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Outcomes of Patients Receiving Streptokinase for ST Elevation Myocardial Infarction at the Georgetown Public Hospital Corporation during November 2023 - April 2024

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ABSTRACT

The use of streptokinase as the primary thrombolytic agent is considered to be outdated because newer drugs offer fewer complications and are easier to administer. GPHC is the national referral hospital and should offer PCI as a first-line treatment for STEMI.

Methods: The patients that presented with STEMI to the GPHC from the 1st November 2023 to the 30th April 2024 were included in this study. The researcher reviewed the charts of the patients admitted with a diagnosis of STEMI. The immediate and delayed outcomes (death, length of stay in hospital, signs of heart failure, bleeding complications, and ischemic chest pain) were documented.

Results: A total of forty-two patients were included in this study. In this study comparing streptokinase to PCI for STEMI patients, 1 out of 14 patients treated with streptokinase died, while 0 out of 25 patients treated with PCI died (p=0.07 chi-squared value) 95% confidence interval (0.03, 0.11). The most common complications of STEMI in this study were ischemic chest pains, heart failure and bleeding. Heart failure was the most prevalent complication after treatment with both streptokinase and PCI (52%). This was followed by bleeding (36%) and chest pains (21%).

Conclusion: This research has demonstrated that streptokinase did confer a higher mortality risk (7%) for patients with STEMI compared to PCI. However, while the p-value of 0.072 suggests a trend towards a higher mortality rate with streptokinase, it is not statistically significant at the standard 0.05 level.

Keywords: Thrombolysis, fibrinolytic therapy, streptokinase, percutaneous coronary intervention, angioplasty, left ventricular dysfunction, reinfarction.

INTRODUCTION

Guyana, the only English-speaking country in South America, is a low to middle-income country located along the borders of Venezuela, Suriname and Brazil.[1] Georgetown Public Hospital Corporation (GPHC) which is located in the capital city of Georgetown is the only national referral hospital in the entire country. The health system is underdeveloped with a major lack of resources especially at the regional and hinterland hospitals. Guyana has the highest rate of cardiovascular mortality in South America.[2] According to the CDC – Guyana,

ischemic heart disease is the number one cause of death in Guyana(15%).[3]

According to the Global Burden of Disease Study, cardiovascular disease prevalence is increasing worldwide, particularly in low- and middle-income countries [4]. While interventions such as cardiac care units and the use of coronary angioplasty have caused a dramatic decline in cardiovascular death in high-income countries [5], the availability of these interventions is limited in Guyana.

Cardiac care in the public health care system in Guyana was almost non-existent just over a decade ago. With the introduction of collaborative efforts from foreign and local parties, it has improved significantly over the past decade. However, there is still a long way to go to achieve the standard of care. The development of strategies at the different levels (preventative, emergency care, advanced cardiac care, and rehabilitation) has to be significant to decrease mortality from ischemic heart disease.

The use of thrombolytics (e.g. Streptokinase) is not common practice in developed countries but has an important role in the management of ST Elevation Myocardial Infarction (STEMI) in Guyana.

Objectives

1. To determine the inpatient mortality of patients that were admitted to GPHC with ST Segment Elevation Myocardial Infarction that received streptokinase from November 2023 to April 2024.
2. To determine outcomes of STEMI patients who received streptokinase only versus streptokinase with PCI in the above time period.
3. To determine the number of patients referred from regional hospitals with a diagnosis of STEMI

LITERATURE REVIEW

STEMI continues to be a significant public health problem in industrialized countries and is becoming an increasingly significant problem in developing countries.[6] All STEMI patients should undergo rapid evaluation for reperfusion therapy and have a reperfusion strategy implemented promptly after contact with the medical system.[7] STEMI patients presenting to a facility without the capability for expert, prompt intervention with primary PCI within 90 minutes of first medical contact should undergo fibrinolysis unless contraindicated.[7] In the absence of contraindications, fibrinolytic therapy should be administered to STEMI patients with symptom onset within the prior 12 hours.[7]

At GPHC the only fibrinolytic agent available is streptokinase. The recommended dose for streptokinase in the setting of acute ST-segment elevation myocardial infarction is 1.5 million units intravenously over 30 to 60 minutes.[8] The diagnosis of STEMI is made by the Emergency Physician who then evaluates if the patient meets the criteria for thrombolysis. This option is deferred if the patient presents during weekdays from 8 a.m. to 4 p.m. due to the availability of PCI. The physician ensures no contraindications or risk of bleeding and obtains consent from the patient. Streptokinase is then administered for 60 minutes under close monitoring. The cardiology service is also contacted for an official consult.

