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Impact of IABP on Clinical Outcomes in Patients with Cardiogenic Shock - A Ten Year Experience: OBSERVATIONAL STUDY

[1]Dr. SAGAR SHAH [1](Author)Dept. of cardiology, Amrita school of Medicine, Amrita institute of medicalsciences & research Centre, Amrita Vishwa Vidyapeetham University, kochi, kerala, Sagar612@gmail.com
[2]Dr. Rajesh Thachathodiyl Clinical professor and Head, Department of Adult Cardiology,drtrajesh@aims.amrita.edu.,
[3]Nisha Annie George, senior house officer, acute medicine in Leicester royal Infirmary, georgethomas.intek@gmail.com.

ABSTRACT

IABP use in cardiogenic shock has seen a degradation in recommendation over the years. IABP Shock II trial concluded that intraaortic balloon counter pulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for whom an early revascularization strategy was planned.[1] But Intraaortic balloon counterpulsation remains the most widely used form of mechanical hemodynamic support in this clinical setting. In our study, we sought to evaluate the outcomes of patient undergoing IABP at our centre over the last 10 years. Our retrospective analysis indicated that incremental risk factors for death were: poor LV function, cause of cardiogenic shock and post procedure insertion of IABP. Vascular complications were the most common complication encountered and incremental risk factor for it was: Poor ejection fraction (EF), whereas associated co-morbidities, age, duration of IABP support did not increase incidence of complications. Vascular complications and sepsis significantly increased the mortality

Keywords cardiogenic shock novel approach, Impact of IABP, clinical study, etc.

II. Introduction

The intra-aortic balloon pump (IABP) is the most frequently used mechanical support device in India, and it is the device interventional cardiologists are most accustomed with. It is inserted easily and quickly, is the least expensive of all the devices, and does not require continuous monitoring by technical support staff. However, use of IABP has shown only minimal hemodynamic support and myocardial protection, clinical trials have failed to demonstrate mortality benefit in cases of cardiogenic shock.[1]

This led to development of newer percutaneous devices like Impella and ECMO, compared with the IABP, they provide greater improvement in hemodynamic parameters. Similar to IABP, there is no evidence to suggest they improve clinical outcomes such as mortality. These devices as compared to

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Dr. SAGAR SHAH Research manuscript on Impact of IABP with cardiogenic shock novel approach.

IABP are expensive, take longer time to insert and have a higher complication rate (ie, bleeding, hemolysis, limb ischemia).[234,5]

The IABP reduces Left Ventricular (LV) afterload Furthermore, it increases blood flow to the coronaries by raising the mean diastolic pressure which might help in cases of cardiogenic shock. Although newer sheathless devices with catheter diameter as low as 7.5 Fr are currently in use, the complication rates especially of peripheral thromboembolism are by no means negligible. Our observational clinical study reports our single centre experience in use of IABP insertion for patients with cardiogenic shock. We attempted to identify variables which would help to decide which cases are likely to benefit with use of IABP.

III. Methods

Data was collected from 134 consecutive patients who underwent non-elective IABP insertion for cardiogenic shock from January 2008 to December 2018, out of which 106 patients were included in this study, and 28 were excluded due to unavailability of data. Data of 106 patients was analysed including cardiovascular history, hemodynamic situation upon admission, angiographic and procedural characteristics, ejection fraction, variables derived from admission to the Coronary Care Unit, outcomes and complications.

IV. Results

In this study, there was data of a total of 106 patients that were analysed. The age distribution was as follows. Youngest patient was 19 years old and the eldest was 88 years old. Maximum patients were in the age group of 61-70 and 2nd being in 51-60 age group followed by 71-80 age group with 71.7% (n=76) being males and 28.3% (n= 30) being females as demonstrated in GRAPH 1.

<u>Sex and Age Distribution (graph 1):</u>

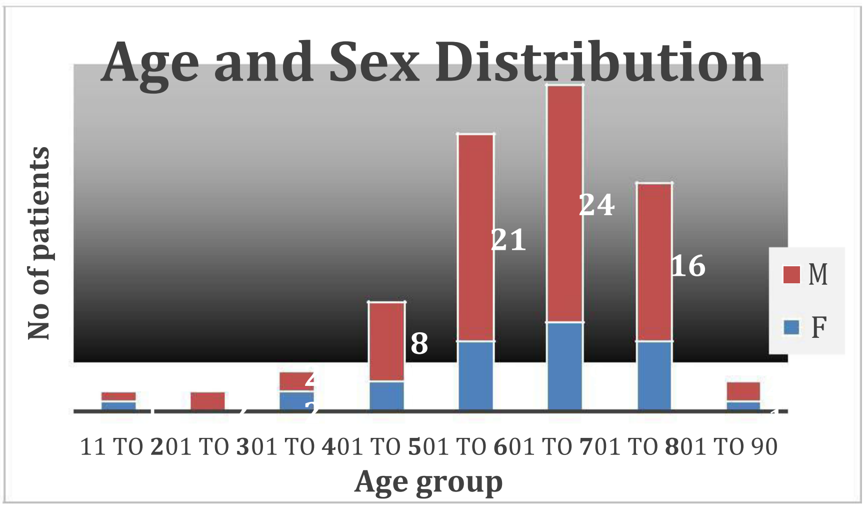

FIG 1.0 Representation of age interval and sex categories of number of patients

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Hypertension (Graph 2):

hypertension (HTN or HT), also known as high blood pressure (HBP), is a long-termmedical condition in which the blood pressure in the arteries is persistently elevated.

