Predictors of mortality and morbidity in soft tissue infections of the lower limb – A prospective nested case control study

A dissertation submitted in partial fulfilment of the requirements of M.S (Branch-I) General Surgery examination of the Tamilnadu Dr. MGR Medical University, Chennai to be held in April 2014.

Abstract

TITLE OF THE ABSTRACT: Predictors of mortality and morbidity in soft tissue infections of the lower limb

OBJECTIVES: To assess the various parameters that predicts the mortality and morbidity in patients with soft tissue infections of the lower limb.

METHODS: A nested case control study was designed with a sample size of fifty five in each arm. Patients were recruited and based on the outcome they were grouped under one of the two arms: non mortality, non morbidity arm and mortality, morbidity arm. From the data collected, univariate and multivariate analysis were done to find significant variables predicting mortality and morbidity.

RESULTS: The significant variables that predict morbidity in patients with soft tissue infections are neutrophilia, low sodium and elevated temperature at presentation. The significant variables that predict mortality in patients with soft tissue infections are diabetes mellitus, requirement of ventilator support and requirement of dialysis.

Certificate

This is to certify that the following work titled, 'Predictors of Mortality and Morbidity in Soft tissue infections of the lower limb is a prospective analysis of cases from 2011-2013,' is an original bonafide work by Vijayan.P, resident in General Surgery at CMC Vellore (2011-2014) in part fulfilment of the requirements of the MS General Surgery branch I exam to be held in April 2014.

Signature

Guide	Head of Department	Principal
Dr. Deepak Abraham	Dr. Benjamin Perakath	Dr. Alfred Job Daniel
Professor	Professor and Head	Professor
Endocrine Surgery	General Surgery	Orthopaedics
CMC Vellore	CMC Vellore	CMC Vellore

Plagiarism online checker

turnitin

Your digital receipt

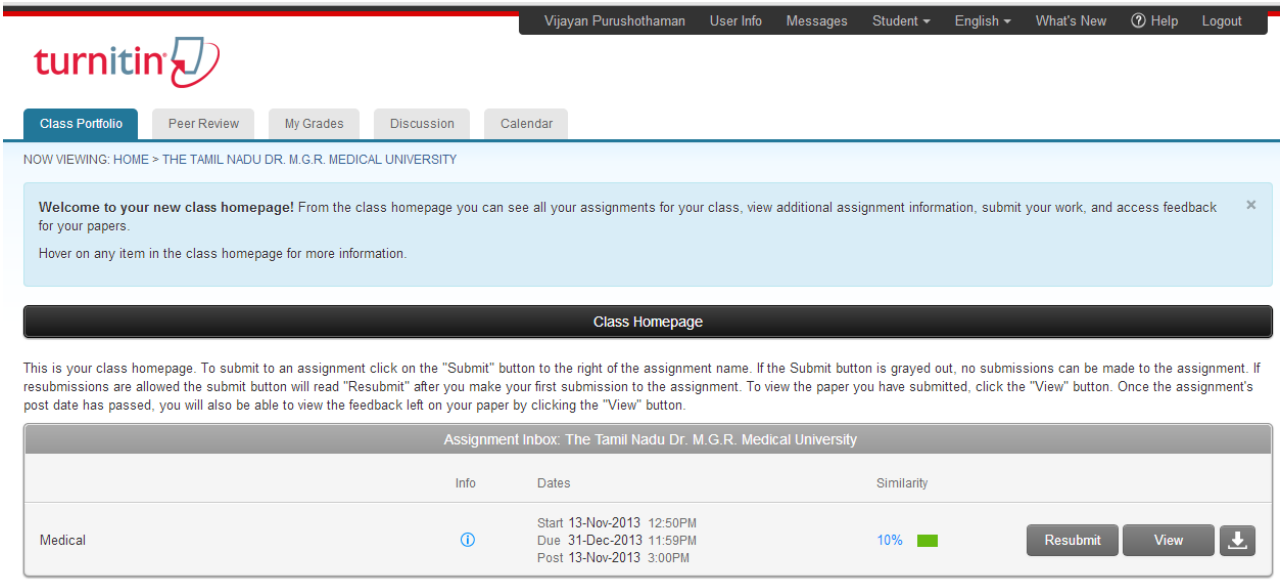
This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

Paper ID	377145981
Paper title	Predictors of mortality and morbidity in soft tissue infections of the lower limb
Assignment title	Medical
Author	Vijayan Purushothaman
E-mail	vijayanpurushothaman@gmail.com
Submission time	25-Nov-2013 08:08PM
Total words	11074

First 100 words of your submission

1. Introduction Soft tissue infections are known to mankind from the times of Hippocrates. Soft tissue infections (STI) are infections of the non skeletal tissue i.e. exclusive of bone, ligaments, cartilage and fibrous tissue. Soft tissue infection affecting the lower extremity comprises of 50% of all soft tissue infection and is one of the most common acute surgical conditions resenting to the emergency department. The incidence of soft tissue infection is about 0.04 per 1000 population in the western world. However the incidence is higher in the developing countries. Despite advances in treatment, the morbidity and mortality rates of soft tissue infection are still high at 25-35%. There...

Copyright 2013 Turnitin. All rights reserved.



Vijayan Purushothaman | User Info | Messages | Student | English | What's New | Help | Logout

turnitin

Class Portfolio | Peer Review | My Grades | Discussion | Calendar

NOW VIEWING: HOME > THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

Welcome to your new class homepage! From the class homepage you can see all your assignments for your class, view additional assignment information, submit your work, and access feedback for your papers.

Hover on any item in the class homepage for more information.

Class Homepage

This is your class homepage. To submit to an assignment click on the "Submit" button to the right of the assignment name. If the Submit button is grayed out, no submissions can be made to the assignment. If resubmissions are allowed the submit button will read "Resubmit" after you make your first submission to the assignment. To view the paper you have submitted, click the "View" button. Once the assignment's post date has passed, you will also be able to view the feedback left on your paper by clicking the "View" button.

Assignment Inbox: The Tamil Nadu Dr. M.G.R. Medical University

	Info	Dates	Similarity	
Medical	ⓘ	Start 13-Nov-2013 12:50PM Due 31-Dec-2013 11:59PM Post 13-Nov-2013 3:00PM	10%	Resubmit View

IRB approval letter

Dept. of Biostatistics

Christian Medical College,
Vellore 632 002.

Ref: Res/10/2011

November 21, 2011

The Treasurer
CMC.

Sub: **FLUID Research grant project NEW PROPOSAL**:
Predictors of Mortality and Morbidity in Soft tissue infections of the Lower limbs – A prospective cohort study
Dr. Vijayan . P, PG Registrar, Assistant, Surgery, Dr. Deepak Abraham, Endocrine Surgery, Dr. Inian Samarasam, Surgery,Dr. Paul. M. J, Dr. Pooja Ramakanth,Endocrine Surgery, Dr. Subramani, Dr. Vinodh M. P, Surgical ICU

Ref: IRB Min. No. 7588 dated 07.09.2011

The Institutional Review Board at its meeting held on September 7, 2011 vide Min. No.7588 accepted the project for 1 year at a total sanction of ₹ 70,000/- (Rupees Seventy thousand only). Kindly arrange to transfer the sanctioned amount to a separate account to be operated by Drs. Vijayan and Deepak Abraham.

Thank you.

Yours sincerely,

Dr. Alfred Job Daniel
Principal & Chairperson (Research Committee)
Institutional Review Board

CC: Dr. Vijayan P, PG Registrar, Department of Surgery, CMC (Emp No. 29019)
Dr. Deepak Abraham, Department of Surgery, CMC
File

Acknowledgements

I would like to place on record my gratitude to the following without whom, this work would not have been possible:

Dr. Deepak Abraham (Professor, Endocrine Surgery) guide, mentor and role model: for all that he has taught me and the support during the study in making this work see the light of day.

Mrs. Gandhimathi, my mother, mentor, guide, friend and teacher for her unconditional love, support and sacrifice at every stage in life without whom I would not be where I am at present.

Dr. Kirthi Sathyakumar, my friend, for her unconditional support and encouragement during my days of difficulty.

CMC Vellore and all my teachers, for making this study and this course a reality.

I would like to express my gratitude to all the patients for their participation despite the burden of their illness. Their fortitude makes our problems seem small.

Last but not least, God for his abundant grace.

Contents

Chapter 1

Introduction

1. Introduction

Soft tissue infections are known to mankind from the times of Hippocrates. Soft tissue infections (STI) are infections of the non skeletal tissue i.e. exclusive of bone, ligaments, cartilage and fibrous tissue.

Soft tissue infection affecting the lower extremity comprises of 50% of all soft tissue infection and is one of the most common acute surgical conditions resenting to the emergency department. The incidence of soft tissue infection is about 0.04 per 1000 population in the western world. However the incidence is higher in the developing countries. Despite advances in treatment, the morbidity and mortality rates of soft tissue infection are still high at 25-35%.

There are various factors associated with these infections. Most common factor is diabetes mellitus. The various other factors associated with STI's are drug abuse, obesity, immunosuppression, recent surgery, malignancy, trauma etc.

Soft tissue infections are of two subtypes: necrotising and non-necrotising infections. Based on the depth of infection it can be further classified as cellulitis, adipositis, fasciitis and myositis.

When classified according to the microbial source of infection, soft tissue infection can be grouped as

Type I	due to polymicrobial source of infection
Type II	due to monomicrobial source of infection
Type III	due to vibrio vulnificus
Type IV	due to fungus

Most common organisms causing soft tissue infections are Group A Streptococci in the developed countries. However polymicrobial source is the most common infection in the developing countries.

Clinical presentation can range from superficial erythema, induration and oedema as in non necrotising infection to myonecrosis as in necrotising soft tissue infections. Patient may also have systemic illness if bacteraemia is present.

The microorganisms enter the tissue through external injury or directly from a perforated viscus. These organisms track along the subcutaneous planes producing endotoxins and exotoxins that cause ischaemia of tissues leading to liquefactive necrosis and often systemic illness. Local inflammation causes thrombosis of the capillaries causing skin necrosis. Infections can spread as fast as 1 – 4 inch per hour with little external changes. As these tissues are necrotic, there is not enough antibiotic supply to this tissue, hence surgical debridement is the mainstay of treatment. An inexperienced surgeon may not identify these skin lesions to be significant causing considerable delay in diagnosis. This leads to systemic illness causing high morbidity and mortality.

There are no standard criteria to predict soft tissue infection and its severity. The LRINEC (Laboratory Risk Indicator for Necrotising fasciitis) score is based on laboratory indicators. This was a retrospective study done on a subset of patients with type III infection which is very uncommon in our setting.

There were various factors identified to predict morbidity and mortality in soft tissue infection but review of studies done in soft tissue infections of the lower limb showed that they were all retrospective studies with varying conclusions and limitations. In addition, there are no studies reported from Indian institutions looking at this common but significant problem.

Hence we need an objective method to predict the severity of soft tissue infection to initiate the appropriate treatment as early as possible to reduce the morbidity and mortality associated with this disease.

Hence we propose this prospective study to analyse various variables (historical, clinical and laboratory) to identify predictors of morbidity and mortality in soft tissue infections.

These variables can be used to assess the severity of infection. If significant, appropriate therapy can then be initiated to improve outcomes of patients suffering from this condition.

Chapter 2

Aim of the study

2. Aim of the study

To assess the various parameters that predict the mortality and morbidity in patients with soft tissue infections of the lower limb.

Chapter 3

Review of literature

3. Review of literature

3.1.0. Definition:

Soft tissue infections are defined as infections of the non skeletal tissue i.e. exclusive of bone, ligaments, cartilage and fibrous tissue(1).

3.2.0. History:

Soft tissue infections are known to mankind from the days of Hippocrates(2). Later it was described as hospital gangrene by British surgeons. Dr. Joseph Jones described the disorder in a large group of patients with a mortality of 46%. This was later described by French and American surgeons. This was called by different names as necrotising erysipelas, Streptococcal gangrene, Suppurative fasciitis. The term necrotising soft tissue infections was coined by Dr. Wilson in 1951(2). Necrotising soft tissue infection (NSTI) now represents a disease spectrum that ranges from necrotising cellulitis to myonecrosis.

3.3.0. Epidemiology:

The overall incidence of necrotising soft tissue infection in the United States was reported as 0.04/1000 people or 1000/year (2)(3). There are about 3.5 cases of invasive group A streptococcus infections per 100,000 persons in the United States; necrotising infections make up approximately 6 percent of these cases (4). In New Zealand, the incidence increased from 0.18 to 1.68 per 100,000 per year between 1990 and 2006 (5). In New Zealand the prevalence was similar among different ethnic groups, but the mortality was greater among older adults and native Pacific Islanders (5). There were also case reports of Clostridium sordellii and C. novyii, causing necrotising soft tissue infections in drug abusers (6). Most of the cases were community acquired whereas 20 percent was hospital acquired.

Despite centuries of knowledge, the cumulative mortality rate of soft tissue infections are still around 25%-35% especially in the necrotising subgroup (3, 7). There needs to be a high index of suspicion for appropriate treatment to be instituted. Delayed recognition is one of the major reasons for increased mortality(7).

Soft tissue infections are more common in the lower extremity, with 50% of infections in the foot and 39% in the leg (7). The other common sites of soft tissue infections are scrotum, head and neck, upper extremity.

There are no studies from India demonstrating the disease burden. In the Christian Medical College and Hospital, a retrospective review of charts in a single unit of the Division of surgery, revealed that there were 71 cases of lower limb soft tissue infections in one year with a morbidity of 40.8 percent and mortality of 5.6 percent.

3.3.1. Associated factors:

There is a higher predilection of this condition in men(8). Diabetes mellitus is also found to have a strong relationship with soft tissue infections, with 75% of the patients with soft tissue infections having diabetes mellitus(8). There is a preceding history of trauma in 40% of patients(8).

The risk factors for necrotising soft tissue infection include diabetes, drug use, obesity, immunosuppression, recent surgery, hepatitis C, malignancy and traumatic wounds(9)(10).

Other risk factors include chronic renal failure, HIV, alcohol abuse, blunt or penetrating trauma, insect bites, surgical incisions, indwelling catheters, chicken pox, vesicles, and perforation of the gastrointestinal tract(2).

3.4.0. Classification:

Soft tissue infections can be classified by various means.

They can be based on necrosis, anatomical, depth of infection and microbiological pattern of infection (2).

Soft tissue infections are classified into two subtypes based on necrosis of the tissues involved as necrotising and non-necrotising infections(2).

3.4.1. Based on depth:

Based on the depth of infection it can be classified as cellulitis, erysipelas, impetigo, adipositis, fasciitis and myositis(2).

a) Cellulitis:

Cutaneous infections include cellulitis, erysipelas, and impetigo. All these are considered to be different presentations of the same condition. Cellulitis means inflammation of the cells just beneath the skin surface. This presents as a painful swelling with associated erythema and tenderness(11).

b) Adipositis:

Adipositis is defined as inflammation of the adipose tissue. This is also called as panniculitis(12).

c) Necrotising fasciitis:

Necrotising fasciitis is defined as soft tissue infection which involves the superficial fascia which also involves the subcutaneous tissue with thrombosis of the cutaneous microcirculation(1, 3).

d) Myonecrosis:

Myonecrosis or necrotising myonecrosis is a rare entity and is defined as inflammation and death of muscle tissues(2). This has been associated with high mortality ranging from 80-100 percent(13).

3.4.2. Microbial source of infection:

Soft tissue infections can be classified according to the organisms isolated on culture(2)(14).

a) Type I STI:

These are due to polymicrobial source of infection. The most common organisms are isolated in this type of infection are Streptococci, Bacteroides, E.Coli, Enterobacter, Klebsiella, Proteus, Acenetobacter baumanii, Enterococcus spp, Pseudomonas aeruginosa.

b) Type II STI:

These are due to monomicrobial source of infection. The most common organism isolated in this type of infection is group A Streptococci and Staphylococcus aureus.

c) Type III STI:

These infections are caused by Vibrio vulnificus. This infection is more common in coastal regions of the tropics.

d) TYPE IV STI:

These infections are caused due to fungus. The most common organisms are Candida, Zygomycotic, Mucor and Rhizopus spp.

3.5.0. Pathophysiology:

The microorganisms enter the skin or subcutaneous tissue through external injury or directly from a perforated viscus. These organisms track along the subcutaneous planes producing endotoxins and exotoxins that cause ischemia of tissues leading to liquefactive necrosis and often systemic illness. Infections can spread as fast as 1 – 4 inch per hour with little external changes(15)(7).

The various exotoxins produced enhance microbial virulence and potentiate the necrosis of the tissues. Increased expression of vimentin potentiates the adherence of group A streptococcus to the tissue and

localises the infection(16). Staphylococcus aureus and Streptococci produce surface proteins M-1 and M-3, exotoxins A, B, C, streptolysin O, and super antigen. The M proteins help the organisms to adhere to tissues and prevent phagocytosis. Toxins A and B damage the endothelium and cause loss of micro vascular integrity. This leads to transfer of plasma, oedema of the tissues and impaired blood flow at the capillary level(17). These toxins, along with streptolysin O, stimulate CD4 cells and macrophages to produce tumour necrosis factor, interleukin-1, and interleukin-6 which potentiate a systemic inflammatory response. Systemic inflammatory response can progress to septic shock, multisystem organ dysfunction, and death (15).

Vibrio vulnificus has capsular polysaccharide which prevents phagocytosis. This along with toxins such as hemolysin, help the organism to overcome the host's immune response(18).

Tumour necrosis factor, released by the host's immune response also injures the vascular endothelium by stimulating neutrophil degranulation. Super antigens stimulate T cells directly, activating complement, the bradykinin-kallikrein system, and the coagulation cascade, thereby worsening small vessel thrombosis and tissue ischaemia(19). Thrombosis is caused by the local hyper-coagualable state, platelet-neutrophil plugging of vessels and increased interstitial pressure together resulting in decreased capillary blood flow to end tissue(19). All these lead to a common pathway leading to tissue ischaemia, impeding the oxidative destruction of bacteria and prevent the adequate delivery of antibiotics.