A few of the significant studies of streptokinase as the fibrinolytic agent used in patients with STEMI are summarized below. Most of these studies were done in the 1980s to 1990s. The incidence of fibrinolysis and also the use of streptokinase as a fibrinolytic agent have since declined. There is limited literature on the use of streptokinase as a thrombolytic for STEMI.

In 1990, Goa et al did a reappraisal of the therapeutic use of streptokinase for STEMI. The results of major trials (GISSI, ISIS-2, and ISAM) comparing streptokinase with standard treatment in more than 30,000 patients prove convincingly that intravenous streptokinase increases patient survival after myocardial infarction[9]. The largest trial, ISIS-2, demonstrated a 23% reduction in 5-week vascular mortality after streptokinase

use[9]. Reperfusion of about 50 to 60% of occluded coronary arteries occurs with intravenous streptokinase, and left ventricular function is improved[9]. The most common adverse events observed during intravenous streptokinase infusion were bleeding complications. An incidence of 3.6% for minor bleeding and 0.4% for major hemorrhage (requiring transfusion) is derived from the combined results of the GISSI and ISIS-2 studies (9). They concluded that streptokinase has been proven to reduce mortality in patients with acute myocardial infarction, with an acceptable risk of bleeding complications.

In 1994 de Boer et al compared PCI vs. intravenous streptokinase and found improved outcomes with PCI.[10] They studied 301 patients with acute myocardial infarction randomly assigned to undergo immediate coronary angioplasty without antecedent thrombolytic therapy or to receive intravenous streptokinase therapy[10]. Before discharge left ventricular ejection fraction was measured by radionuclide scanning[10]. The in-hospital mortality rate in the streptokinase group was 7% (11 of 149 patients) compared with 2% (3 of 152 patients) in the angioplasty group ($p = 0.024$)[10].

In 2013 and 2014 Wu at al investigated the management and 2-year mortality of fibrinolytic-treated patients in China[11]. A total of 19,112 patients with STEMI from 108 hospitals participated in the China Acute Myocardial Infarction (CAMI) registry between January 2013 and September 2014[11]. Non-invasive clinical indexes were used to diagnose successful fibrinolysis or not[11]. Only 1823 patients (9.5%) enrolled in the registry underwent fibrinolysis and 679 (37.2%) were treated within 3 hours after symptom onset[11].

The overall use of rescue PCI was 8.9% and successful fibrinolysis was achieved in 1428 patients (78.3%)[11]. Successful fibrinolysis was strongly associated with a decreased risk of death compared with failed fibrinolysis at 2 years (8.5% vs. 29%)[11].

In 2019 Karthik et al assessed the efficacy of thrombolysis in Acute STEMI patients, to determine resolution of ST-elevation on treatment with streptokinase and predict short term outcome during hospital stay in terms of adverse events and mortality[12]. 60 Acute STEMI patients who had received thrombolytic therapy with streptokinase were studied in three groups namely Category A, Category B and Category C based on ST segment resolution after administration of thrombolytic therapy[12]. Of 60 patients, 9 patients (15%) had <30% ST resolution (no STR), 26 patients (43.3%) had 30-70% ST resolution (partial STR), 25 patients (41.7%) had >70% ST resolution (complete STR)[12]. They concluded that the efficacy of IV streptokinase for thrombolysis in acute STEMI is 41.7%[12]. Patients with no resolution of ST segment 90 minutes following thrombolysis associated with more frequent adverse events and increased mortality compare to partial and complete resolution group[12].

