete as we rely on available patient charts for information

## **10. ETHICAL CONSIDERATIONS**

-approval will be sought from the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu Natal prior to research being started

-permission will be sought from KEH VIII Hospital Manager, and the Head of clinical Surgery Mr R. Chetty

-all patients medical records will be kept strictly confidential and only viewed by those with permission to do so for the purposes of this study

-this is a retrospective chart review study therefore consent from patients will not be a prerequisite



**APPENDIX 2: THE GUIDELINES FOR THE SOUTH AFRICAN JOURNAL OF SURGERY**

See attached PDF document below.



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**Qualification, affiliation and contact details** of ALL authors must be provided in the manuscript and in the online submission process.

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**Journal references:** Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. *Stat Med* 1998;289(1):350-355. [<http://dx.doi.org/10.1000/hgjr.182>] [PMID: 2764753]

**Book references:** Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101. *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.

**Internet references:** World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: World Health Organization, 2002. <http://www.who.int/whr/2002> (accessed 16 January 2010).

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### **APPENDIX 3: ETHICAL APPROVALS**

See attached PDF documents below.





health

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Reference : HRKM 53/15

KZ\_2015RP49\_740

Enquiries : Mr X Xaba

Tel : 033 – 395 2805

Dear Dr GM Makatini

**Subject: Approval of a Research Proposal**

1. The research proposal titled 'A Retrospective Chart Review of Early cholecystectomy in acute cholecystitis in the Third World: A MYTH' was reviewed by the KwaZulu-Natal Department of Health.

The proposal is hereby **approved** for research to be undertaken at King Edward VIII Hospital.

2. You are requested to take note of the following:
  - a. Make the necessary arrangement with the identified facility before commencing with your research project.
  - b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.
3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to [hrkm@kznhealth.gov.za](mailto:hrkm@kznhealth.gov.za)

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

**Dr E Lutge**

Chairperson, Health Research Committee

Date: 17/03/15





health

Department:  
Health  
PROVINCE OF KWAZULU-NATAL

## OFFICE OF THE HOSPITAL CEO

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www.kznhealth.gov.za

Ref.: KE 2/7/1/ (03/2015)  
Enq.: Mrs. R. Sibiya  
Research Programming

27 January 2015

Dr. G. Makatini  
No. 7 Obberreuter Street  
NEW GERMAY  
3610

Dear Dr. Makatini

**Protocol: A retrospective chart review of early cholecystectomy in acute cholecystitis in the third world: A Myth: Degree Purposes (MMed) School of Clinical Medicine. BREC REF: BE347/14**

Permission to conduct research at King Edward VIII Hospital is provisionally granted, pending approval by the Provincial Health Research Committee, KZN Department of Health.

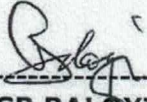
Kindly note the following:-

- The research will only commence once confirmation from the Provincial Health Research Committee in the KZN Department of Health has been received.
- Signing of an indemnity form at Room 8, CEO Complex before commencement with your study.
- King Edward VIII Hospital received full acknowledgment in the study on all Publications and reports and also kindly present a copy of the publication or report on completion.

*The Management of King Edward VIII Hospital reserves the right to terminate the permission for the study should circumstances so dictate.*

Yours faithfully

**SUPPORTED / NOT SUPPORTED**

  
DR. OSIB BALOYI  
ACTING CHIEF EXECUTIVE OFFICER

  
DATE

uMnyango Wezempilo . Departement van Gesondheid

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17 April 2015

Dr Goodman Makatini  
No. 7 Oberreuter Street  
New Germany  
3610  
[mdu.makatini@gmail.com](mailto:mdu.makatini@gmail.com)

Dear Dr Makatini

**PROTOCOL: A retrospective chart review of Early Cholecystectomy in Acute Cholecystitis in the Third World: A Myth: Degree Purposes (MMed) School of Clinical Medicine. BREC REF: BE347/14.**

### EXPEDITED APPLICATION

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 14 July 2014.

The study was provisionally approved pending appropriate responses to queries raised. Your responses received on 13 April 2015 to queries raised on 12 January 2015 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval for all sites for which permission has been granted.

This approval is valid for one year from 17 April 2015. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at <http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx>.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its meeting taking place on 12 May 2015.

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor J Tsoka-Gwegweni  
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee

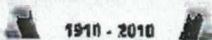
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