Although thrombosis of vessels supplying the skin is the key feature in the pathophysiology of NSTI, the extent of tissue damage may be more, as thrombosis of large number of dermal capillaries is needed for skin changes to occur(2).

Super antigens cause massive activation of T-cells, cytokine release, tissue damage and shock. Shock is due to the capillary leak syndrome causing hypotension and disseminated intravascular coagulation due to super antigen production. Hypoalbuminaemia ensues, with oedema, hypotension and respiratory distress syndrome(14).

3.6.0. Microbiology:

Necrotising soft tissue infection can be classified into four types based on the microbiological source of infection. They are

Type I STI	Due to polymicrobial source of infection
Type II STI	Due to monomicrobial source of infection
Type III STI	Due to Vibrio vulnificus
Type IV	Due to fungus

3.6.1. Type I STI:

Type I STI is due to polymicrobial source which comprises of 55-75 percent of cases. The common organisms in Type I STI isolated are anaerobic Streptococci, Bacteroides, Clostridium, Peptostreptococcus, E.Coli, Enterobacter, Klebsiella, Proteus, Acenetobacter baumanii, Enterococcus fecalis, Streptococcal viridians, Acinetobacter baumannii, and Pseudomonas aeroginosa(9)(3)(7).

Type I STI of head and neck involves mouth anaerobes like Fusobacteria, anaerobic Streptococci and Spirochetes(9).

Fournier's gangrene is a Type I STI which may involve E. coli, Klebsiella, Enterococci along with Bacteroides, Fusobacterium, Clostridium, anaerobic or microaerophilic Streptococci(7).

3.6.2. Type II STI:

Type II STI is also known as Group A Streptococcal gangrene which has a monomicrobial source of infection which comprises of 20-30 percent of cases. The most common organism in the type is group A streptococci or other beta-haemolytic streptococci. They are usually isolated alone or with Staphylococcus aureus. There are also reports of community acquired methicillin resistant Staphylococcus aureus (MRSA) as a cause of necrotising soft tissue infections(10).

The other organisms that were isolated alone were Klebsiella pneumoniae, Hemophilus influenza and Vibrio species(3)(20).

Blood cultures of patient with STI's were predominantly grew Methicillin sensitive and Methicillin resistant Staphylococcus aureus and Vibrio species. There were also reports of E.coli isolated in blood(3).

3.6.3. Type III STI:

Type III STI's are caused by Vibrio vulnificus which were responsible for 0.53 cases per 100 000 in Hong Kong in late 1990's. This is associated with raw oyster ingestion and patients with iron overload. Wound contamination with sea water accounts for 25 percent of these cases. Digestive enzymes contribute for its high mortality which is about 30 percent(20).

3.6.4. Type IV STI:

Type IV STI's are due to fungal infection and include STI's due Candida, Zygomycotic, Mucor and Rhizopus spp. Candida usually affects people who are immunocompromised while others can affect immunocompetent people. Fungal infections are usually associated with trauma(14).

Presence of Vibrio species and fungus in wound culture and presence of group A Streptococcus, Aeromonas species and Vibrio species in blood cultures are associated with high mortality(3).

3.7.0. Clinical presentation:

The clinical presentation depends on the type of infection. It can range from superficial cellulitis with no systemic symptoms to necrotising infection which can be life threatening.

3.7.1. Cellulitis:

Cellulitis usually presents with erythema, pain, swelling, tenderness and local warmth. This may have systemic features of infection. Whereas necrotising cellulitis presents with thin, dark, sometimes foul-smelling wound drainage and necrosis of the skin. Crepitus may be observed in the skin (21).

3.7.2. Adipositis:

An area of skin involved with adipositis feels thickened and woody to touch. It may or may not demonstrate discolouration of the overlying skin. There may be reddening or brownish pigmentation. Associated with areas of tenderness. Most often, the affected area appear as raised nodules or lumps under the skin, but may be a plaque or large flat area of thickened skin. When the inflammation has settled, a depression in the skin may be left behind temporarily or permanently.

3.7.3. Necrotising fasciitis:

Necrotising fasciitis is an infection of the fascia and is more prone to destruction due to its poor blood supply. Underlying muscles and superficial tissue involvement is less in the initial period. Pain is out of proportion to the signs. Within 1-3 days the overlying tissues are also affected because of infection and thrombosis of vessels. This leads to cutaneous changes with appearance of bullae (containing thick pink or purple fluid) and frank cutaneous gangrene. The tenderness is less in the involved region as it becomes anaesthetic because of thrombosis of small blood vessels and destruction of superficial nerves in the subcutaneous tissue. The development of anaesthesia precede skin changes and hence helps in identification of necrotising fasciitis(2,14).

3.7.4. Myositis:

Necrotising myonecrosis has similar presentation as necrotising fasciitis. Clostridial myonecrosis is most common and is associated with trauma. Crepitus is present at the site of infection with associated systemic toxicity. Spontaneous myonecrosis is associated with more aero tolerant bacteria. Crepitus may not be present in this type of infection(22).

Non necrotising myositis presents as a painful swelling with induration with no evidence of necrosis predominantly involving the quadriceps. This is mostly due to a viral aetiology(22).

3.7.5. Compartment syndrome:

All the above infections can have marked swelling and oedema. This leads to increase in the tissue pressure which exceeds perfusion pressure within a closed muscle compartment. This leads to impaired venous flow and accumulation of waste products resulting in pain and paraesthesia due to nerve injury. Delayed recognition leads to myonecrosis.

3.7.6. Other clinical presentations:

Patients usually have fever, tachycardia, and features of systemic toxicity, with temperature elevation in the range of 38.9° to 40.5°C (102° to 105°F). Other symptoms include malaise, myalgias, diarrhoea, and anorexia. Patients may present with low urine output due to renal failure or altered sensorium caused by septicaemia. Hypotension may be present initially or develop with disease progression.

Septic shock is one of the common presentations in the Emergency Department which requires aggressive resuscitation with fluids, antibiotics and source control. Patients presenting with shock have a high morbidity. However hypotension on admission did not influence survival(8).

3.8.0. Diagnosis:

The diagnosis of soft tissue infection is a clinical decision but most often missed due to its varied presentation.

A high clinical suspicion along with a detailed history and a thorough examination is required to avoid a delay in diagnosis. Pain is out of proportion and general unwellness of patient should point to a diagnosis of soft tissue infection in the deeper planes. History should involve questions regarding recent overseas travel, seafood ingestion, trivial trauma, insect bites etc. They also should involve co morbid factors like diabetes mellitus, steroid abuse, drug abuse etc.

Examination should be comprehensive to identify features of systemic inflammatory response syndrome (tachycardia, tachypnoea, fever) and skin changes. This may include mild erythema to frank necrosis of the tissues with haemorrhagic bullae and anaesthesia. The extent of the tissues involved need to be identified as it helps in demarcating the surgical margin of debridement(14,23).

'Finger test' is a bed side test which involves an incision of 2 cm under local anaesthesia and inspection of the fascia which in NSTI will be swollen and grey with lack of bleeding and contractility. If 'dishwater' fluid is found and the index finger dissects the subcutaneous tissue off the deep fascia easily along the tissue plane, the finger test is considered positive(20).

Compartment pressure monitoring can be done to diagnose acute compartment syndrome. Normal compartment pressure at rest is 30-45 mm of Hg. Any compartment pressure more than 30 mm of Hg needs emergency fasciotomy. When the fasciotomy was delayed more than 12 hours, only 8% had normal function of the limb.

Gram staining of the sample will help in identifying the organisms and starting on appropriate antibiotic therapy.

Laboratory investigation may reveal leucocytosis or leucopoenia. Leucocytosis is usually associated with polymicrobial organisms and Streptococcal infection. Staphylococcal infections may have leucopoenia(20). Decreasing haemoglobin may suggest an intravascular haemolysis due to sepsis.

Acute renal failure is usually a sequelae in severe sepsis. Necrotising soft tissue infections may have elevated CRP and creatine kinase. Elevated creatine kinase of more than 600u/l is highly specific for adjacent muscle involvement.

There may be associated hypocalcaemia, hypoalbuminemia and hyponatremia due to sepsis(2,14).

Severe metabolic acidosis with elevated serum lactate and hyponatremia is highly predictive of mortality. The mortality rate is as high as 32 percent when serum lactate levels are more than 6 mmol/l and sodium of less than 135 mg/L(24).

A tissue biopsy will help in diagnosis of necrotising fasciitis. This will reveal underlying thrombi, polymorphic infiltrates and microorganisms(14)(25).

Radiological imaging like plain radiographs, plain computerised tomogram, and magnetic resonance imaging help in identifying gas in the tissue planes which is highly specific for necrotising soft tissue infections. Ultrasonography is helpful in detecting localised abscess but not studied extensively in NSTI's(26). MRI and CT will detect thickened fascial plane which is highly sensitive but less specific(2).

3.9.0. Staging and scoring systems:

3.9.1. For diagnosis:

The diagnosis of necrotising soft tissue infection is crucial as surgical treatment is to be initiated at the earliest. Most often the morbidity and mortality is due to delay in the treatment as diagnosis was missed out. The diagnosis of necrotising soft tissue infection was correct in only about 38 percent(2).

3.9.2. Clinical staging:

Wang et al described a staging system based solely on clinical examination and skin changes in the progression of the disease(27).

The various stages are

Stage I	Early stage; Tenderness to palpation (extending beyond the apparent area of skin involvement), erythema, swelling and calor
Stage II	Intermediate stage; blister or bullae formation with serous discharge
Stage III	Late stage; Crepitus, skin anaesthesia and skin necrosis with dusky discoloration

The initial stage may be indistinguishable from non necrotising soft tissue infection. But as the disease progresses the diagnosis is to be made at the earliest because delay in identification leads to increased mortality rates(27).

The mortality described in each stage according to Wang et al is

Stage I	7.1 percent
Stage II	14.2 percent
Stage III	47 percent

3.9.3. LRINEC score:

Wong et al described a scoring system, LRINEC score which includes laboratory parameters for predicting the possibility of necrotising soft tissue infections(24).

Variable	Value	Score
C-reactive protein (mg/dL)	<150	0
	>150	4
Total white blood cell count (/mm^3)	<15	0
	15125	1
	>25	2
Haemoglobin (g/dL)	>13.5	0
	11-13.5	1
	<11	2
Sodium (mmol/L)	>=135	0
	<135	2
Creatinine (mmol/L)	<141	0
	>141	2
Glucose (mmol/L)	<10	0
	>10	1

This score only includes laboratory parameters. Any score of more than or equal to 6 should raise a suspicion and a score of more than 8 strongly predicts necrotising soft tissue infection(24).

Any patient with a score of 5 or less can be treated with antibiotic. Patient with score more than 8 should undergo surgical treatment whereas patients with a score of 6 or 7 need further assessment.

3.9.4. For prognostication:

Anaya et al suggested a scoring system for prediction of mortality(28). This system includes

Variable (on admission)	Value	Number of points
Heart rate	>110 bpm	1
Temperature	<36^{o} C	1
Serum creatinine	>1.5 mg/dl	1
Age	>50 years	3
White blood cells	>40,000/mcL	3
Hematocrit	>50%	3

The various mortality risks according to the score are(28)

Score	Mortality risk
0-2	6%
3-5	24%
>6	88%

The drawbacks of these scoring systems are

1. All are based on retrospective studies.

2. All are from the east where the causative factors are different as compared to the rest of the world and India.

3. None of the above scoring systems have a validation study.

Hence there is a need for proper and simple scoring system which not only includes laboratory parameters but also clinical history and examination.

3.10.0. Treatment:

Treatment depends on the type of infection: necrotising or non necrotising.

3.10.1. Non necrotising soft tissue infection:

In non necrotising soft tissue infection patient can be treated with oral or IV antibiotics based on the severity of infection. Streptococcus and Staphylococcus needs to be covered and antibiotics of choice are Cephalosporin, Penicillin, Vancomycin or Clindamycin. Antibiotics need to be administered for 7-10 days (28).

This needs to be supported with anti oedema measures like limb elevation, hygroscopic dressings, diuretics or compression stockings(29). Fasciotomy is recommended when anti oedema measures fail and compartment syndrome ensues.

3.10.2. Necrotising soft tissue infection:

a) Surgical therapy:

Necrotising soft tissue infection is a surgical emergency and surgery is the mainstay of treatment in these patients. The aim of surgery is to perform aggressive debridement of all necrotic tissue until healthy, viable (bleeding) tissue is reached(30). Tissue samples are to be sent for Gram stain and culture. The wound needs re-evaluation after 24 hours and re-debridement is to be considered if unhealthy tissue is present. Once the wound is healthy and granulating they can be covered with skin graft or myocutaneous flaps. Multiple debridements may be needed for adequate control of infection(7).

In severe infections amputation may be required for adequate source control. Amputation might be needed when there is severe necrosis of muscle groups rendering it not viable. Twenty percent of patients with NSTI might require amputation(2).

The relative risk of death was 7.5 percent higher in patients with NSTI who did not undergo surgical debridement and the risk was nine fold if the surgical treatment was delayed more than 24 hours(2). Early debridement had a mortality of 4 percent as compared to delayed debridement which had 38 percent mortality(31).

b) Antibiotics in STI:

Antibiotics therapy is an adjunct to surgical therapy in patients with NSTI's. The role of antibiotic alone in NSTI is very limited as thrombosis of vessels leads to inadequate supply to the tissues. Penicillin and Clindamycin are very effective in covering monomicrobial organisms. Recent emergence of MRSA is leading to wide spread use of second line antibiotics like Vancomycin, Linezolid, Daptomycin etc. Clindamycin is still effective as it inhibits the M protein of Group A Streptococci(2,9).

Polymicrobial organisms especially with gram negative bacteria needs carbepenems like Meropenem, Imepenem etc. The antibiotic needs to be adjusted according to the tissue culture report once obtained. The duration of antibiotics is least studied upon. General consensus is to give therapy for 10 – 14 days(2).

c) Immune therapy in STI:

IV Immunoglobulin therapy is advocated in some trials but it is not FDA approved for necrotising soft tissue infections. This use of this agent is based on a theoretical assumptions that it can bind staphylococcal- and streptococcal derived exotoxins, thereby limiting the systemic cytokine release which is associated with systemic inflammatory response syndrome(2).

d) Adjuvant therapy in STI:

Hyperbaric oxygen delivery is based on animal models which showed to inhibit infection of Clostridia. It also was found to augment the oxidative burst and killing ability of leukocytes and can enhance efficacy of antibiotics by increasing local oxygen tension in tissue(32–34). But its use in humans still remains controversial.

e) Secondary prevention in STI:

Post exposure prophylaxis is advocated in patients with group A Streptococcus. Its aim is to prevent the secondary infection due to group A Streptococcus in people who are in close household contacts with type II soft tissue infections(35).

3.11.0. Outcome and Factors predicting disease severity:

The mortality with soft tissue infections especially in the necrotising group can be as high as 25-35 percent despite optimal therapy(3,7). The patients with toxic shock have a mortality of 28 percent(36). Most often the mortality is due to delay in initiating the appropriate treatment which is due to delay in diagnosis. The diagnosis was correct only in 38 percent of the patients at initial evaluation(2).

There are various studies done to identify factors predicting the disease severity. All these studies were retrospective analysis of patients with necrotising soft tissue infections. The various parameters shown to predict severity are as follows

Factors predicting mortality and morbidity in soft tissue infections across various retrospective analysis	
Factors	**References**
Low haematocrit	(8,24,28,37)
High counts	(8,24,28,37)
Left shift of differential counts	(28)
Hypotension (systolic B.P <90 mm c	(3,8,37)
Platelets , 100000/ cu mm	(38)
Coagulopathy	(37)
Hemorrhagic bullae	(3,8)

Factors predicting mortality and morbidity in soft tissue infections across various retrospective analysis	
Factors	**References**
High C- Reactive protein	(24)
Hyponatremia	(24,28,38,39)
High creatinine	(24,28,37,38)
Low Glasgow Coma Scale	(8)
Hypothermia	(28)
High lactate	(39)
Old age	(28,37)
Tachycardia	(28)
Heart disease	(3)
Liver disease	(3)
Malignancy	(8)
Diabetes mellitus	(8,37)
Aeromonas species in culture	(3,8)
Vibrio Species in culture	(3,8)
Fungal species in culture	(3,8)
Bacteraemia	(3,40)

The drawbacks of all these studies were

1. They were all retrospective studies.

2. As they were all done on patients proven to have necrotising soft tissue infection and hence there may be bias which is to be excluded.

3. As there was no regression analysis done on normal controls, these factors actually might not be the actual predictors of severity of the disease.

Hence we propose this prospective nested case control study to predict the factors associated with mortality and morbidity in patients with soft tissue infections.

Chapter 4

Methods and materials

4. Methods and materials

4.1.0. Design:

After discussion with the statistician, a nested case control study was designed.

Patients with no mortality and morbidity were grouped under one arm where as patients with mortality and morbidity was grouped under another arm.

Definition of morbidity and mortality:

In our study, morbidity was defined as any patients requiring

1. Re-debridement
2. Amputation
3. Inotropic support
4. Ventilator support
5. Dialysis
6. Post operative myocardial infarct

In our study, mortality was considered as death that occurred in the hospital during the course of treatment for STI.

4.2.0. Sample size:

Based on the study(3) the sample size was calculated to be 55 in each arm.

$$n = \frac{2PQ\,(Z\alpha+Z\beta)^2}{(P_I-P_0)^2}$$

$$P_I = \frac{P_0(OR)}{P_0\,(OR-1)+1}$$

$$P = \frac{P_0+P_I}{2}$$

n - Sample size

Zα – Significance level – 1.96

Zβ – Power of the study – 0.84

OR – Odds Ratio – 3.5

P0 – Proportion with heart Disease among the control group 0.14

4.3.0. Recruitment:

Institutional research board clearance was obtained before the start of the study.