In 2022 Sahu et al compared the efficacy of streptokinase, tenecteplase, and reteplase in patients of STEMI in terms of post-thrombolytic resolution by observing the reduction of ST-segment elevation at 90 minutes of thrombolytic and assessing for mortality within 30 days of therapy.[13] A prospective, single-centre, observational, hospital-based study was conducted in the Department of Cardiology in collaboration with the Department of Pharmacology at Srirama Chandra Bhanja Medical College and Hospital, Odisha, India, from February 2020 to January 2022.[13] The study involved 300 patients (100 patients in each group) being treated with streptokinase, tenecteplase, or reteplase. [13] A reduction of ≥50% of the initial ST elevation was considered a successful thrombolysis. There was no statistically significant difference between the three groups concerning ST segment reduction. (11) They concluded that streptokinase, tenecteplase, and reteplase were equally efficacious for thrombolysis in terms of thrombus

resolution and preventing mortality when started early. (11)

This study will be done in a low to middle-income country that still uses streptokinase compared to developed countries that use tenecteplase and have PCI readily available for the majority of its population. This study aims to evaluate the modality of treatment for patients presenting with an acute myocardial infarction and to determine the short-term outcomes associated with thrombolytic therapy.

MATERIALS & METHODS

Study Type: Retrospective Descriptive Study

Study Period: 1st October – 31st December 2024

Study Location: The Georgetown Public Hospital Corporation

Permission was sought from the Research Committee and the Director of Medical and Professional Services of GPHC. An IRB for the study was obtained from the Chief Medical Officer's office in Guyana.

The primary researcher conducted a chart review of the patients that were admitted at GPHC with a diagnosis of STEMI during the study period. The diagnosis of STEMI was verified according to the Third Universal Definition for Myocardial Infarction[14]. The researcher reviewed the data at the medical records department for all the admitted patients to the Cardiac Intensive Care unit (CICU) and identified the patients with STEMI. A chart analysis was done to identify demographics, risk factors, co morbidities, ECG diagnosis, and management. The charts were reviewed at the records department of GPHC. The reasons for the administration or non-administration of streptokinase were noted. The use of a standardized checklist to administer streptokinase was reviewed[15]. The dose of streptokinase that was noted as the standard dose is 1.5 Million units over 60 minutes[16]. The implementation of PCI after streptokinase or as the primary treatment was noted.

Immediate post-streptokinase outcomes and complications were documented. The researcher also identified the time from the onset of symptoms to the administration of streptokinase. The immediate outcome of the patients with STEMI that did not receive streptokinase were identified; this included the patients that received PCI or neither PCI nor streptokinase. The variables that were assessed – age, gender, co morbidities, risk factors, time of presentation from onset of symptoms, killip class[17] on presentation. The following outcomes were evaluated: length of stay in the hospital, death, symptoms of heart failure, presence of ischemic chest pains, bleeding disorders, and any other complications.

The average number of patients that present to GPHC with STEMI over a 6-month period is 48. Records for forty-two patients who presented with STEMI to GPHC over the 6-month study period were made available by the records department of GPHC. The estimated sample size that would give a confidence interval of 95% is 40 patients.

The entire assessment was administered by the primary researcher. The results was stored on a secure password-protected flash drive and kept by the primary researcher. The data was inputted into Excel (Microsoft, Washington, USA) on a password-protected computer. The entries were done by the principal investigator and any discrepancies, missing or illegible data were clarified. The length of stay in the hospital, death, symptoms of heart failure, presence of ischemic chest pains, bleeding disorders, and other complications were assessed by the chi squared test. A confidence interval of >95% and a p value of < 0.05 would have made this study statistically significant.

Inclusion Criteria:

Patients diagnosed with STEMI at the ED of GPHC from 1st November 2023 – 30th April 2024.

The diagnosis of STEMI will be made according to the Third Universal Definition for Myocardial Infarction[14].

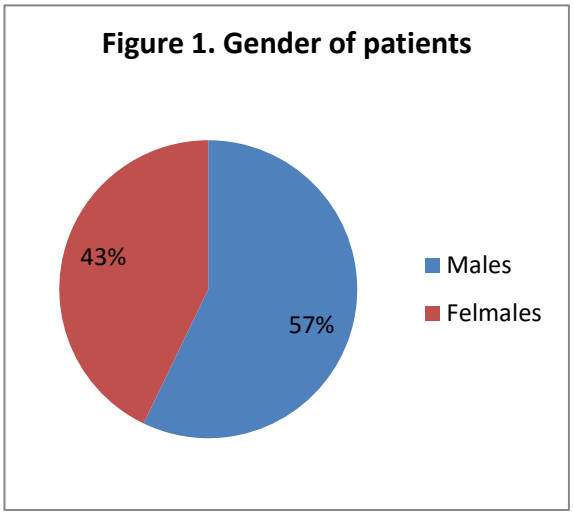
Exclusion Criteria:

