Survey Report

Perception Mapping of Clinicians on Thrombolytic Therapy Consideration Before PCI

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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INTRODUCTION

Acute myocardial infarction (AMI) remains a leading cause of morbidity and mortality worldwide, with ST-segment elevation myocardial infarction (STEMI) requiring immediate and effective reperfusion strategies to improve patient outcomes [1]. The management of STEMI has evolved significantly over the past decades, with primary percutaneous coronary intervention (pPCI) and fibrinolytic therapy emerging as the two primary reperfusion strategies [2]. While pPCI is generally considered the gold standard when available in a timely manner, its accessibility is often limited by various factors, including geographic distance, availability of catheterization laboratories, and skilled personnel [3].

In many clinical scenarios, particularly in regions with limited pPCI capabilities or when there are significant delays in transfer to PCI-capable centers, fibrinolytic therapy plays a crucial role in the initial management of STEMI [4]. The evolution of thrombolytic agents, from streptokinase to more fibrin-specific agents like tenecteplase and reteplase, has improved the efficacy and safety profile of this treatment modality [5]. However, the decision to administer thrombolytic therapy involves careful consideration of various factors, including time from symptom onset, patient characteristics, and the availability of timely PCI [6].

More recently, the concept of a pharmaco-invasive strategy has gained attention in the management of STEMI. This approach combines initial fibrinolytic therapy with subsequent planned PCI, aiming to bridge the gap between immediate thrombolysis and delayed invasive intervention [7]. The pharmaco-invasive strategy may be particularly relevant in settings where immediate pPCI is not feasible, potentially offering a balance between the benefits of early reperfusion and the advantages of mechanical revascularization [8].

Despite these advancements, the optimal approach to STEMI management can vary based on numerous factors, including local resources, patient characteristics, and time from symptom onset. Understanding the perceptions and practices of clinicians regarding thrombolytic therapy and its role in relation to PCI is crucial for optimizing

care strategies and improving patient outcomes [9]. This is particularly important in diverse healthcare settings, such as those found in India, where access to pPCI facilities can vary significantly between urban and rural areas [10].

This study employs a questionnaire-based survey aims to map the perceptions of clinicians on key aspects of thrombolytic therapy and its consideration before PCI in the management of STEMI. By exploring factors such as typical time frames for patient admission, challenges associated with performing primary PCI, preferred reperfusion strategies, and the perceived efficacy of different thrombolytic agents, we seek to provide insights into current clinical decision-making processes.

RATIONALE OF THE STUDY

The rationale for this study is to gather comprehensive insights into the clinical decision-making process and perceptions of Indian clinicians regarding the use of thrombolytic therapy in relation to PCI for STEMI management. By mapping these perceptions, we can identify potential gaps in knowledge, variations in practice, and areas where further education or resources may be needed to support evidence-based decision-making.

The purpose of this study is to evaluate the current practices, challenges, and perceptions associated with thrombolytic therapy and its consideration before PCI in the management of STEMI among Indian clinicians. This investigation aims to assess factors influencing treatment choices, perceived efficacy of different strategies, and the potential role of pharmaco-invasive approaches in the Indian healthcare context.

STUDY OBJECTIVE

The primary objective of the study is to map the perceptions and practices of Indian clinicians regarding the use of thrombolytic therapy in relation to PCI for the management of ST-segment elevation myocardial infarction.

METHODS

This study was designed as a cross-sectional, questionnaire-based survey targeting Indian physicians who manage patients with hypertension. The aim was to gather insights on their clinical experience, prescribing practices, and perceptions regarding the use of thrombolytic therapy for the management of ST-elevation myocardial infarction (STEMI). To achieve this, a 12-question survey was developed. The study commenced with the identification of potential participants through professional networks and medical associations. These physicians were invited to partake in the survey, and detailed information about the study's purpose, procedures, and ethical considerations was provided to them prior to participation. Ensuring participant convenience, the survey was administered electronically.