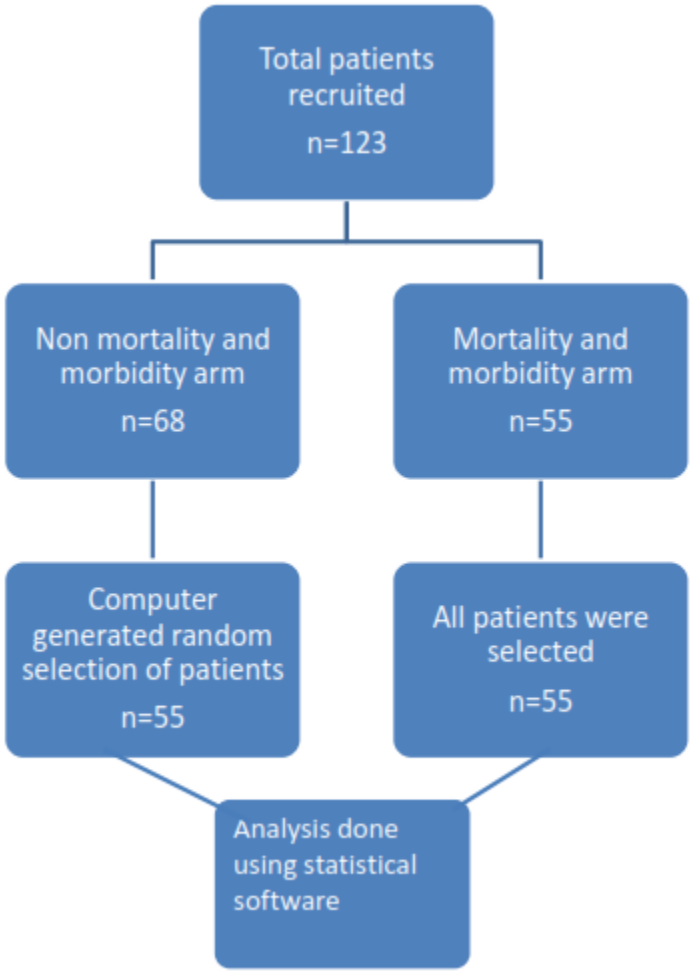


Figure 1: Consort statement of the study

All the patients admitted in the surgical wards with a diagnosis of soft tissue infections were included in the study.

All patients were explained about the study after giving them the information sheet (Annexure 2).

Informed consent (Annexure 3) was taken who were all willing to participate in the study. Those who did not give consent were not recruited in the study.

After informed consent, the details required as per the proforma (Annexure 1) was collected.

They were all followed up during their stay in hospital and their progress was noted for any morbidity or mortality.

Patients were recruited till the sample size was reached in either arm.

There were total of 123 patients recruited. Of which 68 patients were in non mortality and morbidity arm.

The study was conducted till the target sample size was reached in either arm.

Out of 68 patients in non mortality and morbidity arm, random selection of 55 patients was done by computer software.

4.4.0. Analysis:

Analysis was done in SPSS software version 18.0 (licensed by IBM) with the help of the statistician.

The cohort provided the information on mortality, morbidity and 95% confidence interval.

By using nested case control approach we estimated the magnitude of association between selected risk factors and mortality and morbidity.

Simultaneous adjustment for confounders was done using unconditional logistic regression.

All study variables were described using descriptive statistical methods. Continuous variables were summarised using mean with standard deviation.

For skewed variables median with range were used. For categorical variables frequencies with percentages were used.

The association between mortality/morbidity and other categorical parameters (hypotension, etc) were assessed using chi – square test.

For continuous variables either t-test or corresponding non parametric test were used.

Variables with a $p < 0.05$ were considered for the multivariable analysis. Logistic regression analysis were done to identify factors associated with mortality/morbidity.

Chapter 5

Results

5. Results

5.1.0. Descriptive analysis:

5.1.1. Age distribution:

The age distribution was between 28 years to 87 years with a mean of 57 years and median of 58 years.

The disease was predominantly affecting the age group of 40 – 60 years.

Table 1: Distribution of age in patients with soft tissue infections

Age	N	Minimum	Maximum	Mean	Median	Mode	Std. deviation
	110	28	87	56.65	57.5	50	14.26

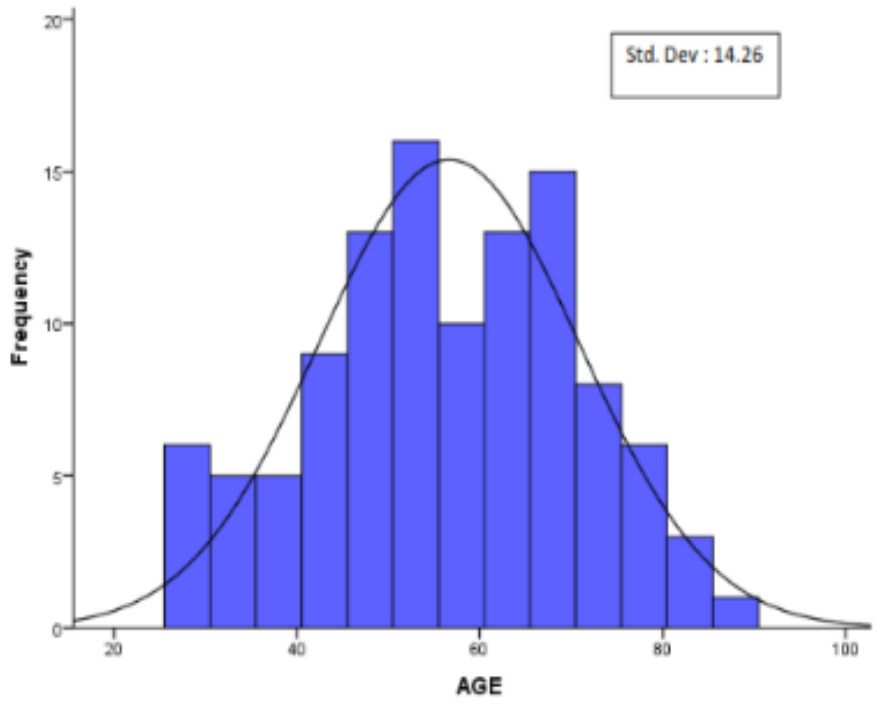


Figure 2: Distribution of age in patients with soft tissue infections.

5.1.2. Gender distribution:

There was a predilection for male population for this disease. 68.2 percent (75 out of 110) of the patients were male as compared to 31.8 percent (35 out of 110) who were female.

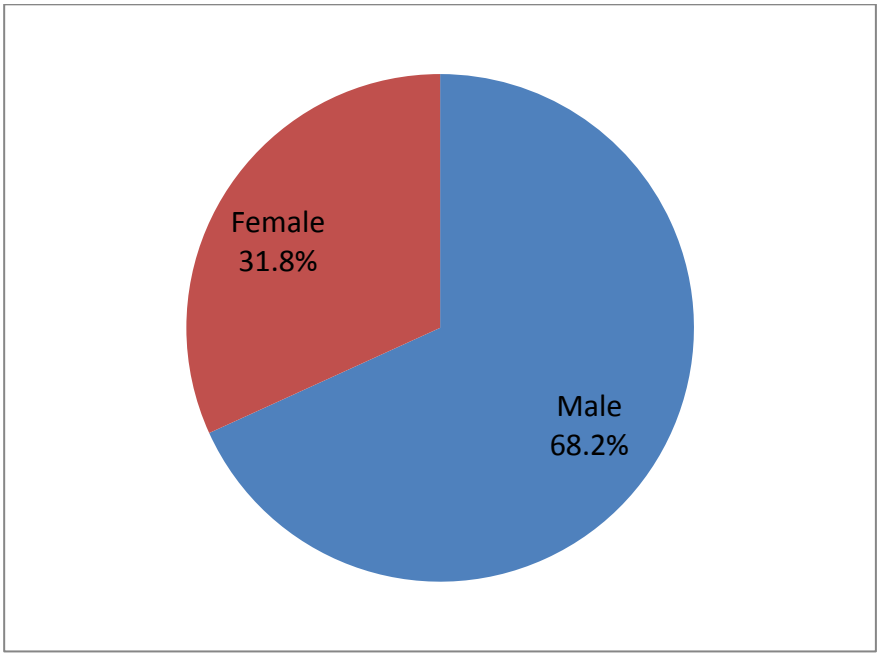


Figure 3: Distribution of gender in patient with soft tissue infections

5.1.3. Duration of presenting illness:

The duration of presenting illness varied from 1 day to 45 days with a mean of 9 days and median of 7 days. Most of the patients presented on the third day after the start of symptoms.

Table 2: Duration of symptoms at presentation to hospital in patients with STI

	N	Minimum	Maximum	Mean	Median	Mode	Std. Deviation
Duration of symptoms	110	1	45	8.83	7	3	8.135

5.1.4. Mode of onset:

Spontaneous mode of onset was the most common followed by trauma. 55.5 percent (61 out of 110) of patients had spontaneous onset but trauma was the cause in 40.9 percent (45 out of 110) of the patients. The other modes of onset included insect bites (0.9 percent) and surgery (2.7 percent).

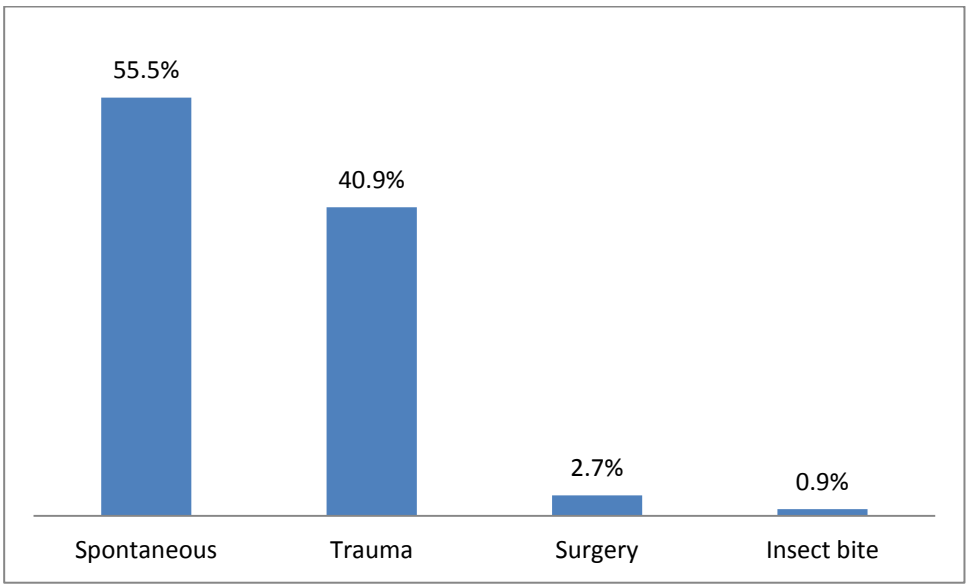


Figure 4: Mode of onset of symptoms in patients with soft tissue infections

5.1.5. Associated illnesses:

69.1 percent (76 out of 110) of patients had associated illnesses at presentation. Diabetes mellitus was the most common associated illness which was seen in 56.4 percent (62 out of 110) of the patients. Hypertension was second most common illness seen in 31.8 percent (35 out of 110) of patients. Cardiac and chronic renal disease was seen in 10 percent and 7.3 percent of the patients respectively. The other illnesses associated were chronic liver disease (2.7 percent), vascular disorders (3.6 percent) and malignancy (1.8 percent). The patient with malignancy had undergone bilateral inguinal block dissection for carcinoma penis.

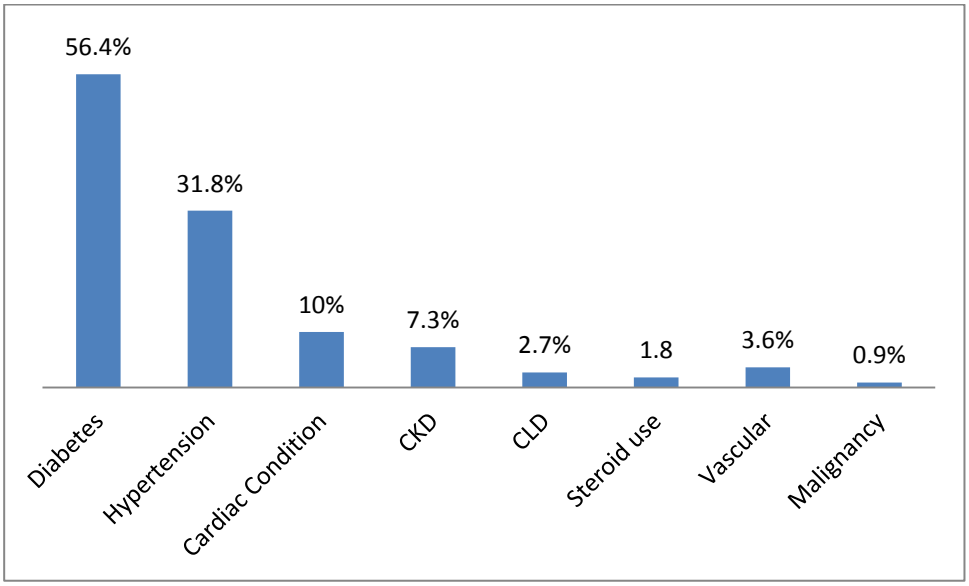


Figure 5: Distribution of associated illnesses in patients with STI

5.1.6. Number of times operated:

10.9 percent (12 out of 110) of patients underwent two operations where as 1.8 percent (2 out of 110) had undergone 3 operations for source control.

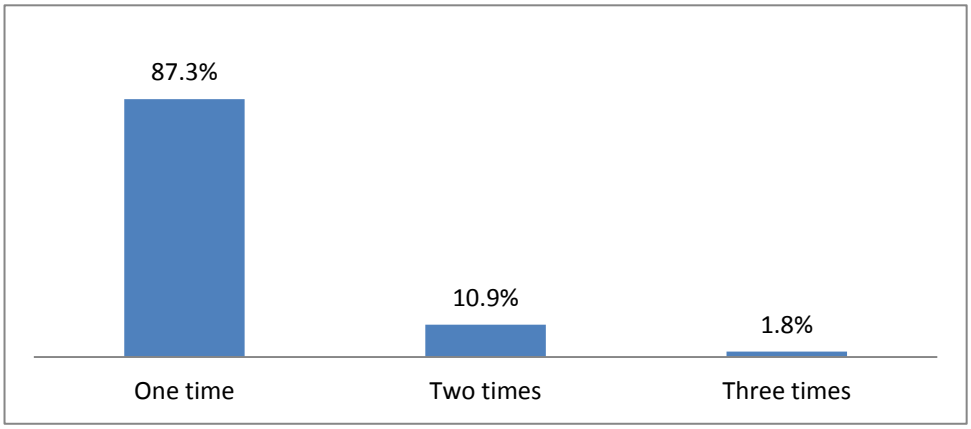


Figure 6: Number of times patients underwent operation for STI

5.1.7. Amputations:

In our study 20 percent (22 out of 110) of the patients had undergone amputation as operation for source control. 18 out of 22 patients who underwent amputation survived where as only 4 out of 22 patients expired during their course of treatment.

Table 3: Mortality rate in patients who underwent amputation for STI

		Mortality		Total
		No	yes	
Amputation	No	77	11	88
	Yes	18	4	22
Total		95	15	110

5.1.8. Inotropic requirements:

Patients who required either preoperative or post operative inotropic support for hypotension comprised of 25.5 percent (28 out of 110).

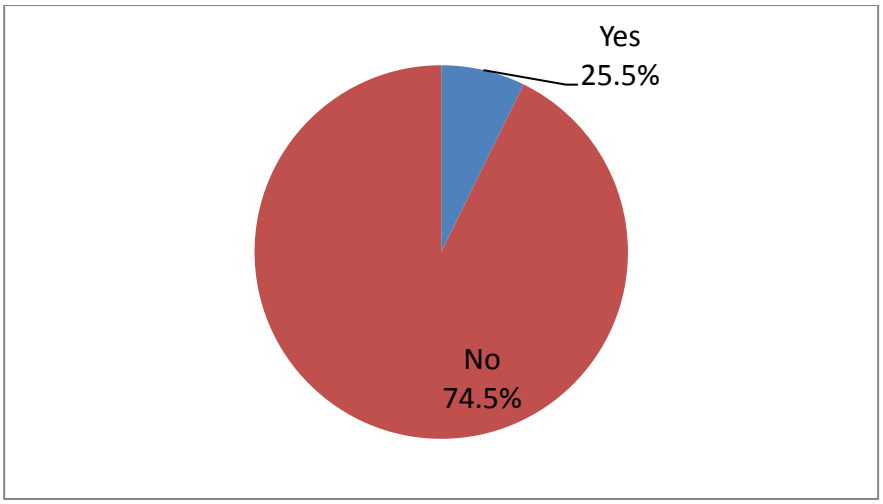


Figure 7: Patients with STI requiring Inotropes perioperatively

5.1.9. Ventilation:

18.2 percent (20 out of 110) of patients required post operative ventilation in view of severe sepsis or acute respiratory distress syndrome. One patient required ventilator support due to pulmonary oedema caused by myocardial infarct.

13 out of 20 patients who required ventilation postoperatively died due to the disease.