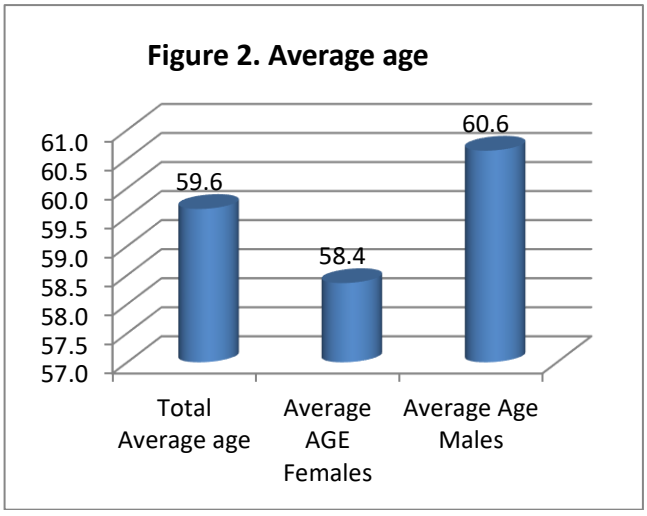
Patients that fail to meet the ECG criteria for diagnosis of STEMI. Patients diagnosed with STEMI that would have received intervention before arrival to GPHC.

RESULT

Section 8: Results

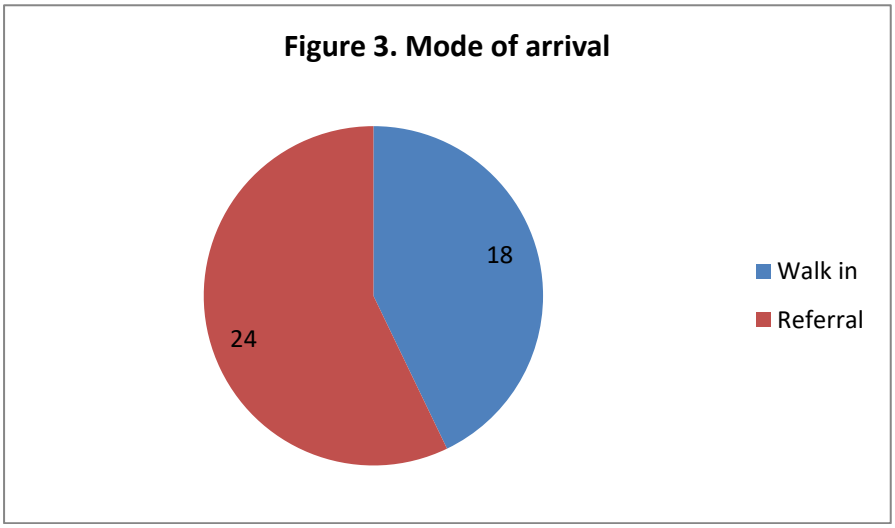
Records of 42 patients that presented to GPHC during the study period with STEMI were retrieved from the records department of GPHC. The records are hardcopy and were retrieved by the clerk at the records department. 57% of the patients were male and 43% were females. (Figure 1)