Confidentiality and ethical standards were stringently maintained throughout the study. All responses were collected and securely stored, guaranteeing anonymity and privacy for all participants. The study adhered to the ethical principles outlined in the Declaration of Helsinki, and ethical approval was obtained from an Independent Ethics Committee. Participants were informed of their right to withdraw from the study at any point without any repercussions. Data collection was followed by rigorous statistical analysis to summarize the findings and identify key trends. The collected data were analyzed to extract meaningful insights into the prescribing practices and perceptions of Indian physicians regarding thrombolytic therapy in STEMI management. The results were compiled into a comprehensive report. These findings are intended for dissemination through scientific publications and presentations at relevant conferences, ensuring the knowledge gained from this study contributes to the broader medical community.

The target sample size for this study was 92 Indian physicians. This number was chosen to ensure a diverse and representative sample, enabling meaningful statistical analysis and robust conclusions from the survey data. Through this methodical approach, the study aimed to provide a clear understanding of current clinical practices and perceptions related to thrombolytic therapy among Indian physicians managing hypertension.

RESULTS

A total of 92 HCPs participated in the survey. Below is the summary of the responses.

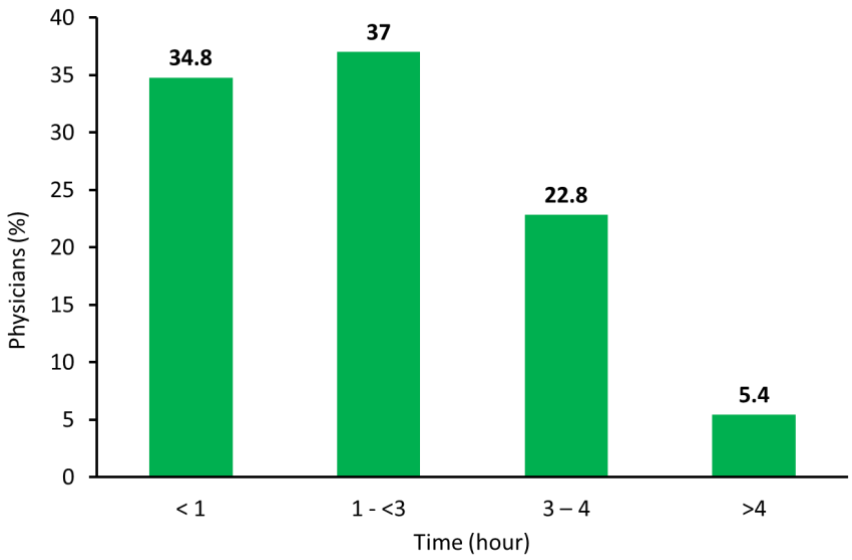
1. What is the usual time taken for the admission of a patient to hospital for MI?

a. < 1 hour

b. 1 - <3 Hours

c. 3 – 4 Hours

d. >4 Hours



- About 34.8% of physicians observed that MI patients were admitted to the hospital in less than one hour.
- Approximately 37% of physicians observed that patients were admitted within one to three hours.
- While 22.8% of physicians observed that patients were admitted within three to four hours.
- However, only 5.4% of physicians observed that patients were admitted after more than four hours.