Table 4: Mortality in patients who had ventilation perioperatively

		Mortality		Total
		No	Yes	
Ventilation	No	88	2	90
	Yes	7	13	20
Total		95	15	110

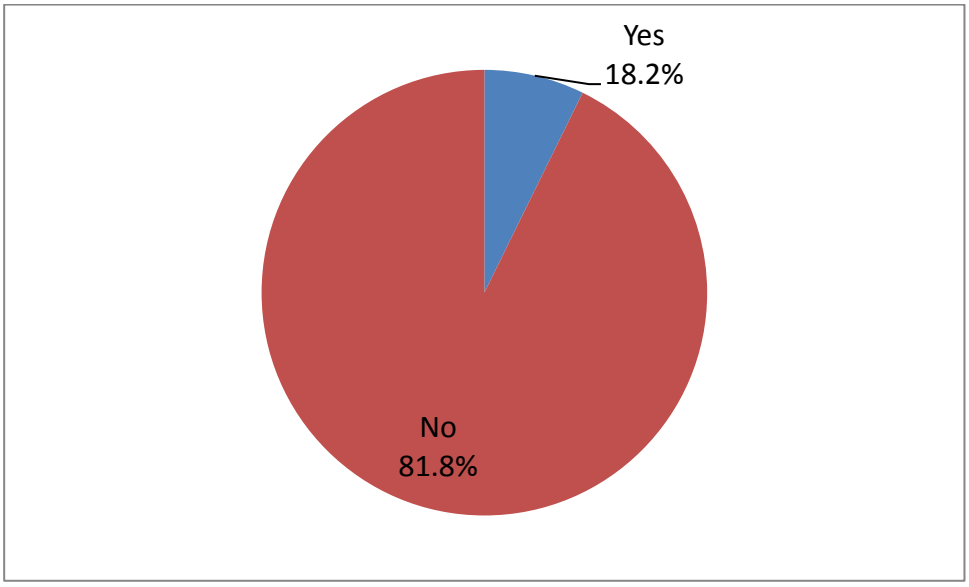


Figure 8: Patient with STI requiring ventilation perioperatively

5.1.10. Need for dialysis:

7.3 percent (8 out of 110) of patients required dialysis due to acute renal failure or acute on chronic renal failure. 3 patients out of 8 who required dialysis were dialysis independent at the time of discharge. The other 5 patients succumbed to illness.

Table 5: Mortality in patients who had dialysis for renal failure

		Mortality		Total
		No	Yes	
Dialysis	No	92	10	102
	yes	3	5	8
Total		95	15	110

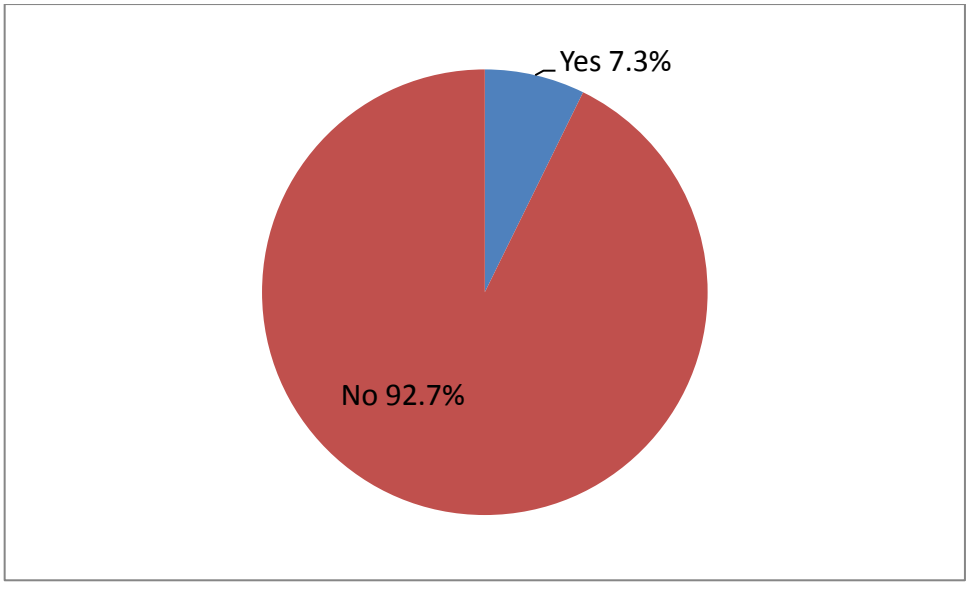


Figure 9: Patients with STI requiring Dialysis for renal failure

5.1.11. Myocardial infarct:

5.5 percent (6 out of 110) of patient had myocardial infarct during the stay in hospital in the immediate post operative period. 4 out of 6 patient who had myocardial infarct expired.

Table 6: Mortality in patients who had myocardial infarct

		Mortality		Total
		No	Yes	
Myocardial infarct	No	93	11	104
	yes	2	4	6
Total		95	15	110

5.1.12. Mortality:

We had total of 15 patients who succumbed to the disease, which comprised 14 percent of patients.

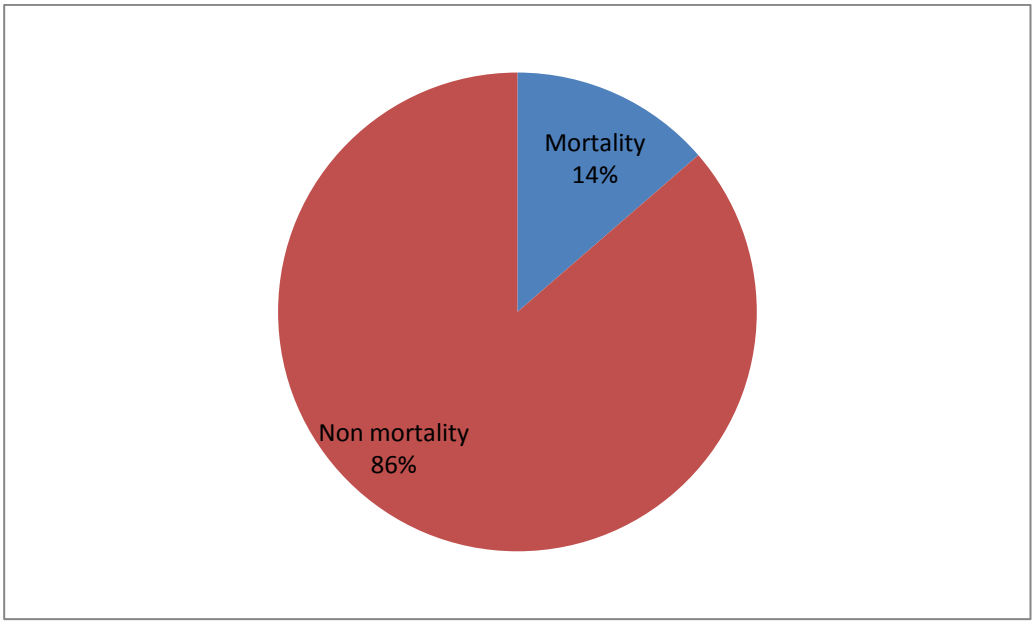


Figure 10: Mortality in patients with STI

5.1.13. Tissue cultures:

Tissue for cultures was sent only for 71.8 percent (79 out of 110) of patients. Of these cultures were positive in 69 patients and sterile in 10 patients.

In the culture positive group 62.3 percent (43 patients) had polymicrobial type I STI where as 37.6 percent (26 patients) had monomicrobial type II STI.

There was no type III and type IV STI found in our study.

8 out of 15 patients (53.3 percent of mortality) died of type II STI in contrast with type I STI where the mortality was 5 out of 15 (33.3 percent).

5.1.14. Organisms in tissue culture:

In type I STI, E. Coli was the most common organism (65.1 percent) followed by Enterococcus (37.2 percent), NFGNB (27.9 percent) and pseudomonas (20.9 percent). The other organisms isolated were MRSA, MSSA, Klebsiella, Enterobacter, Proteus Spp, Morganella, Aeromonas Spp and Bacteroides.

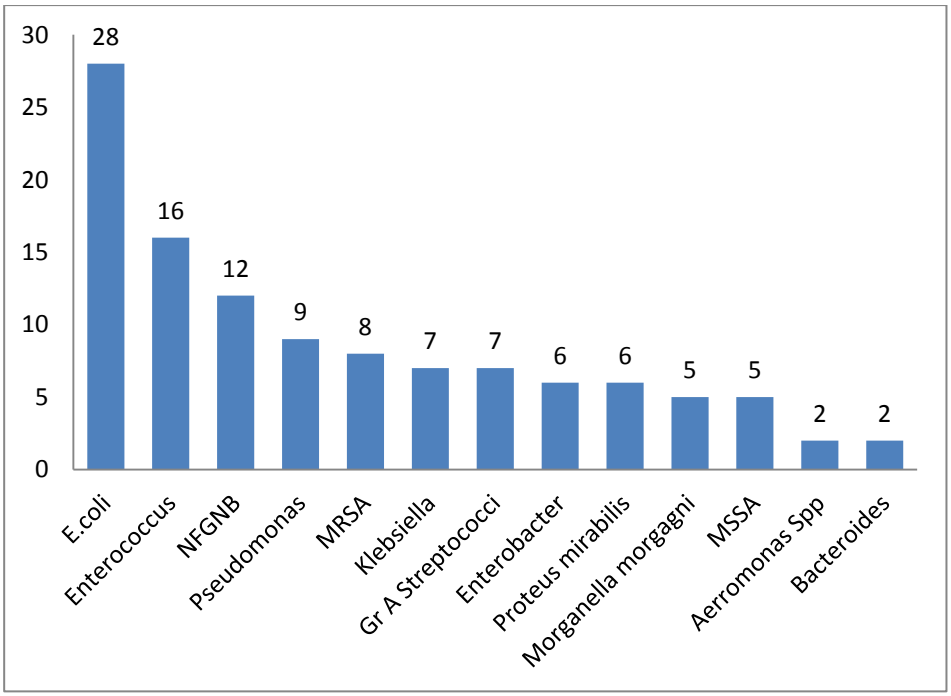


Figure 11: Organisms isolated in type I NSTI

Most common organism seen in the Type II infection is Group A Streptococci comprising of 42.3 percent (11 out of 26 patients) followed by Methicillin sensitive Staphylococcus aureus (MSSA) and Methicillin resistant Staphylococcus aureus (MRSA). The other organisms isolated were Klebsiella, E.coli, Non fermenting gram negative bacteria, Enterococcus.

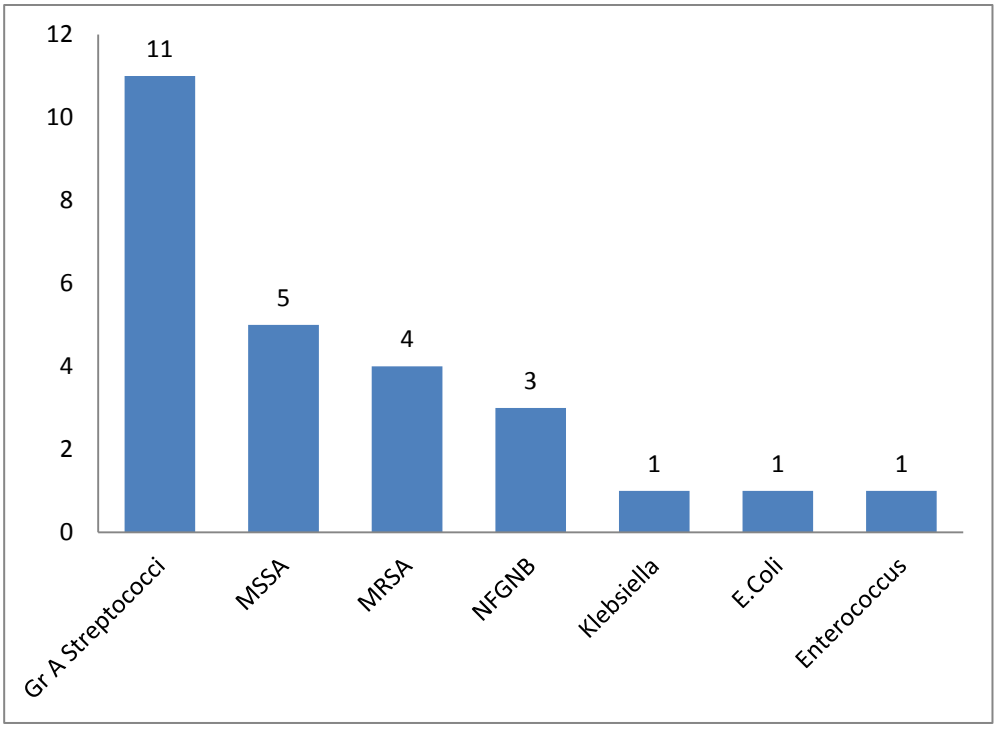


Figure 12: Organisms isolated in Type II NSTI

5.2.0. Analysis of predictors of morbidity in STI

5.2.1. Univariate analysis:

The descriptive analysis (mean, Standard Deviation) of various variables predicting morbidity in STI is as follows

Table 7: Descriptive analysis of variables predicting morbidity in STI

Variables	Outcome	Number (n)	Mean	Standard deviation	Odds ratio
Age	Non-Morbidity	55	58.71	13.67	0.979
	Morbidity	55	54.58	14.664	
Heart rate	Non-Morbidity	55	89.78	11.774	1.071
	Morbidity	55	105.49	19.022	
Systolic blood pressure	Non-Morbidity	55	121.49	15.061	0.974
	Morbidity	55	109.16	26.868	
Diastolic blood pressure	Non-Morbidity	55	72.47	11.674	0.983
	Morbidity	55	68.55	18.051	
Respiratory rate	Non-Morbidity	55	19.49	4.799	1.139
	Morbidity	55	23.45	6.928	
Glasgow coma scale	Non-Morbidity	55	15.00	0.000	0.000
	Morbidity	55	14.49	1.275	
Haemoglobin	Non-Morbidity	55	10.780	2.2390	0.970
	Morbidity	55	10.618	2.4222	

Variables	Outcome	Number (n)	Mean	Standard deviation	Odds ratio
Total counts	Non-Morbidity	55	16401.82	6755.012	1.000
	Morbidity	55	17601.82	8140.718	
Elevated neutrophils	Non-Morbidity	55	77.02	12.027	1.055
	Morbidity	55	83.33	10.736	
Platelets	Non-Morbidity	55	262436.38	110892.461	1.000
	Morbidity	55	246272.73	136938.950	
Prothrombin time	Non-Morbidity	55	14.309	14.6855	0.997
	Morbidity	55	13.962	3.3189	
INR	Non-Morbidity	55	1.293	1.2142	0.970
	Morbidity	55	1.269	0.3150	
APTT	Non-Morbidity	55	36.171	20.5407	0.997
	Morbidity	55	35.324	11.2615	
Urea	Non-Morbidity	55	43.85	25.551	1.022
	Morbidity	55	71.49	49.654	
Creatinine	Non-Morbidity	55	1.631	0.9108	1.484
	Morbidity	55	2.304	1.8573	
Sodium	Non-Morbidity	55	132.96	4.046	0.841
	Morbidity	55	129.11	5.560	
Potassium	Non-Morbidity	55	3.907	0.5405	1.284
	Morbidity	55	4.053	0.9465	
Total bilirubin	Non-Morbidity	55	0.922	0.7208	2.258
	Morbidity	55	1.665	1.6027	

Variables	Outcome	Number (n)	Mean	Standard deviation	Odds ratio
Albumin	Non-Morbidity	55	2.900	0.6374	0.443
	Morbidity	55	2.569	0.6455	
Glucose	Non-Morbidity	55	195.36	92.458	1.001
	Morbidity	55	203.53	117.370	
Serum lactate	Non-Morbidity	55	2.045	1.1519	1.167
	Morbidity	55	2.496	2.2371	
Base deficit	Non-Morbidity	55	3.931	2.7512	1.224
	Morbidity	55	7.149	5.6079	
Serum myoglobin	Non-Morbidity	55	82.29	95.778	1.018
	Morbidity	55	639.93	2311.128	

5.2.2. Independent samples test for continuous variables:

All the variables were analysed with independent samples test with assumption of null hypothesis.

The variables found to be significant for prediction of morbidity using assumption of homogeneity of variance (Levine's test for equality of variance) are heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, Glasgow coma scale, total counts, urea, creatinine, potassium, total bilirubin, serum lactate, base deficit, myoglobin.

This was further analysed by using Levine's test for equality of means. This showed the following variables are the ones that actually violate the assumption of homogeneity. They are heart rate, systolic blood pressure, respiratory rate, Glasgow coma scale, neutrophils, urea, creatinine, sodium, total bilirubin, albumin and base deficit.

The following variables like diastolic blood pressure, total counts, potassium, serum lactate and serum myoglobin though found to be significant by Levine's test for equality of variance were not found to be significant by Levine's test for equality of means.