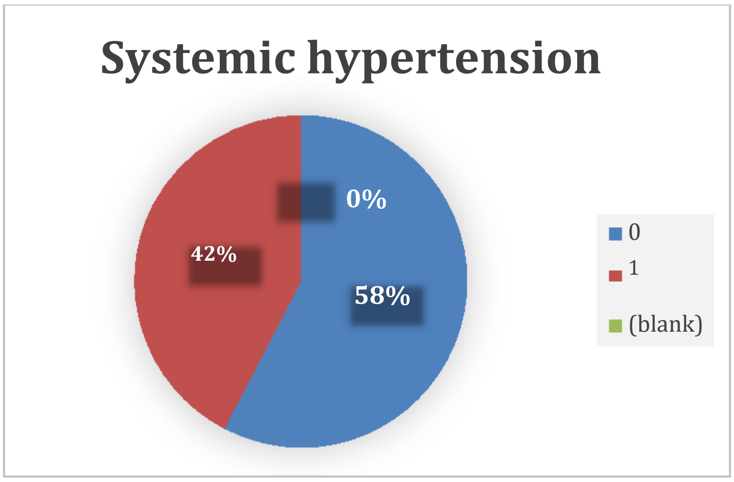

Fig 1.1 Representation of hypertension percentile of number of patients

Type 2 Diabetes (Graph 3)

Diabetes means your blood glucose, or blood sugar, levels are too high. With **type 2 diabetes**, the more common **type**, your body **does** not make or use insulin well. Insulin is ahormone that helps glucose get into your cells to give them energy.

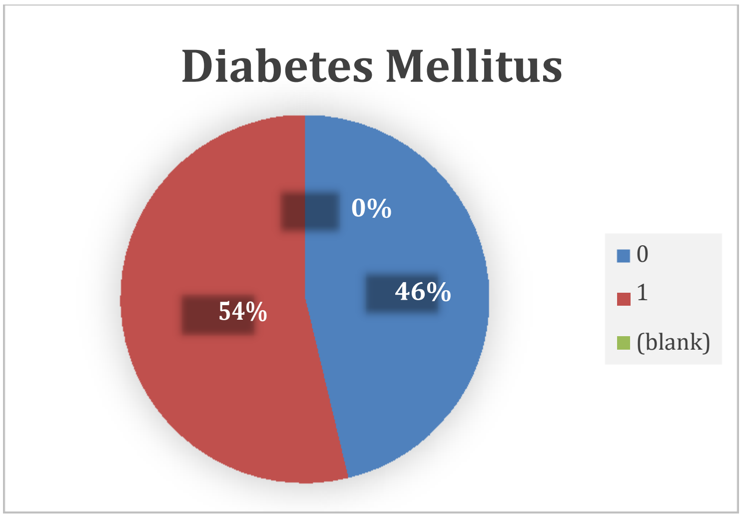

Fig 1.3 Total number of patient's representation the percentile of diabetes type 2 category.

Mortality vs Survival (Graph 4)- Mortality outcomes in total and mortality outcomes at 6 months based on HTN and Diabetes

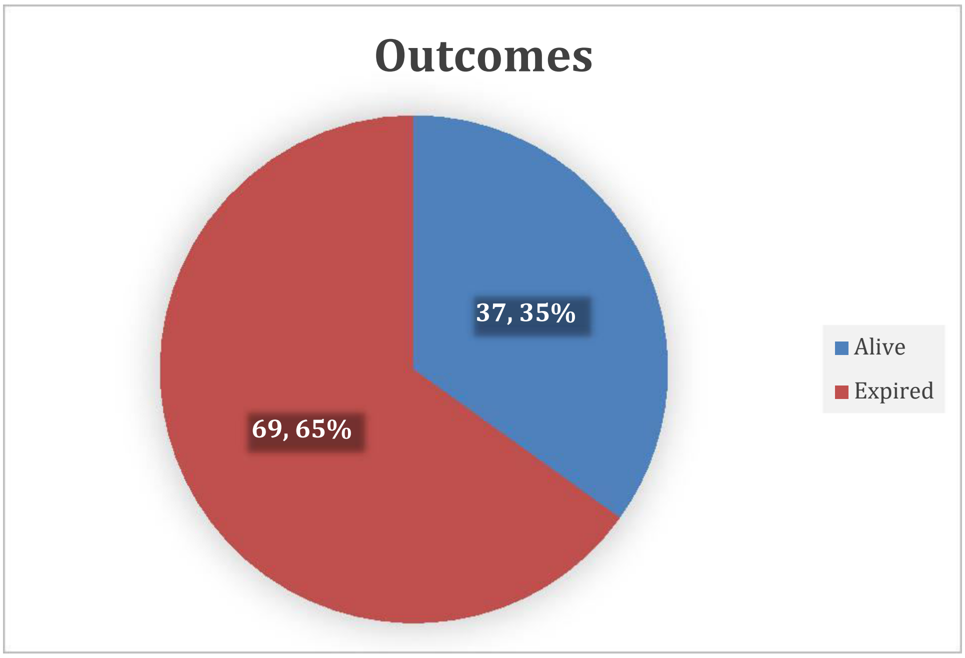

Fig 1.4 Graph representation of mortality outcome on the basis of HTN and Diabetes

Outcomes of IABP in patients with AMI-CS (Graph 5):

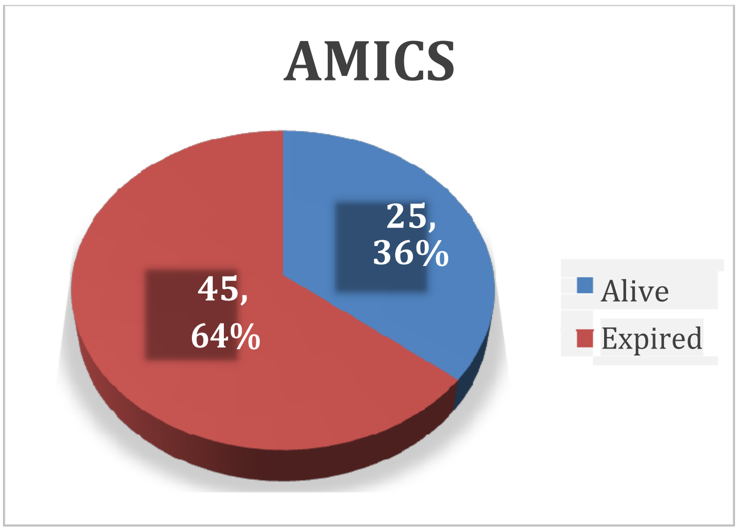

Fig 1.5 Graph 3 shows the outcome of the patients who underwent IABP due to CS because of AMI. Out of a total of 70 patients, 64% of the patients died whereas 36% survived.