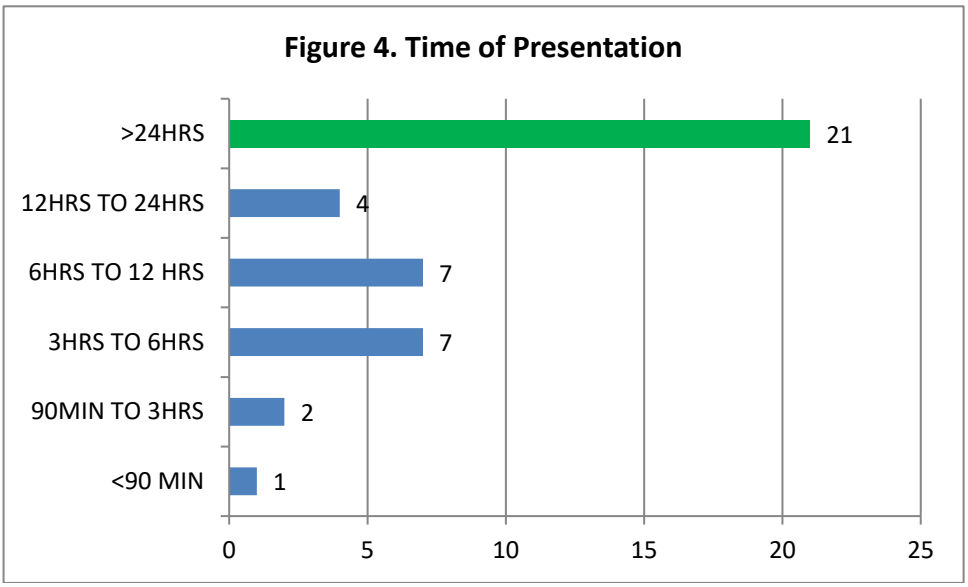




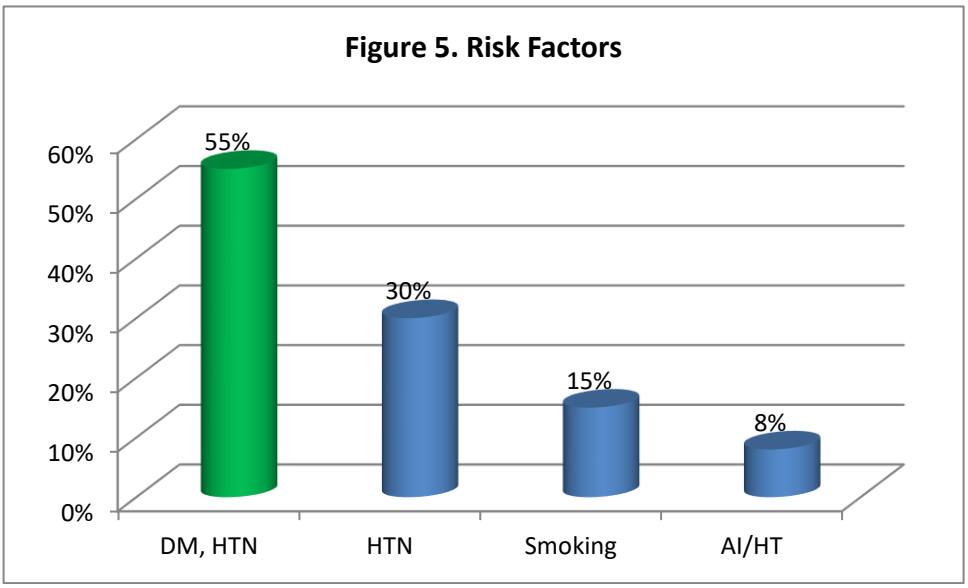
The average age of presentation was 59.6 years. The males and females had a slight age discrepancy, with males presenting at a slightly older age. The youngest person was 38 years old whereas the oldest person was 76 years old.

The majority of patients were referred (24 patients) from other institutions for the management of STEMI. 43% of the patients were walk in. The private hospitals and public hospitals accounted for almost equal amount of referral during this time period.