Table 8: Analysis of variables by independent samples test predicting morbidity in STI

Variables	Variance assumption	Significance by Levine's test for quality of variance	Significance by Levine's test for quality of means	95% Confidence interval	
				Lower	Upper
Age	Equal variance assumed	0.616	0.13	-1.231	9.485
	Equal variance not assumed		0.13	-1.231	9.486
Heart rate	Equal variance assumed	**0.001**	**0**	-1.231	-9.73
	Equal variance not assumed		**0**	-1.231	-9.716
Systolic blood pressure	Equal variance assumed	**0.001**	**0.004**	4.095	20.56
	Equal variance not assumed		**0.004**	4.069	20.585
Diastolic blood pressure	Equal variance assumed	**0.016**	0.178	-1.818	9.673
	Equal variance not assumed		0.179	-1.829	9.684
Respiratory rate	Equal variance assumed	**0.03**	**0.001**	-6.216	-1.711
	Equal variance not assumed		**0.001**	-6.219	-1.708
Glasgow coma scale	Equal variance assumed	**0**	**0.004**	0.168	0.85
	Equal variance not assumed		**0.005**	.164	0.854
Haemoglobin	Equal variance assumed	0.687	0.717	-0.7198	1.0434
	Equal variance not assumed		0.717	-0.7199	1.0435

Variables	Variance assumption	Significance by Levine's test for quality of variance	Significance by Levine's test for quality of means	95% Confidence interval	
				Lower	Upper
Total counts	Equal variance assumed	**0.028**	0.402	-4027.34	1627.341
	Equal variance not assumed		0.402	-4028.43	1628.431
Elevated neutrophils	Equal variance assumed	0.329	**0.004**	-10.618	-2
	Equal variance not assumed		**0.005**	-10.619	-2
Platelets	Equal variance assumed	0.284	0.498	-30932.7	63259.98
	Equal variance not assumed		0.498	-30955.7	63283.05
Prothrombin time	Equal variance assumed	0.252	0.864	-3.6768	4.3713
	Equal variance not assumed		0.865	-3.7143	4.4088
INR	Equal variance assumed	0.286	0.889	-0.3116	0.3589
	Equal variance not assumed		0.889	-0.3146	0.3618
APTT	Equal variance assumed	0.978	0.789	-5.4137	7.1083
	Equal variance not assumed		0.789	-5.4343	7.1289
Urea	Equal variance assumed	**0.003**	**0**	-42.562	-12.711
	Equal variance not assumed		**0**	-42.619	-12.654

Variables	Variance assumption	Significance by Levine's test for quality of variance	Significance by Levine's test for quality of means	95% Confidence interval	
				Lower	Upper
Creatinine	Equal variance assumed	**0.007**	**0.018**	-1.2256	-0.1198
	Equal variance not assumed		**0.018**	-1.228	-0.1175
Sodium	Equal variance assumed	**0.053**	**0**	2.017	5.692
	Equal variance not assumed		**0**	2.015	5.694
Potassium	Equal variance assumed	**0**	0.325	-0.4368	0.1459
	Equal variance not assumed		0.325	-0.4376	0.1467
Total bilirubin	Equal variance assumed	**0.002**	**0.002**	-1.2133	-0.274
	Equal variance not assumed		**0.002**	-1.2157	-0.2716
Albumin	Equal variance assumed	**0.703**	**0.008**	0.0885	0.5734
	Equal variance not assumed		**0.008**	0.0884	0.5734
Glucose	Equal variance assumed	0.084	0.686	-48.098	31.771
	Equal variance not assumed		0.686	-48.123	31.796
Serum lactate	Equal variance assumed	**0.024**	0.187	-1.1234	0.2216
	Equal variance not assumed		0.188	-1.126	0.2242

Variables	Variance assumption	Significance by Levine's test for quality of variance	Significance by Levine's test for quality of means	95% Confidence interval	
				Lower	Upper
Base deficit	Equal variance assumed	**0.001**	**0**	-4.8877	-1.5487
	Equal variance not assumed		**0**	-4.8948	-1.5416
Serum myoglobin	Equal variance assumed	**0.012**	0.077	-1175.88	60.603
	Equal variance not assumed		0.079	-1182.91	67.636

5.2.3. Cross tabs for categorical data:

The following variables were found to be significant predictors for morbidity using Pearson's chi square and Fischer's exact test.

5.2.4. Fever:

Fever as a presenting symptom was found to be a significant variable with a Pearson's chi square value of 0.00 with a risk estimate of 5.701.

Table 9: Analysis of fever as a variable predicting morbidity in STI

			Non morbidity vs. Morbidity		Total
			Non morbidity	Morbidity	
FEVER	No	Count	29	9	38
		% within FEVER	76.3%	23.7%	100%
	yes	Count	26	46	72
		% within FEVER	36.1%	63.9%	100%
Total		Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided) P-value	OR	95% CI	
						Lower	Upper
Pearson chi square	16.082	1	**0.000**		5.70	2.34	13.87
Fischer exact test				**0.000**			

5.2.5. Haemorrhagic bullae:

Haemorrhagic bulla was found to be significant variable with a Fischer's exact test value of 0.000.

Table 10: Analysis of haemorrhagic bullae as a variable predicting morbidity in STI

Haemorrhagic bullae		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
no	Count	54	41	95
	% within Bullae	56.8%	43.2%	100.0%
yes	Count	1	14	15
	% within Bullae	6.7%	93.3%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	13.046	1	**0.000**		18.44	2.32	145.97
Fischer exact test				**0.000**			

5.2.6. Left shift in differential count:

Left shift in the differential counts were found to be significant variable with a Pearson chi square value of 0.057 and an odds ratio of 2.571.

Table 11: Analysis of left shift in differential count as a variable predicting morbidity in STI

Left shift in differential count		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
no	Count	48	40	88
	% within left shift	54.5%	45.5%	100.0%
yes	Count	7	15	22
	% within left shift	31.8%	68.2%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	3.636	1	**0.057**		2.57	0.95	6.92
Fischer exact test				**0.094**			

5.2.7. Number of re-operations:

Patients undergoing multiple operations (more than once) were found to have significant morbidity with a Pearson's chi square value of 0.00.

Table 12; Analysis of multiple operations as a variable predicting morbidity in STI

Number of times operated		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
	0 Count	55	41	96
	% with in multiple operations	57.3%	42.7%	100.0%
	1 Count	0	12	12
	% with in multiple operations	0%	100%	100.0%
	2 Count	0	2	2
	% with in multiple operations	0%	100%	100%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	16.042	2	**0.000**		NA	NA	NA
Fischer exact test				NA			

5.2.8. Amputation:

Amputation for patients with STI was found to be a significant variable predicting morbidity in STI with a Fischer exact test value of 0.000.

Table 13: Analysis of amputation as a variable predicting morbidity in STI

Amputation		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
no	Count	55	33	88
	% within amputation	62.5%	37.5%	100.0%
yes	Count	0	22	22
	% within amputation	0%	100%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	27.5	1	**0.000**		0.38	0.286	0.491
Fischer exact test				**0.000**			

5.2.9. Ventilator support:

Ventilator support for patients with STI was found to be a significant predictor of morbidity with Fischer exact value of 0.000.

Table 14: Analysis of ventilation as a variable predicting morbidity in STI

Ventilation		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
	no Count	55	35	90
	% within ventilation	61.1%	38.9%	100.0%
	yes Count	0	20	20
	% within ventilation	0%	100%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	24.4	1	**0.000**		0.39	0.300	0.504
Fischer exact test				**0.000**			

5.2.10. Inotropes requirement:

Inotropic support for patients with STI was found to be a significant predictor of morbidity with Fischer exact value of 0.000.

Table 15: Analysis of inotropes as a variable predicting morbidity in STI

Inotropes		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
no	Count	55	27	82
	% within inotropes	67.1%	32.9%	100.0%
yes	Count	0	28	28
	% within inotropes	0%	100%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	37.561	1	**0.000**		0.33	0.242	0.448
Fischer exact test				**0.000**			

5.2.11. Dialysis requirement:

Dialysis for patients with STI was found to be a significant predictor of morbidity with Fischer exact value of 0.006.

Table 16: Analysis of dialysis as a variable predicting morbidity in STI

Dialysis		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
no	Count	55	47	102
	% within dialysis	53.9%	46.1%	100.0%
yes	Count	0	8	8
	% within dialysis	0%	100%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	8.627	1	**0.003**		0.46	0.374	0.568
Fischer exact test				**0.006**			

5.2.12. Myocardial infarct:

Myocardial infarct during the hospital course for patients with STI was found to be a significant predictor of morbidity with Fischer exact value of 0.027.

Table 17: Analysis of myocardial infarct as a variable predicting morbidity in STI

Myocardial infarct		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
	no Count	55	49	104
	% within myocardial infarct	52.9%	47.1%	100.0%
	yes Count	0	6	6
	% within myocardial infarct	0%	100%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	6.346	1	**0.012**		0.47	0.384	0.578
Fischer exact test				**0.027**			

5.2.13. Positive tissue culture:

Positive tissue culture for patients with STI was found to be a significant predictor of morbidity with Fischer exact value of 0.001.

Table 18: Analysis of positive tissue culture as a variable predicting morbidity in STI

Tissue culture		Non morbidity vs. Morbidity		Total
		Non morbidity	Morbidity	
	no Count	24	7	31
	% within tissue culture	77.4%	22.6%	100.0%
	yes Count	31	48	79
	% within tissue culture	39.2%	60.8%	100.0%
Total	Count	55	55	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	12.981	1	**0.000**		5.31	2.042	13.801
Fischer exact test				**0.001**			

5.2.14. Other non significant variables:

The other variables analysed like sex, type of onset, diabetes mellitus, hypertension, cardiac co-morbidities, renal disease, liver disease, steroid usage, vascular disease, malignancy or absence of peripheral pulses were not found to be significant.

Table 19: Analysis of variables not significant in predicting morbidity in STI

Variables	OR	P value	95% CI	
			Lower	Upper
Sex	0.464	0.065	0.204	1.058
Type of onset	NA	0.216	NA	NA
Co morbidities	1.186	0.680	0.528	2.665
Diabetes mellitus	0.863	0.701	0.406	1.834
Hypertension	0.777	0.539	0.348	1.738
Cardiac co-morbidity	1.859	0.340	0.512	6.756
Renal disease	0.577	0.463	0.131	2.542
Liver disease	2.038	0.558	0.179	23.151
Steroid usage	1.000	1.00	0.061	16.401
Vascular disease	0.481	0.118	0.395	0.586
Malignancy	0.496	1.000	0.410	0.599
Absence of pulses	0.626	0.580	0.207	1.896

5.2.15. Multivariate analysis:

The variables which were found to be significant by independent samples test, bivariate analysis and logistic regression were analysed by multivariate analysis.

Table 20: Multivariate analysis of significant variables predicting morbidity in STI

Variables	**Odds ratio**	**95% CI**		**P value**
		Lower	**Upper**	
Heart rate	1.037	0.989	1.088	0.136
Blood pressure	0.989	0.959	1.020	0.484
GCS	0.000	0.000	-	0.997
Respiratory rate	0.949	0.826	1.090	0.459
Elevated neutrophils	1.063	0.993	1.139	**0.079**
Urea	1.017	0.990	1.045	0.217
Creatinine	0.734	0.358	1.508	0.400
Sodium	0.838	0.735	0.955	**0.008**
Albumin	1.012	0.351	2.913	0.983

Variables	Odds ratio	95% CI		P value
		Lower	Upper	
Total bilirubin	1.458	0.832	2.554	0.187
Base deficit	1.033	0.882	1.210	0.686
Fever	4.300	1.161	15.920	**0.029**
Haemorrhagic bullae	12.373	0.570	268.497	0.109

After multivariate analysis it was concluded that the following variables predict morbidity in soft tissue infections.

The variables were

1. **Neutrophilia in differential count with a p value of 0.079.**
2. **Low sodium at presentation with a p value of 0.008.**
3. **Elevated temperature at presentation with a p value of 0.029.**

5.3.0. Analysis of predictors of mortality in STI

5.3.1. Univariate analysis:

The descriptive analysis (mean, Standard Deviation) of various variables predicting mortality in STI is as follows.

Table 21: Descriptive analysis of variables predicting mortality in STI

Variables	Outcome	Number (n)	Mean	Standard deviation
Age	Non –mortality	95	57.34	14.589
	Mortality	15	52.27	11.436
Heart rate	Non- Mortality	95	96.63	16.471
	Mortality	15	104.00	23.312
Systolic blood pressure	Non- Mortality	95	117.64	20.624
	Mortality	15	100.67	28.900
Diastolic blood pressure	Non- Mortality	95	71.64	14.199
	Mortality	15	63.33	19.881
Respiratory rate	Non- Mortality	95	20.72	5.158
	Mortality	15	26.27	9.881
Glasgow coma scale	Non- Mortality	95	14.85	0.785
	Mortality	15	14.07	1.438
Haemoglobin	Non- Mortality	95	10.646	2.347
	Mortality	15	11.033	2.209

Variables	Outcome	Number (n)	Mean	Standard deviation
Total counts	Non- Mortality	95	17426.32	7241.32
	Mortality	15	14313.33	8567.78
Neutrophils	Non- Mortality	95	80.35	11.54
	Mortality	15	79.07	13.625
Platelets	Non- Mortality	95	260326.33	121289.912
	Mortality	15	216533.33	140446.16
Prothrombin time	Non- Mortality	95	13.895	11.193
	Mortality	15	15.660	5.514
INR	Non- Mortality	95	1.258	0.928
	Mortality	15	1.427	0.516
APTT	Non- Mortality	95	34.52	16.13
	Mortality	15	43.49	17.23
Urea	Non- Mortality	95	54.44	38.39
	Mortality	15	78.13	55.76
Creatinine	Non- Mortality	95	1.84	1.39
	Mortality	15	2.773	1.86
Sodium	Non- Mortality	95	131.24	5.012
	Mortality	15	129.73	6.386
Potassium	Non- Mortality	95	3.941	0.704
	Mortality	15	4.227	1.105

Variables	Outcome	Number (n)	Mean	Standard deviation
Total bilirubin	Non- Mortality	95	1.107	0.877
	Mortality	15	2.473	2.47
Albumin	Non- Mortality	95	2.789	0.643
	Mortality	15	2.387	0.6871
Glucose	Non- Mortality	95	200.75	97.04
	Mortality	15	191.20	151.41
Serum lactate	Non- Mortality	95	1.985	1.13
	Mortality	15	4.080	3.491
Base deficit	Non- Mortality	95	4.471	3.155
	Mortality	15	12.313	6.859
Serum myoglobin	Non- Mortality	95	148.38	221.106
	Mortality	15	1708	4320.674

5.3.2. Independent samples test for continuous variable

All the variables were analysed with independent samples test with assumption of null hypothesis.

The variables found to be significant for prediction of mortality are systolic blood pressure, diastolic blood pressure, respiratory rate, GCS, urea, creatinine, total bilirubin, albumin, serum lactate and base deficit.

Table 22: Analysis of variables predicting mortality by independent samples test

Variables	Odds ratio	P Value	95% confidence interval	
			Lower	Upper
Age	0.975	0.203	0.938	1.014
Heart rate	1.022	0.139	0.993	1.052
Systolic B.P	0.967	**0.009**	0.942	0.992
Diastolic B.P	0.967	**0.058**	0.935	1.001
Respiratory rate	1.121	**0.004**	1.036	1.213
GCS	0.564	**0.011**	0.363	0.878
Haemoglobin	1.078	0.548	0.845	1.375
Total counts	1.000	0.138	1.000	1.000
Neutrophils	0.991	0.695	0.949	1.036
Platelets	1.000	0.206	1.000	1.000
Prothrombin time	1.011	0.567	0.973	1.051

Variables	Odds ratio	P Value	95% confidence interval	
			Lower	Upper
INR	1.162	0.516	0.739	1.829
APTT	1.022	0.133	0.994	1.050
Urea	1.011	**0.052**	1.000	1.022
Creatinine	1.349	**0.043**	1.010	1.801
Sodium	0.948	0.299	0.858	1.048
Potassium	1.587	0.185	0.802	3.140
Total bilirubin	1.809	**0.005**	1.200	2.727
Albumin	0.399	**0.033**	0.172	0.927
Glucose	0.999	0.743	0.994	1.005
Serum lactate	1.730	**0.002**	1.214	2.465
Base deficit	1.521	**0.000**	1.240	1.867
Serum myoglobin	1.002	0.078	1.000	1.004

5.3.3. Cross tabs for categorical data:

The following variables were found to be significant predictors for morbidity using Pearson's chi square and Fischer's exact test.

5.3.4. Diabetes mellitus:

Diabetes mellitus in patients with STI was found to be a significant variable predicting mortality with a significant p value of 0.013.

Table 23: Analysis of Diabetes mellitus as a variable predicting mortality in STI

Diabetes mellitus	Non mortality vs. Mortality			Total
		Non Mortality	Mortality	
no	Count	37	11	48
	% within DM	77.1%	22.9%	100.0%
yes	Count	58	4	62
	% within DM	93.5%	6.5%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	6.228	1	**0.013**		0.23	0.069	0.783
Fischer exact test				**0.023**			

5.3.5. Chronic Liver Disease:

Chronic liver disease in patients with STI was found to be a significant variable predicting mortality with a Pearson chi square of 0.007 and Fischer's exact test value of 0.048.

Table 24: Analysis of Chronic liver disease as a variable predicting mortality in STI

Chronic liver disease (CLD)		Non mortality vs. Mortality		Total
		Non Mortality	Mortality	
no	Count	94	13	107
	% within CLD	87.9%	12.1%	100%
yes	Count	1	2	3
	% within CLD	33.3%	66.7%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	7.365	1	**0.007**		14.46	1.224	170.89
Fischer exact test				**0.048**			

5.3.6. Fever:

Fever as a presenting symptom in patients with STI was found to be nearly a significant variable predicting mortality with a Pearson chi square value of 0.063 and Fischer's exact value of 0.082.

Table 25: Analysis of fever as a variable predicting mortality in STI

Fever		Non mortality vs. Mortality		Total
		Non Mortality	Mortality	
no	Count	36	2	38
	% within fever	94.7%	5.3%	100%
yes	Count	59	13	72
	% within fever	81.9%	18.1%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	3.456	1	**0.063**		3.966	0.846	18.59
Fischer exact test				**0.082**			

5.3.7. Haemorrhagic Bullae:

Haemorrhagic bullae as a presenting symptom in STI was found to be a significant variable predicting mortality with a Pearson chi square value of 0.000 and Fischer's exact value of 0.001.

Table 26: Analysis of haemorrhagic bullae as a variable predicting mortality in STI

Haemorrhagic bullae		Non mortality vs. Mortality		Total
		Non Mortality	Mortality	
no	Count	87	8	95
	% within bullae	91.6%	8.4%	100%
yes	Count	59	13	72
	% within bullae	53.3%	46.7%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	16.090	1	**0.000**		9.516	2.736	33.09
Fischer exact test				**0.001**			

5.3.8. Left shift in differential count:

Left shift in differential count was found to be a significant variable predicting mortality in patients with STI with a Pearson chi square value of 0.005 and Fischer's exact value of 0.011.