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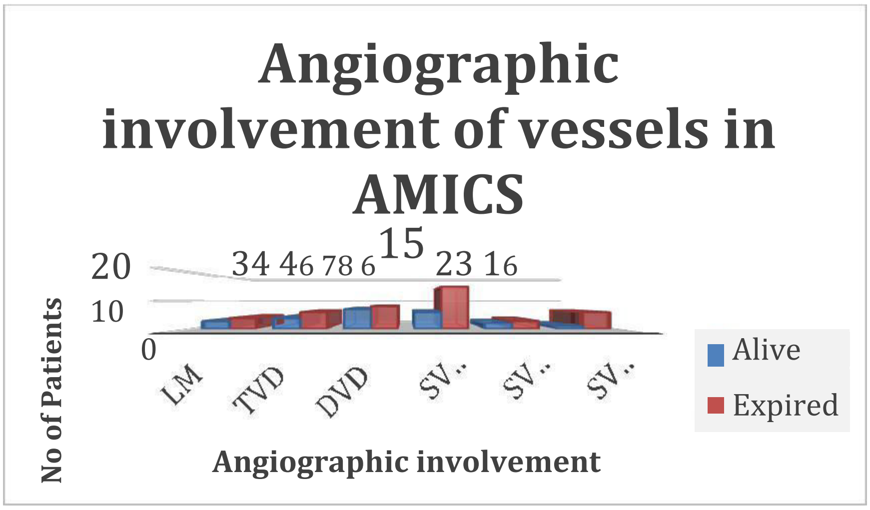
Outcomes of patients with AMI-CS based on angiographic vessel involvement (graph 6)



Graph 1.6 shows the Angio-graphical involvement of coronary arteries in AMI associated cardiogenic shock in whom IABP was used and shows almost similar number with expiry and survival, apart from right coronary artery and left anterior descending. Of the 21 patients that had LAD associated MI- 71% expired, with around 85% of the patients died with RCA associated MI.

Outcomes with IABP use in AMI-CS with successful revascularisation (Graph 7)

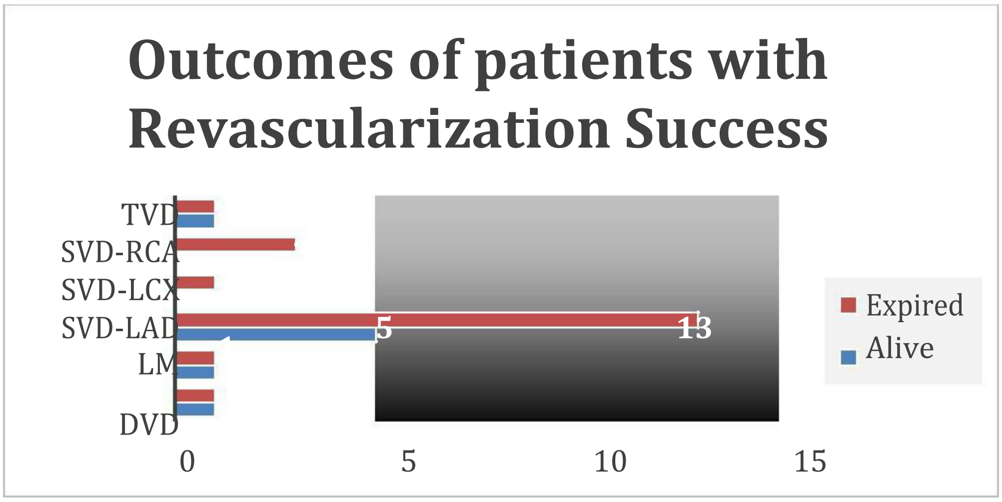


Fig 1.7 graph representation of the patients that survived and had a successful CABG and revascularisation done- t

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There was a higher number of patients that died (72%) from LAD involvement compared to the survival rate (27%), with no patients surviving with RCA involvement. The other arteries had equal deaths and survival rates. The left circumflex artery also had no survivors.

Outcomes associated with complications of PCI prior to IABP (Graph 8)