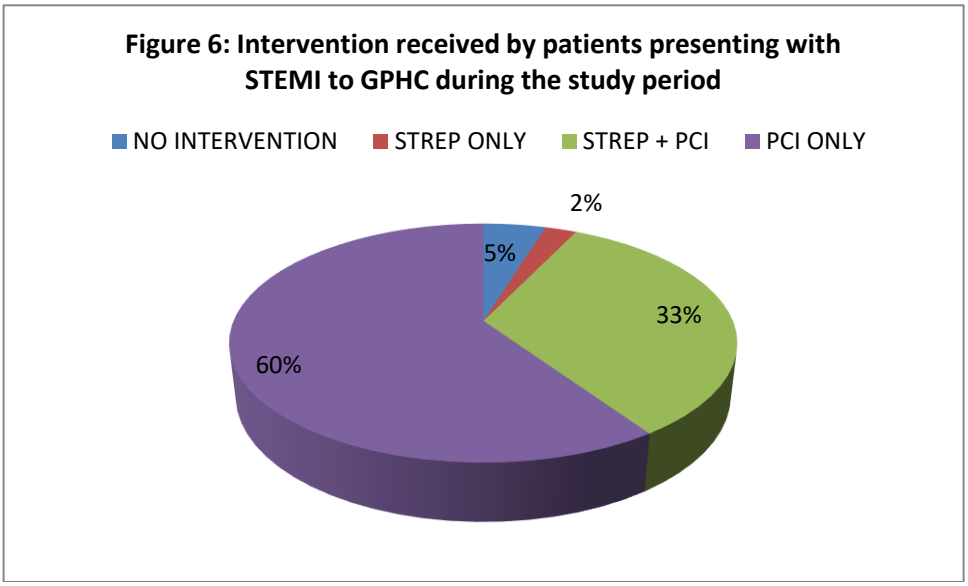




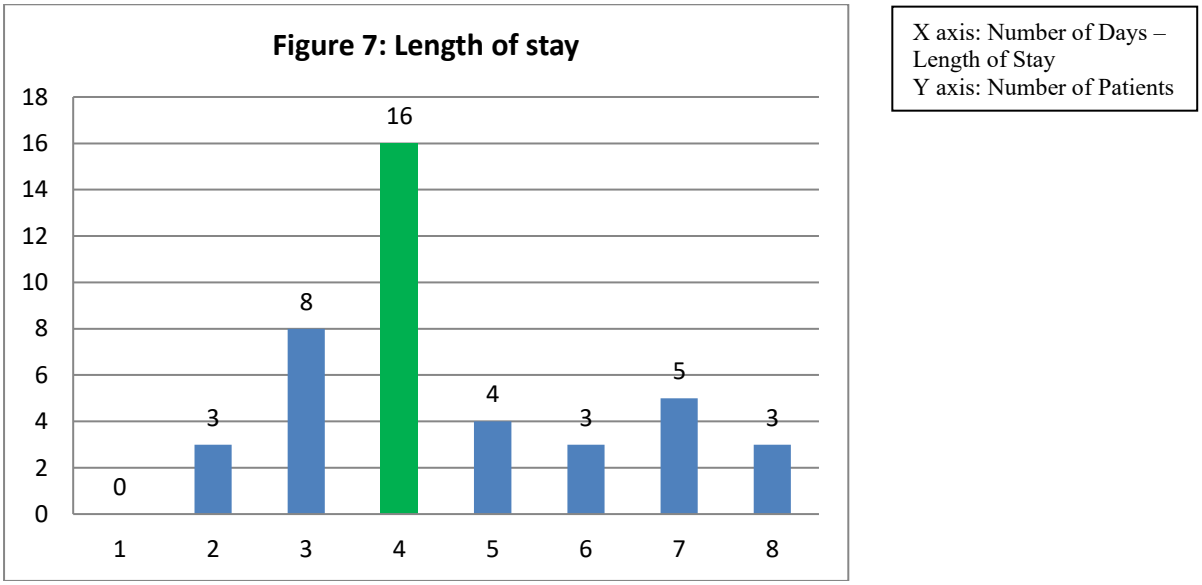
The vast majority of patients (21) presented after 24 hours, 4 patients presented between 12 and 24 hours. Only 17 patients presented to the hospital within 12 hours of symptoms.



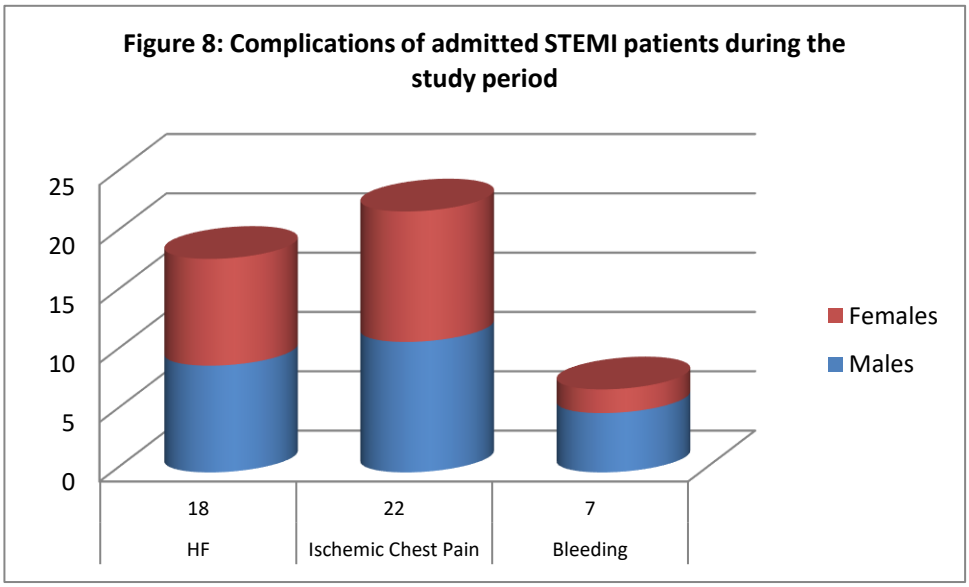
Patients with both diabetes and hypertension were at the highest risk for STEMI (55%). All the patients that were included in this study had at least one risk factor. Hypertension was the second most frequent risk factor with smoking also contributing to the risk of STEMI in the patients included.