Table 27: Analysis of left shift as a variable predicting mortality in STI

Left shift	Non mortality vs. Mortality			Total
		Non Mortality	Mortality	
no	Count	80	8	88
	% within left shift	90.9%	9.1%	100%
yes	Count	59	13	72
	% within left shift	68.2%	31.8%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	7.719	1	**0.005**		4.667	1.471	14.81
Fischer exact test				**0.011**			

5.3.9. Ventilation:

Ventilation in patient with STI was found to be a significant variable predicting mortality with a Pearson chi square value of 0.000 and Fischer's exact value of 0.000.

Table 28: Analysis of ventilation as a variable predicting mortality in STI

Ventilation		Non mortality vs. Mortality		Total
		Non Mortality	Mortality	
no	Count	88	2	90
	% within ventilation	97.8%	2.2%	100%
yes	Count	7	13	20
	% within ventilation	35.0%	65.0%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	54.76	1	**0.000**		81.714	15.292	436.65
Fischer exact test				**0.000**			

5.3.10. Inotropes:

Inotropes in patient with STI was found to be a significant variable predicting mortality with a Pearson chi square value of 0.000 and Fischer's exact value of 0.000.

Table 29: Analysis of inotropes as a variable predicting mortality in STI

Inotropes	Non mortality vs. Mortality			Total
		Non Mortality	Mortality	
no	Count	79	3	82
	% within inotropes	96.3%	3.7%	100%
yes	Count	16	12	28
	% within inotropes	57.1%	42.9%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	27.33	1	**0.000**		19.75	4.996	78.076
Fischer exact test				**0.000**			

5.3.11. Dialysis:

Dialysis in patient with STI was found to be a significant variable predicting mortality with a Pearson chi square value of 0.000 and Fischer's exact value of 0.001.

Table 30: Analysis of dialysis as a variable predicting mortality in STI

Dialysis		Non mortality vs. Mortality		Total
		Non Mortality	Mortality	
no	Count	92	10	102
	% within dialysis	90.2%	9.8%	100%
yes	Count	3	5	8
	% within dialysis	37.5%	62.5%	100%
Total	Count	95	15	110

	Value	df	Asymp sig (2 sided)	Exact Sig (2 sided)	OR	95% CI	
						Lower	Upper
Pearson chi square	17.49	1	**0.000**		15.33	3.180	73.93
Fischer exact test				**0.001**			

5.3.12. Other non significant variables:

The other variables analysed like sex, type of onset, hypertension, cardiac co-morbidities, renal disease, steroid usage, vascular disease, malignancy, repeated operations and amputation were not found to be significant.

Table 31: Analysis of variables not significant in predicting mortality in STI

Variables	OR	P value	95% CI	
			Lower	Upper
Sex	0.751	0.645	0.221	2.548
Type of onset	NA	0.476	NA	NA
Co-morbidities	0.454	0.155	0.150	1.374
Hypertension	0.492	0.380	0.130	1.870
Cardiac co-morbidity	1.470	0.644	0.285	7.574
Renal disease	0.898	1.000	0.103	7.863
Steroid usage	0.861	1.000	0.798	0.929
Vascular disease	2.190	0.449	0.213	22.558
Malignancy	0.682	1.000	0.800	0.930
Repeated operations	NA	0.713	NA	NA
Amputation	1.556	0.495	0.444	5.452

5.3.13. Multivariate analysis:

The variables which were found to be significant by independent samples test, bivariate analysis and logistic regression were analysed by multivariate analysis.

Table 32: Multivariate analysis of significant variables predicting mortality in STI

Variables	Odds ratio	95% CI		P value
		Lower	Upper	
Diabetes mellitus	0.065	0.007	0.573	**0.014**
Ventilator support	0.009	0.001	0.074	**0.000**
Dialysis	0.053	0.004	0.701	**0.026**

After multivariate analysis it was concluded that the following variables predict mortality in soft tissue infections.

The variables were

1. **Diabetes mellitus as a co morbid illness with a p value of 0.014.**
2. **Requirement of ventilator support with a p value of 0.000.**
3. **Requirement of dialysis with a p value of 0.026.**

Chapter 6

Discussion

6. Discussion

In the study done in our institution to find factors predicting mortality and morbidity, we found the following results.

Soft tissue infections have a male predilection with 68.2 percent (75 out of 110) of population being male which is in comparison with the international population which is 67.2 % (8).

The mean age of population having this problem was 57 years which is in comparison with international population which range from 48 years to 56 years (24)(12).

Duration of presenting symptoms vary from 1 day to 45 days with a mean of 9 days and median of 7 days where as in other study it was 3.4 days (12).

The mode of onset is predominantly spontaneous comprising of 55.5% of the population followed by trauma comprising of 40.9%. Surgery and insect bite comprised the remaining population. Whereas in the Western literature, trauma (38.3%) and spontaneous (31.2%) causes were the most common mode of onset (8).

69.1 percent (76 out of 110) of patients had associated illnesses at presentation. Diabetes mellitus was the most common associated illness which was seen in 56.4 percent (62 out of 110) of the patients where as in literature it is 58.6% - 70.8% (7,8).

Hypertension was second most common illness seen in 31.8 percent (35 out of 110) of patients. Cardiac and chronic renal disease was seen in 10 percent and 7.3 percent of the patients respectively. The other illnesses associated were chronic liver disease (2.7 percent), vascular disorders (3.6 percent) and malignancy (1.8 percent)(2,9,10).

There were 15 (15/110) mortalities in our study comprising of 13.6% of the total population where as in western literature it ranges form 25-35% (3,4,7).

22% of the patients had undergone amputation in our study. 18.18% of population who had undergone amputation had expired where as 81.82% of the population who had amputation survived. Of all the patients who had died, 73.33 did not have an amputation.

25.5 percent (28 out of 110) of the patients required inotropic requirement perioperatively whereas it is 25% in literature (8).

18.2 percent (20 out of 110) of patients required post operative ventilation. Of all the patients who had died, 86.66% of the population required ventilation.

7.3 percent (8 out of 110) of patients required dialysis due to acute renal failure or acute on chronic renal failure. 33.33& of patients who had died required dialysis.

5.5 percent (6 out of 110) of patient had myocardial infarct during the stay in hospital in the immediate post operative period. 4 out of 6 patient who had myocardial infarct expired.

Tissue for cultures was sent only for 71.8 percent (79 out of 110) of patients. Of these cultures were positive in 69 patients and sterile in 10 patients.

In the culture positive group, 62.3 percent (43 patients) had polymicrobial type I STI where as 37.6 percent (26 patients) had monomicrobial type II STI. The most common type of infection in the literature was Type I STI which comprises of 55-75% of cases (3,7,9).

8 out of 15 patients (53.3 percent of mortality) died of type II (monomicrobial)STI in contrast with type I (polymicrobial) STI where the mortality was 5 out of 15 (33.3 percent). There were no Type III or type IV infections noted in our study.

In type I STI, Escherichia Coli was the most common organism (65.1 percent) followed by Enterococcus (37.2 percent), NFGNB (27.9 percent) and pseudomonas (20.9 percent). These organisms were the common isolates in type I soft tissue infections (3,7,10,28).

Most common organism seen in the Type II infection is Group A Streptococci comprising of 42.3 percent (11 out of 26 patients) followed by Methicillin sensitive Staphylococcus aureus (MSSA) and Methicillin resistant Staphylococcus aureus (MRSA) which is same as in literature where Group A Streptococci is the most common comprising of 30% followed by Staphylococcus infection (3,10,14).

Heart rate, systolic blood pressure, respiratory rate, Glasgow coma scale, neutrophils, urea, creatinine, sodium, total bilirubin, albumin and base deficit, fever, haemorrhagic bullae, left shift in differential counts, number of re operations, amputation, ventilation, inotropic support, dialysis, positive tissue culture were found to be significant variables by logistic regression analysis in predicting morbidity in patients with soft tissue infections.

These are the variables that were identified as predictors of morbidity and mortality in soft tissue infection in various studies with varying significance (3,8,24,28,29,37–40).

However multivariate analysis in our study revealed the following variables to be significant in predicting morbidity in soft tissue infections. The variables are

1. **Neutrophilia in differential count with a p value of 0.079.**
2. **Low sodium at presentation with a p value of 0.008.**
3. **Elevated temperature at presentation with a p value of 0.029.**

These above variables were found to predict morbidity in soft tissue infection in literature (24,28,38,39).

Similarly systolic blood pressure, diastolic blood pressure, respiratory rate, GCS, urea, creatinine, total bilirubin, albumin, serum lactate, base deficit, diabetes mellitus, chronic liver disease, fever, haemorrhagic bullae, left shift in differential counts, ventilation, inotropic support and dialysis were found to be significant variables by logistic regression analysis in predicting mortality in patients with soft tissue infections.

However multivariate analysis in our study revealed the following variables to be significant in predicting mortality in soft tissue infections. The variables are

1. **Diabetes mellitus as a co morbid illness with a p value of 0.014.**
2. **Requirement of ventilator support with a p value of 0.000.**
3. **Requirement of dialysis with a p value of 0.026.**

The variables that predict mortality in soft tissue infections according to literature are tachycardia, hypothermia, elevated serum creatinine, age more than 50 years, elevated haematocrit, left shift in differential count, hypotension, malignancy, haemorrhagic bullae, Aeromonas and Vibrio infections(3,8,28,37,38).

Chapter 7

Conclusions and future directions

7.1.0. Conclusions

The significant variables that predict **morbidity** in patients with soft tissue infections are

1. **Neutrophilia in differential count with a p value of 0.079.**
2. **Low sodium with a p value of 0.008.**
3. **Elevated temperature at presentation with a p value of 0.029.**

The significant variables that predict **mortality** in patients with soft tissue infections are

1. **Diabetes mellitus as a co morbid illness with a p value of 0.014.**
2. **Requirement of ventilator support with a p value of 0.000.**
3. **Requirement of dialysis with a p value of 0.026.**

7.2.0. Future direction:

Based on the factors predicting mortality and morbidity in soft tissue infection, a scoring system is to be devised. Further studies are required for the validation of the scoring system.

8. Bibliography

1. From Cecil Textbook of Medicine, 19th ed, p1688 - fbDownloader Search [Internet]. [cited 2013 Aug 7]. Available from: http://search.fbdownloader.com/search.php?channel=msus200fbdgy6&q=From+Cecil+Textbook+of+Medicine%2C+19th+ed%2C+p1688

2. Sarani B, Strong M, Pascual J, Schwab CW. Necrotizing fasciitis: current concepts and review of the literature. J Am Coll Surg. 2009 Feb;208(2):279–88.

3. Chen I-C, Li W-C, Hong Y-C, Shie S-S, Fann W-C, Hsiao C-T. The microbiological profile and presence of bloodstream infection influence mortality rates in necrotizing fasciitis. Crit Care Lond Engl. 2011;15(3):R152.

4. O'Loughlin RE, Roberson A, Cieslak PR, Lynfield R, Gershman K, Craig A, et al. The epidemiology of invasive group A streptococcal infection and potential vaccine implications: United States, 2000-2004. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007 Oct 1;45(7):853–62.

5. Das DK, Baker MG, Venugopal K. Increasing incidence of necrotizing fasciitis in New Zealand: a nationwide study over the period 1990 to 2006. J Infect. 2011 Dec;63(6):429–33.

6. Kimura AC, Higa JI, Levin RM, Simpson G, Vargas Y, Vugia DJ. Outbreak of necrotizing fasciitis due to Clostridium sordellii among black-tar heroin users. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004 May 1;38(9):e87–91.

7. Wong C-H, Chang H-C, Pasupathy S, Khin L-W, Tan J-L, Low C-O. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. J Bone Joint Surg Am. 2003 Aug;85-A(8):1454–60.

8. Hsiao C-T, Weng H-H, Yuan Y-D, Chen C-T, Chen I-C. Predictors of mortality in patients with necrotizing fasciitis. Am J Emerg Med. 2008 Feb;26(2):170–5.

9. Anaya DA, Dellinger EP. Necrotizing soft-tissue infection: diagnosis and management. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007 Mar 1;44(5):705–10.

10. Miller LG, Perdreau-Remington F, Rieg G, Mehdi S, Perlroth J, Bayer AS, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles. N Engl J Med. 2005 Apr 7;352(14):1445–53.

11. Kilburn SA, Featherstone P, Higgins B, Brindle R. Interventions for cellulitis and erysipelas. In: The Cochrane Collaboration, Kilburn SA, editors. Cochrane Database Syst Rev [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2010 [cited 2013 Aug 6]. Available from: http://summaries.cochrane.org/CD004299/interventions-for-cellulitis-and-erysipelas

12. Shaikh N. Necrotizing fasciitis: A decade of surgical intensive care experience. Indian J Crit Care Med. 2006;10(4):225.

13. Jahnson L, Berggren L, Björsell-Ostling E, Bonnerstig J, Holmberg H. Streptococcal myositis. Scand J Infect Dis. 1992;24(5):661–5.

14. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect. 2010 Aug;75(4):249–57.

15. Salcido RS. Necrotizing fasciitis: reviewing the causes and treatment strategies. Adv Skin Wound Care. 2007 May;20(5):288–293; quiz 294–295.

16. Bryant AE, Bayer CR, Huntington JD, Stevens DL. Group A streptococcal myonecrosis: increased vimentin expression after skeletal-muscle injury mediates the binding of Streptococcus pyogenes. J Infect Dis. 2006 Jun 15;193(12):1685–92.

17. Cainzos M, Gonzalez-Rodriguez FJ. Necrotizing soft tissue infections. Curr Opin Crit Care. 2007 Aug;13(4):433–9.

18. Jones MK, Oliver JD. Vibrio vulnificus: Disease and Pathogenesis. Infect Immun. 2009 May 1;77(5):1723–33.

19. Olsen RJ, Musser JM. Molecular pathogenesis of necrotizing fasciitis. Annu Rev Pathol. 2010;5:1–31.

20. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect. 2010 Aug;75(4):249–57.

21. MACLENNAN JD. The histotoxic clostridial infections of man. Bacteriol Rev. 1962 Jun;26:177–276.

22. Stevens DL. Streptococcal toxic-shock syndrome: spectrum of disease, pathogenesis, and new concepts in treatment. Emerg Infect Dis. 1995 Sep;1(3):69–78.

23. Majeski J, Majeski E. Necrotizing fasciitis: improved survival with early recognition by tissue biopsy and aggressive surgical treatment. South Med J. 1997 Nov;90(11):1065–8.

24. Wong C-H, Khin L-W, Heng K-S, Tan K-C, Low C-O. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004 Jul;32(7):1535–41.

25. Stamenkovic I, Lew PD. Early recognition of potentially fatal necrotizing fasciitis. The use of frozen-section biopsy. N Engl J Med. 1984 Jun 28;310(26):1689–93.

26. Schmid MR, Kossmann T, Duewell S. Differentiation of necrotizing fasciitis and cellulitis using MR imaging. AJR Am J Roentgenol. 1998 Mar;170(3):615–20.

27. Wang Y-S, Wong C-H, Tay Y-K. Staging of necrotizing fasciitis based on the evolving cutaneous features. Int J Dermatol. 2007 Oct;46(10):1036–41.

28. Anaya DA, Bulger EM, Kwon YS, Kao LS, Evans H, Nathens AB. Predicting death in necrotizing soft tissue infections: a clinical score. Surg Infect. 2009 Dec;10(6):517–22.

29. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: executive summary. Clin Infect Dis Off Publ Infect Dis Soc Am. 2011 Feb 1;52(3):285–92.

30. Sudarsky LA, Laschinger JC, Coppa GF, Spencer FC. Improved results from a standardized approach in treating patients with necrotizing fasciitis. Ann Surg. 1987 Nov;206(5):661–5.

31. Bilton BD, Zibari GB, McMillan RW, Aultman DF, Dunn G, McDonald JC. Aggressive surgical management of necrotizing fasciitis serves to decrease mortality: a retrospective study. Am Surg. 1998 May;64(5):397–400; discussion 400–401.

32. Mader JT, Brown GL, Guckian JC, Wells CH, Reinarz JA. A mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. J Infect Dis. 1980 Dec;142(6):915–22.

33. Kaye D. Effect of hyperbaric oxygen on Clostridia in vitro and in vivo. Proc Soc Exp Biol Med Soc Exp Biol Med N Y N. 1967 Feb;124(2):360–6.

34. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. A comparison of the effects of inspired oxygen concentration and antibiotic administration on in vivo bacterial clearance. Arch Surg Chic Ill 1960. 1986 Feb;121(2):191–5.

35. Prevention of Invasive Group A Streptococcal Infections Workshop Participants. Prevention of invasive group A streptococcal disease among household contacts of case patients and among postpartum and postsurgical patients: recommendations from the Centers for Disease Control and Prevention. Clin Infect Dis Off Publ Infect Dis Soc Am. 2002 Oct 15;35(8):950–9.

36. Darenberg J, Luca-Harari B, Jasir A, Sandgren A, Pettersson H, Schalén C, et al. Molecular and clinical characteristics of invasive group A streptococcal infection in Sweden. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007 Aug 15;45(4):450–8.

37. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. Arch Surg Chic Ill 1960. 2005 Feb;140(2):151–157; discussion 158.

38. choosak. Predictor of mortality from necrotisinng infections. Chiang Mai Med J. 2009(48(4)):135–142.

39. Yaghoubian A, de Virgilio C, Dauphine C, Lewis RJ, Lin M. Use of admission serum lactate and sodium levels to predict mortality in necrotizing soft-tissue infections. Arch Surg Chic Ill 1960. 2007 Sep;142(9):840–846; discussion 844–846.