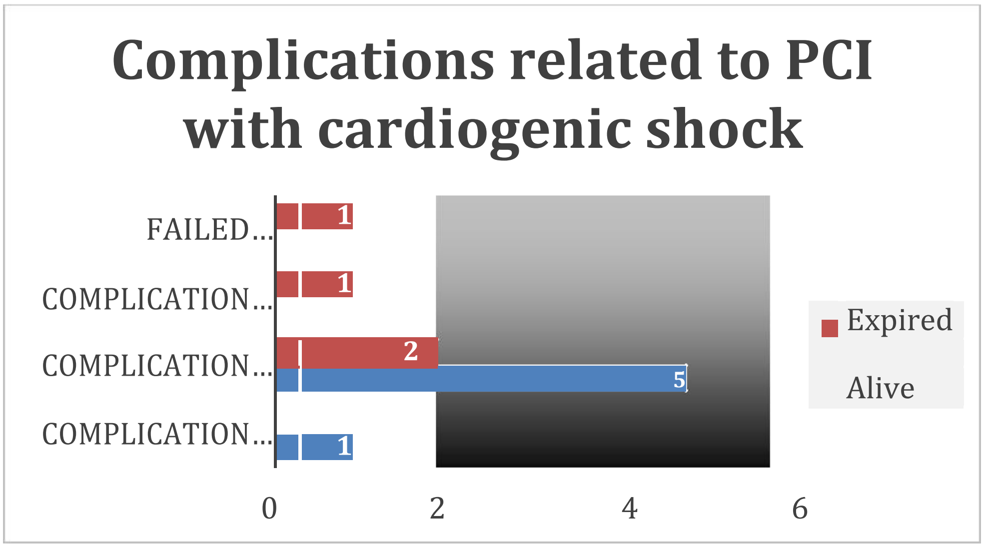
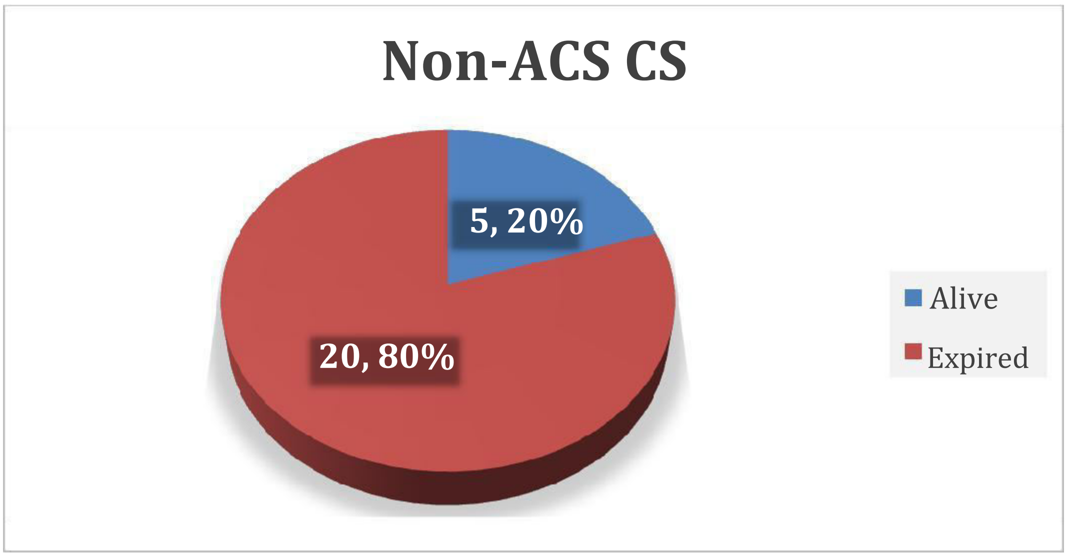


Fig 1.7 Graph 11 shows the complications that were associated with the PCI with cardiogenic shock with most of the complications occurring during PCI-

No Reflow- leading to 5 patients out of 7 that survived. Artery dissection was also a complication which occurred to one patient- and they survived the complication. Failed PTCA, stent deformation and 2 patients who had PCI-no reflow died. There was greater survival than the number of deaths associated with complications of PCI.

Outcomes of IABP use in non- ACS related CS (Graph 9)



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In comparison to Graph 3- which showed 36% survival, this graph shows the outcomes of the use of IABP in non-ACS related CS- with 80% of the patients had expired and only 20% surviving. There was a total of 25 patients that were in CS due to non-AMI related causes.

Causes and outcomes of Non-ACS related CS (Graph 10)