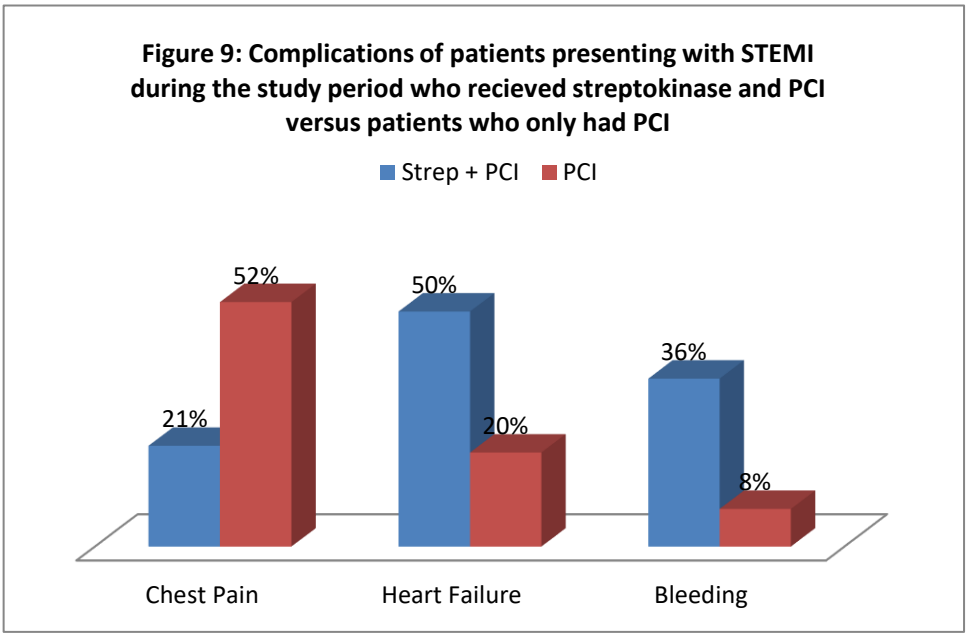
60% of the patients in this study received PCI only; 33% received streptokinase and PCI. Only one patient had streptokinase as the sole therapy.



16 patients were discharged after 4 days of hospital admission. This accounted for the majority of patients. The average stay in the hospital for all of the patients accounted for in this study was 4.7 days. There were two patients that only stayed for two days; one was referred to a regional hospital while the other one died. There was one death due to cardiogenic shock. The majority of patients with complications stayed beyond four days.



Heart failure, ischemic chest pains, death and bleeding were the most common complications studied. The most prevalent complication was ischemic chest pains (52%).



DISCUSSION

A total of forty-two patients were included in this study after conducting a chart review of the admissions to the hospital for STEMI during the study period of November 2023 to April 2024. These patients were either walk-in (43%) or referrals (57%) from public and private hospitals. The patients that were referred from the regional hospitals were mainly due to lack of resources, lack of inpatient cardiology service and the absence of a cardiac catheterization laboratory. The most common cause for the referral from the private hospital was due to financial constraints. The referrals caused a significant delay in the time of presentation to GPHC, hence the large number of patients (50%) presenting after 24 hrs from onset of symptoms (Figure 4). Only 17 patients presented to the hospital in a time frame (<12hrs) to be eligible for streptokinase. The average age of presentation was 59.6 (Males: 60.6;

Females: 58.4). There was only a minor discrepancy of age difference from males and females in this study (Figure 2). The major risk factor was the presence of both diabetes mellitus and hypertension. The other significant risk factors identified were smoking, hypercholesteremia, and autoimmune disease. This was another finding that is consistent with prior studies of STEMI.