40. Micek ST, Hoban AP, Pham V, Doherty JA, Zilberberg MD, Shorr AF, et al. Bacteremia increases the risk of death among patients with soft-tissue infections. Surg Infect. 2010 Apr;11(2):169–76.

9.1.0. Annexure 1

Pro forma for data collection

Christian Medical College, Vellore

Department of General Surgery

An Observational study on factors predicting mortality and morbidity in patients with soft tissue infections

Proforma for Data Collection

Serial number: Hospital number: Place:

Name: Age: Sex: Occupation:

Time of onset of problem (onset to hospital admission):

Type of onset: Traumatic [ ] Insect bite [ ] Spontaneous [ ] Surgical [ ]

Previous co morbid illness:

Number of co morbid illness:

Hr: B.P: R.R: Temperature: GCS:

Oedema: Icterus: Swelling: Haemorrhagic Bullae

Peripheral pulses: left right

Femoral

Popliteal

Dorsalis pedis

Haemoglobin: Total counts: Differential counts:

Platelet : Pt/INR: APTT:

Creatinine: Urea: Sodium: Potassium:

Calcium: Albumin: Glucose:

Bicarbonate: Lactate: Base excess: Anion gap:

Saturation: P/F ratio:

Procalcitonin: Serum Myoglobin:

Tissue culture:

Organisms:

Sensitivity:

Blood Culture:

Organisms:

Sensitivity:

Debridement: Number of times of debridement

Time taken for intervention: Amputation:

Ventilation: Number of days in ventilator

Inotropes: Number of days on inotropes:

Myocardial infarct:

Renal failure: Need for dialysis:

Number of days of hospital stay:

Mortality:

9.2.0. Annexure 2

Patient information sheet

Christian Medical College, Vellore

Department of General Surgery

An Observational study on factors predicting mortality and morbidity in patients with soft tissue infections

Information sheet

You are invited to be part of a study to improve the current knowledge about your disease condition. This study will help other patients who later come to hospital with the same complaints. By agreeing to be a part of this study, you will contribute to recognizing early how severe the disease is and thereby starting appropriate treatment immediately. The severity of your disease and the final treatment received will be compared to the information collected from you in the beginning.

The information collected from you will include

1. History – This includes details regarding your general health and the present illness

2. Clinical examination – Includes evaluation by the attending doctor on admission to the hospital

3. Investigations – Includes the results of relevant blood and urine tests

Whether you accept or decline to be a part of this study will not affect your further treatment at this hospital.

The benefits of joining in this study will be that you don't have to pay for a particular laboratory test which is called "arterial blood gas". The money for this particular test alone will be provided by the study team.

There is no disadvantage or complication that can happen to you by participating in this study as this study does not interfere in the treatment provided by the caretaker.

All details including personal data, assessment of the doctor during and after the operation will be kept confidential.

We aim to include about 150 people from this hospital in this study in the next 2 years.

Participation in this study is purely voluntary, and you can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which you are otherwise entitled.

In case of doubts/ questions, please contact Dr. Vijayan P, Dept of General Surgery, CMCH Vellore. Ph no: +919840529964

9.3.0. Annexure 3

Patient consent form

Informed Consent form to participate in a clinical trial

Christian Medical College, Vellore

Department of General Surgery

An Observational study on factors predicting mortality and morbidity in patients with soft tissue infections

Study Number:

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age: _____

Please initial box

(i) I confirm that I have read/been read to and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am

free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date: _____/_____/_____

Name of the Witness: _____

9.4.0. Annexure 4

Data sheet

arm	id	hosp	hosp1	age	sex	dos	tos	comorbid
1	1	17578	D	79	1	10	3	1
0	2	70462	D	67	2	3	3	1
0	3	83216	D	70	2	4	1	0
1	4	107599	F	49	1	10	1	0
1	5	113903	f	60	2	15	3	1
1	6	113027	f	80	2	3	1	0
1	7	111102	f	84	2	3	2	1
1	8	123478	f	62	2	1	1	1
1	9	117878	f	55	2	30	3	1
1	10	912940	d	62	1	15	3	1
1	11	126007	f	31	1	7	3	1
1	12	126514	f	51	1	15	4	1
1	13	192121	c	62	1	3	3	0
1	14	133305	f	37	2	5	3	0
1	15	972711	d	53	1	20	1	1
1	16	153669	f	58	1	15	3	1
1	17	156110	f	30	1	7	1	0
1	18	162024	f	74	1	4	3	1
1	19	180309	f	45	2	15	1	1
0	20	189619	f	64	2	7	3	1
0	21	936475	d	28	1	15	3	0
1	22	207801	f	37	1	3	3	1
1	23	781612	d	66	1	3	3	0
1	24	138781	F	61	1	2	3	1
0	25	893005	A	46	2	7	3	1
0	26	107606	F	53	1	3	1	0
0	27	757917	D	52	1	10	3	0
0	28	620904	b	70	1	7	3	1
0	29	119326	f	50	1	3	3	0
0	30	124992	f	55	1	20	1	0
1	31	867395	d	71	1	3	3	1
0	32	126491	f	63	1	4	1	1
0	33	925276	d	66	1	5	3	0
1	34	133273	f	43	1	30	1	1
1	35	133072	f	46	1	5	3	1
1	36	992929	d	40	2	4	3	1
0	37	91821	f	65	2	2	3	1
0	38	107148	f	62	1	3	1	0
0	39	119325	f	29	2	2	4	0
0	40	136093	f	69	1	5	3	1
0	41	194122	d	70	1	3	1	1
0	42	384910	b	33	2	30	1	1
0	43	497534	f	40	2	3	3	0
0	44	476631	f	87	1	10	3	1
1	45	485882	f	73	1	4	1	1
1	46	485978	f	51	1	8	3	1
0	47	295943	f	45	1	2	4	0
0	48	295941	f	45	1	3	3	1
0	49	485943	f	65	1	30	1	1
1	50	142667	f	71	1	8	3	1
0	51	582137	d	71	1	10	3	0
0	52	133167	d	68	2	7	3	1
0	53	617880	d	77	1	8	3	1
0	54	474668	f	71	1	2	1	0
1	55	406429	f	66	1	1	1	1
0	56	476627	f	30	2	7	3	0
0	57	626565	c	44	2	6	1	1
0	58	70462	d	69	2	10	3	1
1	59	6565	b	44	1	20	1	1
0	60	74224	f	49	1	20	3	1
0	61	113001	f	58	1	2	3	1
1	62	120095	o	77	2	15	1	0
1	63	126930	c	57	1	5	1	1
1	64	232316	d	85	1	9	3	1
1	65	240631	f	71	1	1	1	1
0	66	286858	d	69	2	7	3	1
0	67	879658	D	43	1	10	1	1
1	68	353117	F	51	1	10	1	0
0	69	448581	F	60	2	7	3	1
0	70	338761	F	63	1	9	3	1
0	71	270867	F	70	2	3	3	1
0	72	472563	F	51	1	14	1	1
1	73	269191	F	43	1	30	1	1
1	74	296410	F	66	1	10	3	1
0	75	105398	f	54	1	15	3	1
0	76	251731	f	70	1	7	1	1
0	77	295401	f	59	1	5	1	1
0	78	623470	f	85	2	7	3	1
0	79	327659	f	50	2	5	3	1
1	80	299496	f	50	1	4	3	1
1	81	448582	f	59	1	40	1	1
1	82	441140	f	33	1	45	1	1
1	83	434516	f	59	1	10	3	1
0	84	455412	f	79	1	10	1	1
1	85	264069	f	52	1	3	1	1
1	86	500723	f	30	2	15	3	1
1	87	441165	f	47	1	2	1	0
0	88	611888	f	75	1	7	3	0
1	89	455954	f	50	1	15	3	0
0	90	389835	d	54	1	10	3	1
0	91	184264	b	77	1	2	3	1
1	92	425139	f	50	1	7	1	1
1	93	476393	f	65	1	4	3	0
0	94	490621	f	47	1	3	1	0
1	95	476056	f	34	1	2	1	0
1	96	476399	f	50	2	1	1	1
0	97	406245	f	42	2	4	1	1
0	98	625856	f	58	1	3	1	1
0	99	476350	f	63	1	7	3	0
0	100	783402	d	47	2	3	3	1
0	101	329922	F	60	2	7	3	1
1	102	591295	F	68	1	5	3	1
0	103	330809	F	55	2	4	3	1
0	104	389494	F	65	2	15	3	0
1	105	338598	F	30	1	14	1	0
1	106	485979	F	51	1	8	3	1
1	107	149391	F	35	2	10	1	0
1	108	312485	F	55	1	10	1	0
1	109	500642	F	39	2	7	1	1
1	110	401186	F	52	1	3	1	0

dm	htn	ihd	ckd	cld	steroid	vascular	malignancy	hr
1	1	1	0	0	0	0	0	110
1	1	0	0	0	0	0	0	74
0	0	0	0	0	0	0	0	78
0	0	0	0	0	0	0	0	78
1	0	1	1	0	0	0	0	100
0	0	0	0	0	0	0	0	122
0	1	1	0	0	0	0	0	114
1	1	0	0	0	0	0	0	100
1	1	0	0	0	0	0	0	96
0	1	0	0	0	0	0	0	114
0	0	1	0	0	0	0	0	88
1	1	1	1	0	0	0	0	80
0	0	0	0	0	0	0	0	106
0	0	0	0	0	0	0	0	120
0	0	0	0	1	0	0	0	100
1	0	0	0	0	0	0	0	100
0	0	0	0	0	0	0	0	120
1	0	0	0	0	0	0	0	108
1	0	0	0	0	0	0	0	82
1	0	0	0	0	0	0	0	100
0	0	0	0	0	0	0	0	100
0	0	0	0	1	0	0	0	96
0	0	0	0	0	0	0	0	80
0	0	1	0	0	0	1	0	100
1	0	0	0	0	0	0	0	100
0	0	0	0	0	0	0	0	124
0	0	0	0	0	0	0	0	94
1	1	1	0	0	0	0	0	80
0	0	0	0	0	0	0	0	90
0	0	0	0	0	0	0	0	72
1	1	1	0	0	0	0	0	120
0	1	0	1	0	0	0	0	90
0	0	0	0	0	0	0	1	70
1	0	0	0	0	0	0	0	120
1	0	0	0	0	0	0	0	108
1	0	0	1	0	1	1	0	125
1	1	0	0	0	0	0	0	110
0	0	0	0	0	0	0	0	108
0	0	0	0	0	0	0	0	90
1	1	0	0	0	0	0	0	88
1	0	0	0	0	0	0	0	82
0	0	0	1	0	1	0	0	90
0	0	0	0	0	0	0	0	98
0	0	0	0	0	0	0	0	86
0	0	0	0	0	0	0	0	150
1	1	1	1	0	0	0	0	84
1	1	1	0	0	0	0	0	92
1	1	0	0	0	0	0	0	98
0	0	0	0	0	0	0	0	120
0	0	0	0	0	0	0	0	106
0	0	0	0	0	0	0	0	70
1	0	0	0	0	0	0	0	106
1	1	0	0	0	0	0	0	100
1	0	0	0	0	0	0	0	80
0	0	0	0	0	0	0	0	110
1	1	0	0	0	0	0	0	92
1	0	0	0	0	0	0	0	90
1	1	0	0	0	0	0	0	108
1	1	0	0	0	0	0	0	96
0	0	0	0	0	0	0	0	80
0	0	0	0	0	0	0	0	80
1	0	0	0	0	0	0	0	132
0	0	0	0	0	0	0	0	110
0	0	0	0	0	0	0	0	110
1	0	0	0	0	0	0	0	90
0	0	0	0	0	0	0	0	140
0	1	0	0	0	0	0	0	80
0	1	0	0	0	0	0	0	78
1	0	0	0	0	0	0	0	119
0	0	0	0	0	0	0	0	90
1	1	0	0	0	0	0	0	78
1	0	0	0	0	0	0	0	66
1	0	0	0	0	0	0	0	90
0	0	0	0	0	0	0	0	98
1	0	0	0	0	0	0	0	92
1	0	0	0	0	0	0	0	96
0	0	0	0	0	0	0	0	88
0	0	0	0	0	0	0	0	94
0	0	0	0	0	0	0	0	88
0	0	0	0	0	0	1	0	94
1	1	0	0	0	0	0	0	60
0	0	0	0	0	0	1	0	106
1	0	0	0	0	0	0	0	90
1	1	0	0	0	0	0	0	88
0	0	0	0	0	0	0	0	76
1	1	0	0	0	0	0	0	84
1	1	0	0	0	0	0	0	130
1	0	0	0	0	0	0	0	90
1	0	0	0	0	0	0	0	96
1	0	0	0	0	0	0	0	104
0	0	0	0	0	0	0	0	120
1	0	0	0	0	0	0	0	80
1	0	0	1	0	0	0	0	88
1	1	0	0	0	0	0	0	90
1	1	0	0	0	0	0	0	90
1	0	0	0	0	0	0	0	110
1	1	0	0	0	0	0	0	84
1	1	1	0	0	0	0	0	96
1	0	0	0	0	0	0	0	88
1	1	0	0	0	0	0	0	96
1	1	0	1	0	0	0	0	100
1	0	0	0	0	0	0	0	72
1	1	0	0	0	0	0	0	170
1	1	0	0	0	0	0	0	106
1	0	0	0	0	0	0	0	102
1	1	0	0	0	0	0	0	92
0	0	0	0	0	0	0	0	76
0	0	0	0	0	0	1	0	120
1	0	0	0	0	0	0	0	116
0	0	0	0	0	0	0	0	134

bp	bp1	rr	gcs	fever	bullae	pulses	hb	tc
130	90	24	15	1	0	1	12.4	13100
110	60	38	15	0	0	1	11.8	12200
118	70	14	15	1	0	1	9.9	11000
90	70	18	15	0	1	1	10.2	24700
90	60	24	15	1	0	1	6.7	32800
70	60	28	15	1	0	1	12.4	14300
110	80	20	15	1	0	1	15.1	27400
140	80	20	15	1	0	0	10	22900
170	100	22	15	1	0	0	7.5	14200
110	70	28	15	1	0	1	10	9900
120	70	18	15	1	0	0	13.4	6500
140	80	28	15	1	0	1	8.8	28000
80	50	44	12	1	1	1	14.1	15000
110	70	18	15	1	0	1	12.9	12000
110	70	20	15	1	1	1	12.6	8000
130	80	22	15	1	1	1	10.4	12700
100	60	22	15	1	0	1	13.9	10800
110	90	20	15	1	1	1	10.6	29100
100	60	14	15	0	0	1	8.6	16200
110	70	18	15	1	0	1	5.8	25200
100	70	24	15	0	0	1	12.9	17000
110	60	22	15	1	0	1	9.4	5000
110	80	22	15	1	0	1	12	12000
120	70	16	15	0	0	0	13.1	29200
130	90	17	15	0	0	1	7.7	15100
100	60	22	15	0	0	1	6.5	23500
140	90	14	15	1	0	1	12.8	9100
130	70	20	15	1	0	1	13.1	31000
110	70	16	15	0	0	0	11.7	17600
122	60	22	15	1	0	1	12.1	11800
70	50	38	12	1	0	1	14.3	11400
110	70	18	15	0	0	1	9	3000
130	70	11	15	0	0	1	10	23000
100	70	18	15	1	0	1	8	21100
80	60	25	10	1	1	1	12.5	16300
70	50	50	15	1	0	0	8.9	20600
110	70	22	15	1	0	1	11.6	8400
116	70	22	15	1	0	1	12	15600
90	60	18	15	1	0	1	12.2	15100
120	70	20	15	1	0	0	8.5	14400
130	80	14	15	1	0	1	10	11800
120	70	14	15	1	0	1	12.7	16100
110	70	20	15	1	0	1	12.1	11400
130	90	20	15	0	0	0	11.3	15000
110	60	14	15	0	0	1	13.3	9500
130	60	28	15	1	0	0	10.6	21200
150	90	20	15	1	0	1	13.9	17800
118	70	22	15	1	0	1	7.8	18000
100	50	12	15	0	0	0	9.9	7800
150	100	28	15	1	1	1	10.9	8000
108	60	18	15	0	0	1	5.1	37000
130	50	20	15	1	0	1	11.8	10500
140	90	22	15	0	0	1	13.4	12100
100	50	18	15	0	0	0	11.8	24400
118	90	15	15	1	0	1	10.3	12500
120	70	12	15	0	0	1	11.5	14400
100	70	16	15	1	0	1	6.6	22000
130	50	14	15	0	0	1	11.4	12200
126	76	20	15	1	0	1	10	28500
120	56	18	15	1	0	0	12.4	17800
130	90	14	15	0	0	1	14.8	18500
110	80	17	15	0	1	1	11.2	6200
130	80	16	15	1	0	1	11.8	15500
140	90	22	15	1	1	1	11.1	28100
100	60	20	15	0	0	1	10.9	17500
140	70	22	15	0	0	1	10.6	10800
140	90	22	15	0	0	1	10.7	22000
150	70	22	15	1	0	1	9.3	28800
130	90	18	15	0	0	1	10.6	18800
160	90	20	15	1	0	1	10.5	8500
130	90	18	15	1	0	1	10.2	17200
110	70	22	15	0	0	1	10.1	27800
130	94	20	15	1	0	1	8.5	15000
110	70	19	15	0	0	0	9.6	18200
140	70	18	15	1	0	1	13.5	11400
150	80	22	15	1	0	1	11.6	8400
120	70	20	15	0	0	1	11.2	16700
100	60	28	15	1	1	1	8.3	20700
130	80	28	15	1	0	1	8.4	7700
50	10	42	15	1	1	0	10.6	14900
80	40	24	15	0	0	1	8.5	15500
110	70	22	15	1	0	1	8.7	14500
140	80	28	15	1	0	1	5.8	24600
110	70	16	15	0	0	1	8.6	12200
70	40	26	15	1	0	0	11.8	10700
100	60	14	15	1	0	1	6.4	29600
110	70	18	15	1	0	1	7.7	34600
110	60	20	15	0	0	1	11.7	15100
80	60	28	10	1	1	1	8.6	26200
140	80	12	15	0	0	1	12.6	9400
130	80	20	15	1	0	1	15.4	18900
140	90	20	15	1	0	1	13.8	22900
70	50	50	11	1	1	1	10.6	6100
140	80	24	15	0	0	1	11.7	16500
70	50	46	13	1	0	1	14.4	3000
80	60	24	15	1	0	1	8.8	4800
110	80	22	15	0	0	1	8.9	14900
110	70	20	15	0	0	1	12.5	19900
120	80	32	15	1	0	1	10.2	25500
110	70	20	15	1	0	1	7.9	34600
130	90	20	15	0	0	1	12.4	17800
150	80	22	15	1	0	1	10.7	21900
110	70	18	15	0	0	1	15.2	16200
130	70	20	15	0	0	1	8.2	11500
120	80	22	15	0	0	1	13.4	22600
100	60	50	15	1	1	1	3.5	21200
90	60	20	12	1	1	1	11	15200
90	60	24	14	1	0	1	13.3	30600
110	80	20	15	1	0	1	8.9	15700
170	100	28	15	1	0	1	12.4	15900