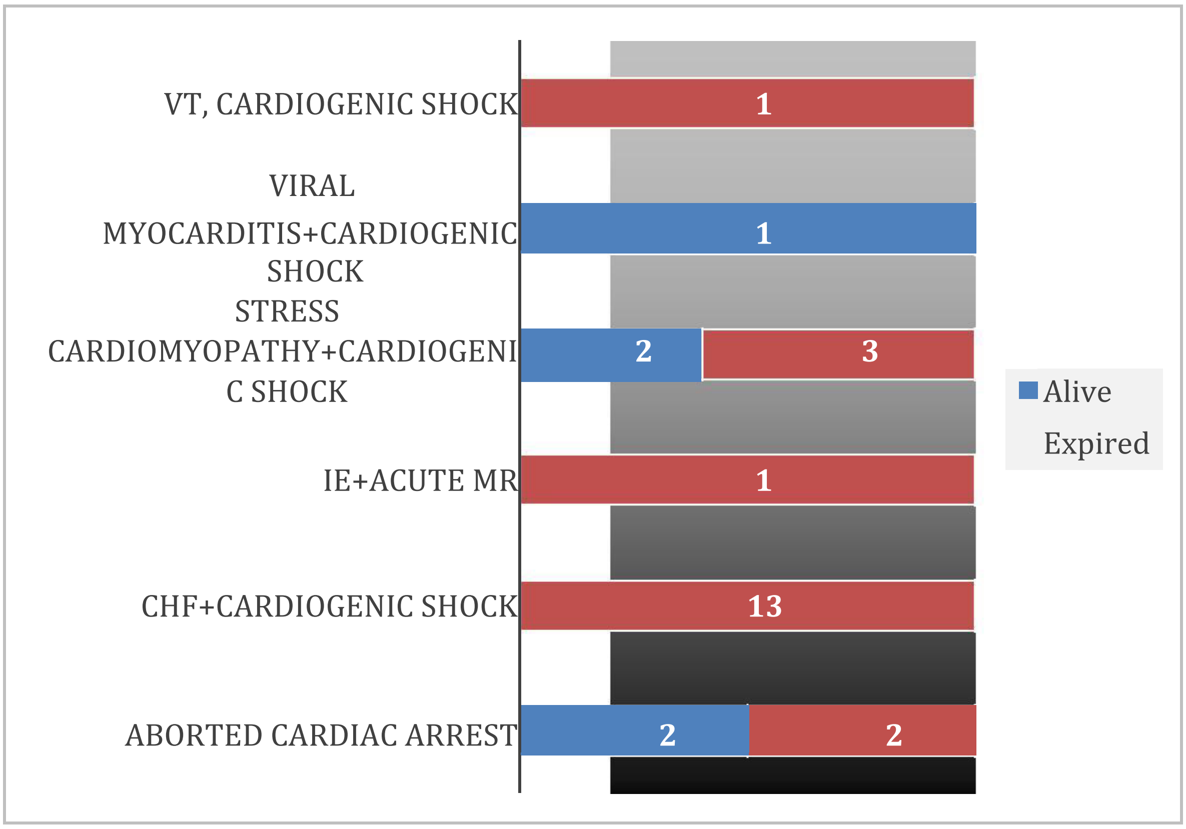

Fig 1.8 Graph 2 shows the non-ACS causes of cardiogenic shock with a vast majority of the patients that expired were due to CHF- accounting for 13 patients.

One patient expired due to infective endocarditis causing acute MR which might be attributed to the contaminated equipment used during the admission. Aborted cardiac arrest resuscitation accounted for 2 deaths and 2 survivals along with stress cardiomyopathy accounting for 2 survivals and 3 deaths. The only non-ACS associated CS that resulted in 100% survival rate was viral myocarditis as per our study population.

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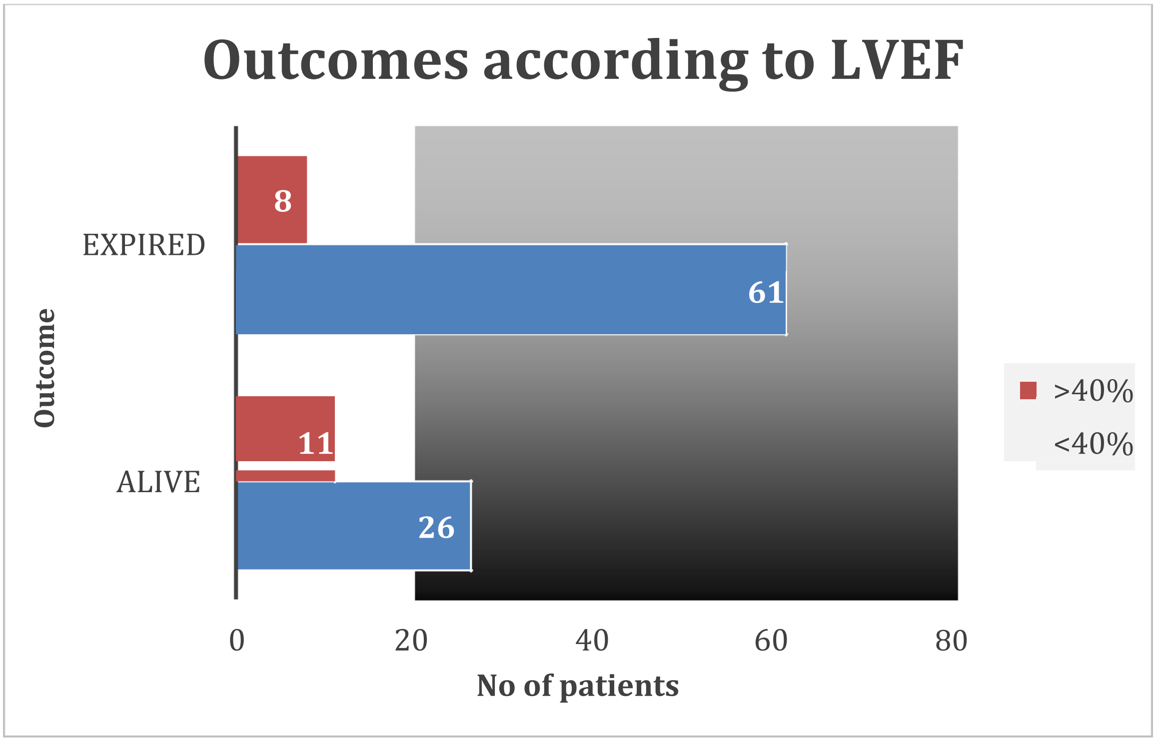
Outcomes of IABP insertion- based on the LVEF (Graph 11)



Graph 6 shows a 6-month mortality rate of the patients based on the ejection fraction. Of the 106 patients, 69 patients expired which accounts for 65% of the patients, with 35% (37 patients) surviving. Comparing this data to Graph 6.1-

shows that majority of the patients that expired had LVEF of less than 40%, with a smaller proportion of 26 patients surviving with an LVEF of <40%. When comparing the number of patients that survived with the AIBP- total of 37 patients- accounting for 11 patients with LVEF of >40% and 26 patients <40%. Post IABP LV function assessment done and 18 patients with severe LV dysfunction survived out of which 11 patients showed improvement in LV function post IABP and revascularization, and 7 patients did not show any improvement.