The majority of patients that presented with STEMI to GPHC during the study period had PCI as the only intervention. This was because the majority of patients presented beyond the window for thrombolytic therapy. These patients were admitted and had scheduled PCI. PCI was often delayed for a period of 24 to 72 hours depending on the time of presentation and the number of patients scheduled for PCI. To note, this interventional therapy was only available from 8am to 4pm on weekdays. Therefore, patients presenting with STEMI on weekends would need to wait until Monday to have PCI done. The majority of patients that received thrombolytics eventually had PCI. Only one patient had streptokinase as the primary treatment modality. This was due to a non- functional cardiac catheterization laboratory. The average length of hospital stay was 4.7 days and most of the patients were admitted for a total of 4 days.

In this study comparing streptokinase to PCI for STEMI patients, 1 out of 14 patients treated with streptokinase died, while 0 out of 25 patients treated with PCI died (p=0.07 chi-squared value) 95% confidence interval (0.03, 0.11). The study's findings show a trend towards higher mortality with streptokinase compared to PCI, but the p-value is not statistically significant. The observed mortality rates in this study (7.14% for Streptokinase, 0% for PCI) are within the range of expected mortality rates following STEMI, which can range from 2.7% to 8%. Other studies have shown varying results, and the timing of reperfusion and patient characteristics are crucial factors to consider when comparing streptokinase and PCI for STEMI treatment. The one patient that died had thrombolytic therapy with subsequent PCI to the RCA followed by cardiogenic shock post intervention. This patient was also 76 years old with a history of diabetes and a prior myocardial infarction.

The most common complications of STEMI in this study were ischemic chest pains, heart failure and bleeding. Heart failure was the most prevalent complication after both streptokinase and PCI (52%). This was followed by bleeding (36%) and chest pains (21%) (Figure 9). The seven patients that experienced bleeding were all discharged without further complications. Five patients with bleeding were given streptokinase with subsequent PCI. The most common bleeding diatheses were hemoptysis and mucosal bleeds (5 patients), followed by hematuria (2 patients). Bleeding does not appear to be more frequent or severe with intravenous streptokinase than with the more fibrin-selective agent, rt-PA. The most common complication after PCI was ischemic chest pains (52%). Only eight percent of patients who had PCI done experienced bleeding. The other complications noted were: one death (cardiogenic shock), ischemic stroke, hospital acquired pneumonia and one patient developed a thrombus in the left ventricle.

This study had various limitations. The main limiting factor was record keeping and access to medical records. There are only hard copies of patients' medical records. The filing system does not account for the diagnosis; hence it was difficult to locate all the patients that were admitted for STEMI during the study period. The admitting diagnosis did not always reflect the diagnosis of STEMI. There may have been a few patients admitted for STEMI during the study period that were not reflected in this study. The patients that presented to the emergency department and died prior to admission were not captured. This study had a small sample size and should be extended

for a longer duration in order to acquire a more significant sample size.

This study was limited to assessing patient's progress during their stay in the hospital. A more comprehensive study that follows up patients 30 days post hospital discharge would have given more significant data. The accuracy and completeness of the data collected were limited by the information that was written in the charts.

CONCLUSION

In conclusion, this research has demonstrated that streptokinase did confer a higher mortality risk (7%) for patients with STEMI compared to PCI. However, while the p-value of 0.072 suggests a trend towards a higher mortality rate with streptokinase, it's not statistically significant at the standard 0.05 level. Additionally, there was a risk of non-life-threatening bleeds post thrombolytic therapy which was alleviated prior to patient discharge. There was only one death from the forty-two patients that were included in this study. Notably, the death was attributed to cardiogenic shock in an elderly patient with multiple co-morbid conditions who had streptokinase and PCI.

A significant number of patients were referred from private and regional hospitals due to financial constraints and the lack of adequate resources respectively. The other findings of this study regarding risk factors for cardiovascular diseases and complications in patients with STEMI are consistent with another notable research.

The limitations of this study are mostly due to the lack of adequate record keeping and relying on chart documentation to provide accurate information. Additionally, the sample size was not large enough to provide a more comprehensive analysis of patients that received thrombolytic therapy for management of STEMI.

Declaration by Authors

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