dc	dc1	platelets	pt	inr	aptt	urea	creatinine	sodium
88	0	146000	11.8	1	38	67	1.5	126
88	0	160000	9.2	0.9	31	97	2.2	150
69	0	308000	12.8	1.2	34	24	1	132
86	1	224000	11.9	1.1	35.5	225	4.2	127
90	1	215000	11.2	1	24	78	4.4	123
89	0	215000	15.6	1.4	25.9	51	1.7	131
91	0	199000	15.4	1.4	33.1	62	2.5	131
88	0	441000	12.7	1.2	41.3	78	1.6	132
87	0	284000	11.8	1	67.1	70	2	123
57	0	613000	13	1.2	30.2	18	0.8	128
73	0	12000	12.4	1.1	32.7	85	1.4	135
90	0	374000	11	1	29.6	132	6.1	124
69	1	114000	28.2	2.6	78.6	124	3.5	134
80	0	225000	18.9	1.7	43.7	22	0.8	134
82	1	61000	19.9	1.8	37.8	36	0.8	140
89	0	219000	12	1.1	28.9	46	2.5	131
90	0	33000	14.4	1.3	30	42	1.8	135
70	1	494000	15.5	1.4	29.2	52	1.5	128
68	1	66000	16.3	1.6	26	91	1.2	120
87	0	350000	13.2	1.2	27.3	45	2	150
85	0	421000	12	1.1	27.4	27	1	126
88	1	49000	26.9	2.5	73.5	42	2.3	159
85	0	258000	13.1	1.2	36	72	2.5	150
84	0	297000	14.2	1.3	42.6	41	1	125
87	0	258000	12.2	1.1	30.6	80	4.6	125
89	0	91000	13.6	1.2	40.5	72	1.1	133
71	1	221000	11.1	1	31.5	64	0.9	137
26	0	341000	11.8	1	30.2	25	0.9	133
86	1	176000	10.9	1	32	40	1.2	131
72	0	432000	10.9	1	37.7	54	0.9	131
90	0	182000	17	1.6	38.2	47	2.9	131
85	0	360000	12.1	1.1	28.1	115	3.4	127
87	0	208000	11.8	1	33	33	1.9	137
87	0	244000	11.6	1.1	36.8	36	1.4	122
92	1	128000	11.4	1	25.1	222	1.5	131
92	0	254000	14.6	1.3	26.7	80	2.1	114
69	0	212000	11	1	33	20	0.9	135
84	0	217000	13.2	1.3	38	35	1	137
71	0	265000	11.4	1	24.5	18	0.9	134
81	0	296000	15.2	1.4	34.4	67	2.8	150
69	0	22000	10.6	1	35.2	31	2	133
81	0	374000	25.2	2.3	46.2	23	0.8	135
84	0	220000	11	1	36.6	25	1.2	131
82	0	222001	11.5	1	37.6	77	1.7	131
95	0	269000	14.6	1.3	29.7	57	3.2	139
99	0	254000	12.4	1.1	28.9	56	1.2	127
89	0	48000	120	10	180	29	1.1	137
85	0	384000	12.5	1.1	31.4	33	1.9	136
62	0	353000	11.1	1	28.3	37	1.3	135
97	1	195000	11.1	1	38.5	144	7.5	128
95	1	237000	13.5	1.2	39.5	35	1.1	136
55	0	349000	11.9	1	32.2	23	1.1	132
83	0	253000	12.6	1.1	29	22	1.1	138
87	0	332000	12.2	1.1	29	44	1.1	131
74	0	354000	11.9	1	29.7	33	1.7	130
79	0	278000	11	1.1	37.6	13	0.9	136
67	0	22000	16.9	1.5	50.3	32	1.3	132
88	0	166000	9.2	0.9	31.2	97	2.2	150
95	0	437000	16.1	1.4	46.4	178	10.2	128
72	0	321000	12.2	1.1	35	25	1.3	137
86	0	156000	14.2	1.2	39.2	26	1.3	134
55	0	252000	14.9	1.4	33.2	45	1.5	131
83	0	506000	11.4	1	28.5	24	0.8	124
94	0	233000	13.1	1.2	26.5	72	2.3	130
82	0	222000	13.1	1.2	28	44	1.2	128
57	0	321000	14.1	1.3	32.3	27	0.9	135
83	0	565000	10.9	0.9	29.2	23	1.6	126
95	0	158000	12.9	1.2	25.3	52	1.6	132
76	0	278000	11.2	1.1	25	19	1.4	138
78	0	156000	12	1.1	42.2	48	4.7	143
78	0	377000	11.9	1.1	32.8	33	1.4	130
56	1	212000	11.2	1	30.4	22	1	133
81	0	386000	12.3	1.1	39.3	16	1	122
84	0	212000	14.4	1.3	41.2	34	1.2	132
71	0	110000	13.4	1.2	29.4	57	2.3	140
66	0	318000	10.5	0.9	39.7	36	1.4	139
94	0	116000	12.2	1.1	36.6	42	1.4	134
81	0	211000	12.3	1.1	27.6	68	3	131
69	0	289000	11.9	1.1	35.1	102	4.5	134
84	1	222000	13	1.2	33	93	3.1	137
90	0	292000	16.5	1.5	37.2	72	2.4	134
80	0	441000	14.2	1.3	41	23	0.7	116
85	0	350000	12.1	1.1	26.6	121	1.4	133
89	0	319000	11.7	1.1	31	79	2.1	132
88	0	174000	12.4	1.1	38.5	73	2.9	135
83	1	509000	12.2	1.1	24	46	1.6	127
88	0	158000	14.4	1.3	32.5	26	1.2	130
83	0	170000	12	1.1	27.5	10	1.3	131
74	1	526000	13.4	1.2	24.7	194	3.3	124
72	0	212000	12.6	1.2	28.2	20	1.9	138
82	0	195000	11.2	1.2	29	35	1.4	126
81	0	316000	11.1	1.1	32.4	42	1.4	131
91	0	66000	13.4	1.2	45.5	161	8	128
70	1	218000	10.8	1	27.7	15	1	134
43	1	302000	16.5	1.5	51.6	85	2.9	130
86	0	73000	13.1	1.2	38.8	48	2.1	128
78	0	245000	10.3	0.9	43.2	64	1.4	133
90	0	207000	13.2	1.2	27	34	1.3	139
76	1	301000	12.5	1.1	47.1	44	1.4	124
65	1	325000	13.8	1.3	31.8	88	2.2	127
83	0	517000	12.2	1.3	38.9	78	1.3	130
90	0	291000	11.3	0.9	29.4	80	1.7	125
65	0	324000	14.2	1.3	31.2	37	1.2	130
77	0	395000	12.9	1.2	35.2	45	1.3	134
79	1	253000	11.6	1.1	28.2	17	1.1	131
90	0	254000	12.4	1.1	28.9	56	1.1	127
71	0	101000	10.9	1	24.4	59	2.8	117
82	1	74000	13.8	1.3	31.2	99	1.3	135
69	0	125000	13.2	1.2	28.2	30	0.8	132
92	0	197000	13.4	1.3	39.2	35	1.3	136

potassium	total	albumin	glucose	lactate	base	myoglobin	multiple	amputation
3.8	1	3.2	241	1.1	5.7	29	0	0
3.9	0.5	3.6	251	3.5	6.8	44	0	0
3.5	1.2	3.7	141	1.4	1.3	34	0	0
5.4	1.7	2.6	64	1	19.8	52	0	0
6.2	0.4	2.5	630	1.7	10.6	640	1	1
3.6	0.7	2.8	81	0.8	10.1	84	1	0
3.7	1	2.9	114	0.9	6.6	88	1	0
4.5	1	2.8	230	1	5.4	57	0	0
4.2	0.4	1.4	322	0.5	7.6	133	0	0
4.4	1.8	2.2	83	2.6	7	123	0	0
3.1	0.8	2.1	108	0.9	3	146	1	0
4.8	0.4	0.9	128	0.7	14.8	188	0	0
5.2	6.4	2.5	200	9.8	12.2	16548	0	1
5	1.1	1.3	110	12.7	29.7	155	0	0
3.6	3.6	3.4	161	6.6	8.6	625	0	0
3.6	1.9	3.2	110	2.7	13.9	192	0	0
3.7	2.5	2.2	110	2	5.1	188	0	0
4.9	1.1	2.5	544	1.1	5.5	98	0	0
4	2.7	1.9	180	2.6	5.7	197	1	1
3.8	0.5	2.2	198	0.5	10.2	102	0	0
5.1	1.8	2.3	83	0.9	0.5	36	0	0
4.5	9.4	1.5	112	4.4	11	129	0	0
2.5	3	1.9	208	4.9	9.5	425	0	0
3	1	3.5	547	0.9	0.1	208	0	1
4.7	0.4	1.7	180	2	5	56	0	0
3.3	5.1	2	155	3.2	6.2	182	0	0
4.2	1.2	3.2	145	1	3.2	32	0	0
4.2	0.3	3.2	158	2	2.1	98	0	0
3.9	0.5	3	308	0.6	2.3	20	0	0
3.9	0.5	3.2	144	2	3	61	0	0
3.8	1	4	105	2.4	9.1	1608	0	0
4.2	0.4	3	434	4	9.1	122	0	0
4.7	0.7	3.2	111	1.6	2.2	44	0	0
4.1	1.2	3.2	545	2	4	432	0	1
3.5	0.8	2	203	2.4	7.3	401	1	0
4.1	0.7	2.7	297	5.3	10.2	104	0	0
5.1	0.8	3	201	2	4	20	0	0
3.5	1	2.8	186	0.8	2.3	44	0	0
4	0.4	2.3	104	0.6	2.9	62	0	0
2.7	0.5	2.1	159	3.2	10.1	103	0	0
3.2	0.4	3.3	145	1.8	6.3	50	0	0
4.1	1	3.8	106	2.1	3.2	76	0	0
3	0.5	2.8	120	2.4	5.4	55	0	0
4	0.7	2.5	80	1.9	6.3	58	0	0
4.5	0.7	3.4	98	1.7	5.5	241	0	0
3	2	2.2	166	0.9	0.3	476	0	1
3.1	0.8	2.6	118	3	4.7	234	0	0
4.5	0.4	2	198	2.2	5.6	326	0	0
4.4	0.4	3.6	224	0.9	0.9	45	0	0
5.5	0.4	2.4	322	0.8	8.7	314	0	0
3.8	1.9	2.2	136	2	6.6	84	0	0
4.5	0.5	3	172	1	7	21	0	0
3.8	1	3.9	168	1.8	3.5	110	0	0
3.7	1.5	1.5	188	1.4	4.5	57	0	0
4.5	1.2	3	173	2	3.3	59	1	0
3.3	1	3.4	156	3	0.3	23	0	0
4	2.1	2.3	108	2.2	3.2	20	0	0
3.9	0.5	3.6	444	3	6.7	52	0	0
5.1	3.3	2.6	100	1.9	11.9	234	0	0
4.8	0.3	3.2	177	0.8	1.2	20	0	0
3.6	0.6	3.4	188	0.8	2.3	23	0	0
5	1.3	2.6	156	0.2	1	33	0	1
4.8	1	3.3	144	2	4.2	69	1	0
3.9	1.7	2.7	99	1.4	11.5	45	0	0
3.6	1.1	2.3	242	2.8	4.3	33	2	0
4.4	0.7	3.2	298	4.7	0.8	31	0	0
3.9	0.4	3.3	346	0.8	3.5	20	0	0
2.7	0.3	3.5	130	0.9	1.3	71	0	1
4.3	1.2	3.3	256	0.3	0.9	66	0	0
4.6	0.5	1.4	214	2	9	43	0	0
3.3	0.4	2.7	559	2	3.2	55	0	0
3.8	1.2	2.6	188	0.3	2.3	31	0	0
4.5	0.4	2.3	197	0.6	2.7	63	0	1
3.5	0.8	3.4	244	1.2	0.7	146	0	1
2.9	1.3	3	88	3	7.2	78	0	0
4.2	1.3	3.4	245	0.8	0.9	39	0	0
3.8	0.5	3.4	164	3.6	4.5	75	0	0
3.6	1.8	2.3	288	1.9	6.7	112	0	0
4.5	0.8	2.5	210	2.3	8.2	102	0	0
5.9	0.4	2.3	217	2	8.7	182	0	1
2.7	1	2.2	333	2.2	3.9	425	0	1
4	1.5	3.2	161	2.2	0.9	98	0	1
5.3	0.4	3.3	212	1.3	3.4	81	0	1
4.2	0.7	2.1	135	4.2	8.2	141	0	0
3.7	1.2	2.2	139	1.3	3.3	564	0	1
3	1.3	3.2	289	1.9	2.3	289	0	1
3.9	2	2.9	152	1.2	1.9	129	0	1
3.3	0.9	3.9	153	2.3	0.9	91	0	0
6.3	0.4	2.2	188	2.3	0.8	982	1	1
3.9	0.6	3.3	267	1.2	0.9	172	0	0
3.6	1.2	3.4	190	2.1	1.2	61	0	0
5.4	1.7	3.4	328	3.4	1.2	20	0	1
4.7	3	2.5	58	1.7	16.2	297	0	0
3	0.6	2.4	217	3.2	5.6	153	0	0
3.9	1.5	2.2	196	6.1	18.8	5462	0	0
3.8	2.2	2.1	404	2.9	5.2	139	0	0
4.6	0.8	2.9	216	4.2	2.8	61	0	0
4.1	1.1	4	98	2.1	4.2	72	0	0
3.7	1	2.5	122	2.4	0.4	35	0	0
3.6	1.3	2.2	290	5.1	3.2	645	0	0
3.7	0.7	3	194	2	1.3	41	0	0
4.8	0.9	2.9	328	3.9	6.2	49	2	1
4.2	1	3.7	207	0.5	0.9	20	0	0
3.5	1.3	3.4	114	1.9	0.9	72	0	0
2.8	1.2	2.7	110	2.3	1.7	97	1	0
3	2	2.2	378	2.8	8.8	626	0	1
3.3	1.5	2.8	50	3.6	11	457	0	0
3.4	4.1	1.1	109	2.7	9.8	217	0	0
2.5	0.8	2.3	232	1.3	4.2	20	1	1
2.9	2.9	2.7	206	4.8	7.2	432	1	0

ventilatio	inotropes	dialysis	mi	mortality	tissue	organisms
1	1	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	1	1	2
1	1	1	0	1	1	1
0	0	0	0	0	1	2
0	0	0	0	0	1	2
1	0	0	0	0	1	2
1	0	0	0	1	1	2
1	1	0	0	1	1	2
0	0	0	0	0	1	2
0	0	1	0	0	1	0
1	1	1	0	1	0	0
1	1	0	0	1	1	1
1	1	0	0	1	1	1
1	1	1	0	1	1	1
0	1	0	0	0	1	2
0	1	0	0	0	1	1
0	1	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	1
1	1	0	0	1	1	1
1	1	1	0	1	1	1
0	0	0	1	1	1	2
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	0
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	1	0	1	0	0	0
0	0	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	2
1	1	0	0	0	1	2
0	1	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	0	0

inguinal dissection

0	0	0	0	0	1	1
0	1	0	0	0	0	0
0	0	0	0	0	1	1
0	0	0	0	0	0	0
0	0	0	0	0	1	1
0	0	0	0	0	1	2
0	0	1	0	0	1	1
0	0	0	0	0	1	1
0	0	0	0	0	1	1
0	0	0	0	0	1	0
0	0	0	0	0	1	1
0	0	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	1	1	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	1	0
0	0	0	0	0	1	2
0	1	0	0	0	1	0
0	0	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	0	0	1	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	1	1
0	0	0	0	0	1	1
0	0	0	0	0	0	0
0	0	0	0	0	1	1
0	0	0	0	0	1	1
0	0	0	0	0	0	0
1	1	1	1	1	1	2
1	1	0	0	0	1	1
0	0	0	0	0	1	2
0	1	0	0	0	1	2
0	0	0	0	0	1	2
0	1	0	0	0	1	1
0	0	0	0	0	0	0
0	0	0	0	0	1	0

0	0	0	0	0	1	0
1	1	0	0	0	1	2
0	0	0	0	0	1	0
0	0	0	0	0	0	0
0	0	0	0	0	1	1
1	1	0	0	1	1	0
0	0	0	0	0	1	2
1	1	0	1	1	1	1
1	1	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	0
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	0	0	0	0	0	0
0	0	0	0	0	1	2
0	0	0	0	0	1	2
0	0	0	0	0	1	1
1	1	0	1	1	1	1
1	1	0	0	0	1	1
0	0	0	0	0	1	2
0	0	0	0	0	1	2