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Duration of IABP (Graph 12)

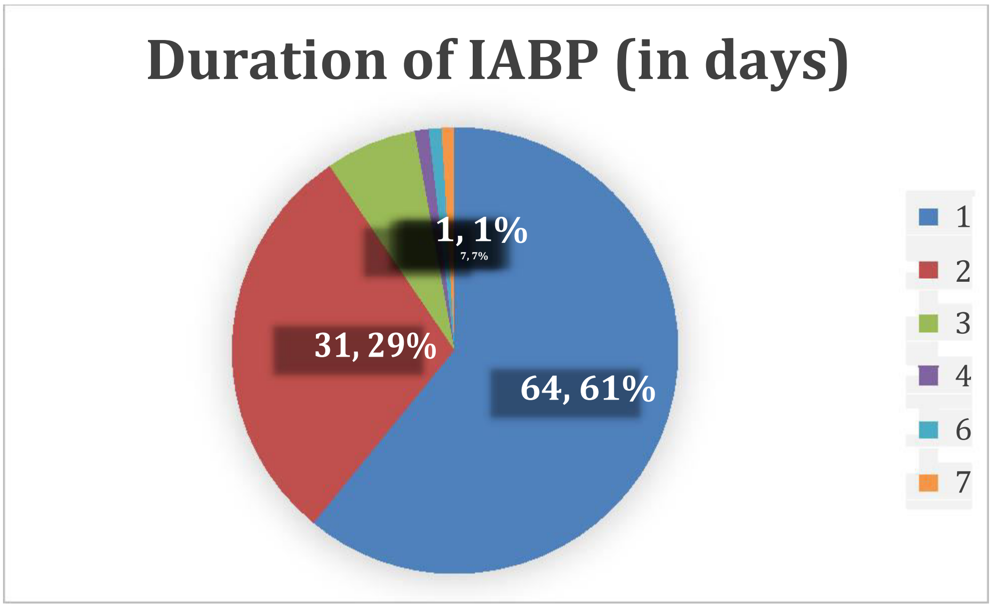

Fig 1.09 graph represent the IABP duration of 12 days only.

Majority of the patient were having IABP for less than 48 hours, with majority of the IABP removal occurring after 24 hours (**60.4%) with remaining 29.2. %** accounting for the removal after 48 hours. Out of the 10 patients having IABP for more than 48 hours only 3 survived and their IABP was removed within 72 hours. No patient with IABP for more than 48hours survived in our study. Complications also rose to 50% in the group who had duration of IABP more than 48 hours.

Complications

Serial number		Frequency	Percent
Valid	No Complications	69	65.1
	Complications present	37	34.9
	Total	106	100.0

69 patients which accounts for 65.1% of the study population did not have any complications whilst 37 patients (34.9%) had complications associated with the procedure of which 24.32% were due to sepsis with an equal distribution of 18.9% having an embolic complication and arrythmia.

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Most common complication was embolic complication occurring in 10% of the patients followed by sepsis which occurred in 8.5 %. Mortality was significantly higher in the embolic complication group and only 2 patients which had embolic complications survived.

Outcomes related to complications secondary to IABP use (Graph 13)

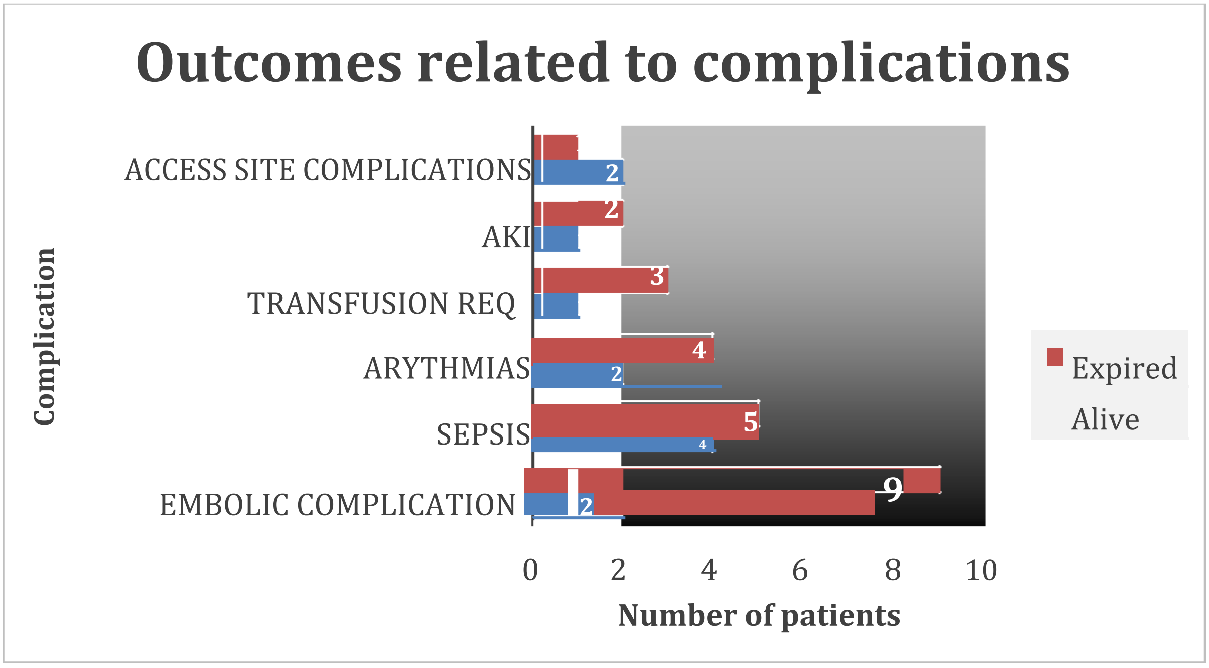

Fig 1.10 graph representationnumber of patient's outcomes related to complications

VIII. Discussion:

Cardiogenic shock (CS) is defined as SBP <90mmHg for >30 mins or the use of inotropes to maintain the SBP at <90 mmHg with end organ failure and clinical features of reduced cardiac output (Vahdatpour & Collins, 2019). The most common cause of CS is acute coronary syndrome which accounts for 70-80% of the cases with left ventricular failure accounting for 78.9% of the cause of CS in ACS (Suarez, et al., 2019) . The management of CS compromise of a two- part strategy: 1) Stabilisation and resuscitation with intravenous fluids, oxygenation and ventilation, vasopressors (Suarez, et al., 2019), continuous renal replacement therapy 2) Revascularisation- with PCI/CABG. There is use of bridging therapy with mechanical circulatory support devices such IABP, Impella, ECMO prior to the use of vasopressors and PCI treatment (Vahdatpour & Collins, 2019). As a general trend, there has been an increase in the incidence of cardiogenic shock secondary to an AMI with the mean age reducing from 67 to 63 years and a greater incidence in the Asian/Pacific Islander population compared to other ethnicities. There has also been an increasing trend in the use of IABP for the mechanical management of cardiogenic shock (D, et al., 2014).

Our retrospective study highlighted the main prognostic determinants in the use of IABP were the cause of cardiogenic shock, poor ejection fraction before and after IABP insertion, severe LV dysfunction, post-procedural insertion of IABP with associated complications with IABP insertion. Factors such as gender, age, presence of co-morbidities did not have a significant impact.

In our study, the two major causes of cardiogenic shock were AMI (acute myocardial infarction) and CHF. Though studies have shown the use of IABP in AMI to have a neutral effect on mortality with no association with long term mortality (Iqbal, et al., 2016) (Timóteo, 2016), there have been studies to show a beneficial impact on the use IABP in CS secondary to CHF (Fried, 2018) (Sintek, 2015). There was an increase in the 30-day survival of 84% and IABP was used as a bridging therapy for heart replacement therapy or were discharged without further escalation. This difference in hemodynamic stability achieved in CHF compared to AMI can be attributed to the chronicity of CHF with the adaptability to lower cardiac output. This also reinforces data present of greater clinical deterioration with ICM (ischemic cardiomyopathy) in IABP support (Fried, 2018) (Unverzagt, 2011). Some studies have showed that IABP should only be used as bridging therapy for the mechanical stabilisation in cardiogenic shock secondary to myocardial infarction. It mainly acts as a bridging method for subsequent re-vascularisation procedure by decreasing the size of the infarct and decreasing intra-operative mortality (Stone GW, 2003). The use IABP does not significantly reduce the mortality rate if early re-vascularisation was planned (Thiele, 2012)- which re-iterates that IABP has a neutral effect on mortality (Iqbal, et al., 2016). IABP use in patients with previous MI may have a detrimental effect (Timóteo, 2016). With the varying evidence in the survival rate with IABP use in AMI, our study supported the findings of (van Nunen, 2013) and (Thiele, 2012) that the use of IABP does not affect the long term mortality rate in AMI patients. Another approach was evaluated where IABP was used as a adjunct method to PCI in reducing the infarct size in the absence of CS- which showed no added benefit (Patel MR, 2011).

Another factor that was highlighted in our study were the vessels that were involved which were established angiographically. It was noted there was an almost equal distribution of deaths and survival with the coronary arteries apart from single vessel disease of Left anterior descending artery and right coronary artery where majority of the patients expired. It has been noted that the right ventricular myocardial infarction (RVMI) tends to have higher mortality rate, with greater propensity for arrythmias such as ventricular tachycardia and fibrillation, cardiogenic shock, ventricular failure, and atrioventricular blocks. This was in comparison with LVMI (Mehta, 2001) (Jacobs, 2003). Other studies have reiterated that despite the shorter time to shock diagnosis, similar mortality with re-vascularisation, younger patients presenting with RVMI, when compared to only LVMI, there is a higher mortality rate in patients with RVMI (Ondrus, 2013)

The management for majority of the patients with AMI was PCI (percutaneous coronary intervention), which are associated with their own complications such as dissection, no-reflow phenomenon, coronary perforation, stent deformation and failed PCI. In our study, out of 10 patients who encountered complications during PCI, 7 of them experienced no-reflow periprocedure with 2 deaths and 5 survivals. No-reflow is generally a poor prognostic marker due to reduction in the salvageability of the myocardium post-AMI especially STEMI (Micheal, 2011). No-reflow phenomenon is a complication noted in more than 30% of patients post-thrombolysis/PCI, also acting as a strong indicator for long-term and short-term mortality. These patients tend to have a higher incidence of heart failure, MI and subsequently death (Wang, 2015). These findings are counterintuitive to the results from the study where 5 out of the 7 patients with no-reflow survived. One of the possibilities is that these patients had collateral circulations to compensate which may have decreased the extent of the infarct. (Wang, 2015) tabulated that well-developed coronary collateral circulation is shown to have a protective effect and can lead to lower propensity for no-reflow phenomenon especially in STEMI patients, thus is an independent predictor for the incidence of no-reflow phenomenon. We believe that the use of IABP would be beneficial during a no-reflow event-to help sustain vitals long enough for the collateral circulation to develop and be maintained.

Another factor in our study that was significant parameter was severe LV dysfunction and poor ejection fraction ($P=<0.003$). Studies have showed that the use of IABP in severe LV dysfunction and in patients with ejection fraction of 36% and above have shown a reduction in in-hospital mortality (He, 2019), reduced hospital stay and more cost effective approach in CS (Charles A. Dietl, 1996). It has been noted to play a protective role (He, 2019).

The clinical outcomes for patients who either deteriorated after IABP implantation or did not have an improvement in the ejection fraction or diastolic function had worse outcomes with longer hospital stay, with use of inotropes (Khan TM, 2020). Based on the mechanism utilised by IABP for circulatory support, severe cardiogenic shock is unlikely to have a positive outcome with IABP support (Parissis, 2016) or escalation to another MCSD (such as left ventricular assist device (LVAD)) (Timóteo, 2016). It should be noted that patients with severe LV dysfunction with <35% ejection fraction usually have a higher mortality score compared to those with better cardiac reserve (He, 2019). The survival of patients is better when using IABP as the primary method of circulatory support as opposed to ionotropes (den Uil, 2019). Though using IABP did not show any significant difference in 30-day mortality for CS secondary to right or left heart failure- there was a need for early escalation to stronger MCSD with biventricular failure (Krishnamoorthy A, 2017) (Timóteo, 2016).

Throughout the literature, the mortality rates range from 10% to 85% [2,3]. This is probably due to the various groups of patients considered. Within its wide range of indications, some series have included low risk patients in whom the device was inserted as a prophylactic measure, with a more favourable outcome. The overall mortality in our series was 65%. This obviously reflects a heterogeneous population of high-risk patients for which IABP was inserted on an emergency basis. Since the introduction of IABP, the incidence of complications has decreased over the years. (Valente, et al., 2012). Our study also showed 34.9% of the patients with IABP developed secondary complications- with higher mortality rate in patients that developed complications compared to those that did not. These results are like the findings of (Valente, et al., 2012). Majority of the complications in our study were associated with sepsis, embolic events and arrythmias followed by bleeding episodes requiring transfusion. Multiple factors are known to be independent factors for the development of complications. These factors are age above 75 (Parissis, 2016), the degree of hemodynamic instability (Valente, et al., 2012), presence of peripheral vascular disease, diabetes (Meco, 2002) (A.Piozzi, 2016) (Valente, et al., 2012) and duration of implantation more than 24 hours (Valente, et al., 2012) (Parissis, 2016) (A.Piozzi, 2016).

Sepsis-24.3% of the patients in our study developed sepsis. Majority of them growing theorganism Burkholderia, supported by (Shaban, 2020). They determined that Burkholdia

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bacteremia is a nosocomial infection associated with exposure to contaminated products and equipment with 125 documented outbreaks affecting 3287 patients. A high SOFA score was associated with increased mortality rate. We treated our patients with Ceftazidime or Cefuroxamine which is in keeping with the other studies that used either Meropenem, Ceftazidime or Piperacillin-Tazobactam as antibiotics (Chun-Hsing Liao, 2011). (Crystal, 2001) found that majority of the patients developed fever with 12% developing sepsis with recommendations given to initiate prophylactic antibiotic prior to IABP insertion. (Vales, Kanei, Ephrem, & Misra, 2011) noted that the presence of diabetes and the duration of IABP implantation increased the risk of developing fever with the only risk factor for a positive blood culture being the duration of IABP support. The organisms that was cultured was coagulase negative Staphylococcus (Vales, Kanei, Ephrem, & Misra, 2011), Klebsiellapneumoniae and Pseudomonas aeruginosa (Kohsaka, Menon, Iwata, & Lowe, 2007). The school ofthought for the higher mortality rate is associated with fever presenting with leucocytosis (Kohsaka, Menon, Iwata, & Lowe, 2007) and the release of pro-inflammatory cytokines that facilitates shock and induces oxidative stress (JS, 2003). In comparison with the 24.3% who developed sepsis, a recent study showed the incidence of infection with IABP was 0.1% (Khan TM S. A., Jan 2020 (updated May 2020)).

Our study noted that of the people that had IABP- 35% had developed a complication, of which 30% (29.7%) developed an embolic event. 11 patients who experienced consequences of embolic events namely 5 strokes, 5 acute limb ischemia (1 had loss of limb) and 1 bowel ischemia. There were no pulmonary embolism or further MI. Compared to (Khan TM S. A., 2020), where 3.9% were noted to have an embolic event with 0.5% leading to major limb ischemia with 0.1% needing amputation. There was also an incidence of 0.1% of visceral ischemia. An incidence of 3.3% was noted in the IABP SHOCK II trial of peripheral ischemia and sepsis with 0.7% leading to stroke (our study showed 45%) (Khan TM S. A., 2020). (Sara Hocker, 2014) denoted that a transthoracic approach usually predisposes a patient to lower extremity neurological deficits due to limb ischemia whereas a femoral artery approach causes neurological deficits secondary to obstructive blood flow or thromboembolic event. Stroke, on the other hand, due to IABP can be caused by either mobile atheroma present in the thoracic aorta, spontaneous thromboembolic events during the point of insertion or a delayed response or cerebral air embolism. The propensity of embolic events occurring greatly increases with a background history of peripheral vascular disease (60% v 5%) (Kvilekval, 1999) and diabetes (Parissis, 2016). It was interesting to note that the type of complication that developed had an impact on the mortality i.e. embolic events had a higher mortality rate compared to bleeding episodes which was supported by our study (p- value <0.001). This was further supported by a German study (Sirbu, 2000).

Though the incidence of complications have decreased since the introduction of IABP, major bleeds are still frequent (Valente, et al., 2012). The use of IABP increases the risk of moderate to severe bleeding (Bahekar, 2012) which is contrary to the findings of (Altayyar, 2015) where IABP is not associated with complications including stroke, limb ischemia and major bleeding.

IX. Limitations:

In our results it was noted that the patients without a background of hypertension or diabetes were more likely to have complications. Patient's whose background comorbidities were unknown were considered under the bracket of no history of hypertension or diabetes.

In the patients that had a significant improvement in the LV function had collective management of IABP and PCI/CABG as opposed to improvement in the LV function with IABP alone.

Compared to multivariant studies with a higher sample size, our small sample size of 106 and heterogenicity of the sample may have contributed to some of the insignificant data.

Criteria of bleeding (minor or major) and if it was secondary to thrombocytopenia or raised INR secondary to coagulation. We also did not have the data for the time of onset of chest pain to the time taken to conduct the PCI- this would have greatly influenced the mortality rate in the patients with AMI. Another factor which may impact our data was the involvement of LV with

X. Conclusions:

While IABP is an excellent means of support for the failing heart, its mortality and complication rates are high, and this is attributed to the high risk population supported. Furthermore, vascular adverse outcome correlates with significantly high mortality rates especially in patients with poor heart performance. The drawbacks of this report are highlighted by the fact that the population studied was small and slightly heterogeneous. Nevertheless, we consider our observations to be important and highly representative of day to day practice.

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