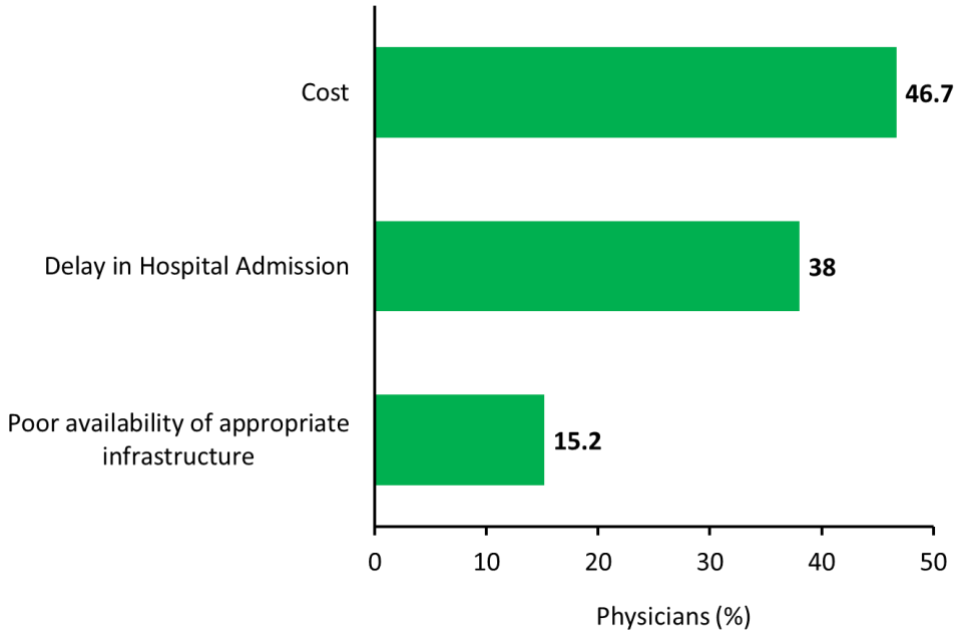
- This survey data highlighted that timely admission was a critical focus, with the majority of patients being admitted within the first few hours of experiencing MI symptoms.

2. What do you consider are the challenges associated with performing a primary PCI in patients with MI?

a. Cost

b. Delay in Hospital Admission

c. Poor availability of appropriate infrastructure



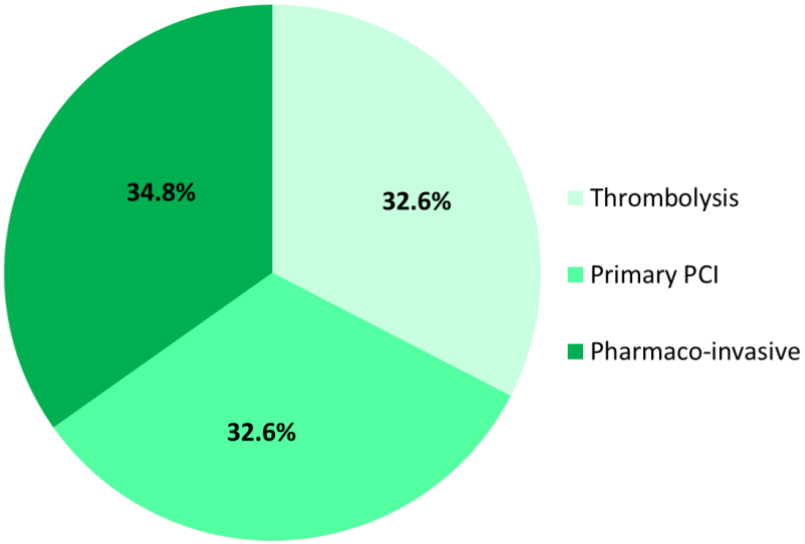
- About, 46.7% of physicians considered cost as a challenge associated with performing primary PCI in patients with MI.
- However, 38% of physicians considered delay in hospital admission as a challenge associated with performing primary PCI in patients with MI.
- While, 15.2% of physicians considered poor availability of appropriate infrastructure as a challenge associated with performing primary PCI in patients with MI.

3. In your clinical Practice which reperfusion strategy do you prefer?

a. Thrombolysis

b. Primary PCI

c. Pharmaco-invasive



- About, 34.8% of physicians preferred the pharmaco-invasive approach in their reperfusion strategy during clinical practice.
- About 32.6% of physician has preferred thrombolysis approach in their reperfusion strategy during clinical practice.
- Similarly, 32.6% of physicians preferred primary PCI approach in their reperfusion strategy during clinical practice.
- This distribution indicates a balanced preference among different reperfusion strategies, with a slight inclination towards the pharmaco-invasive approach.

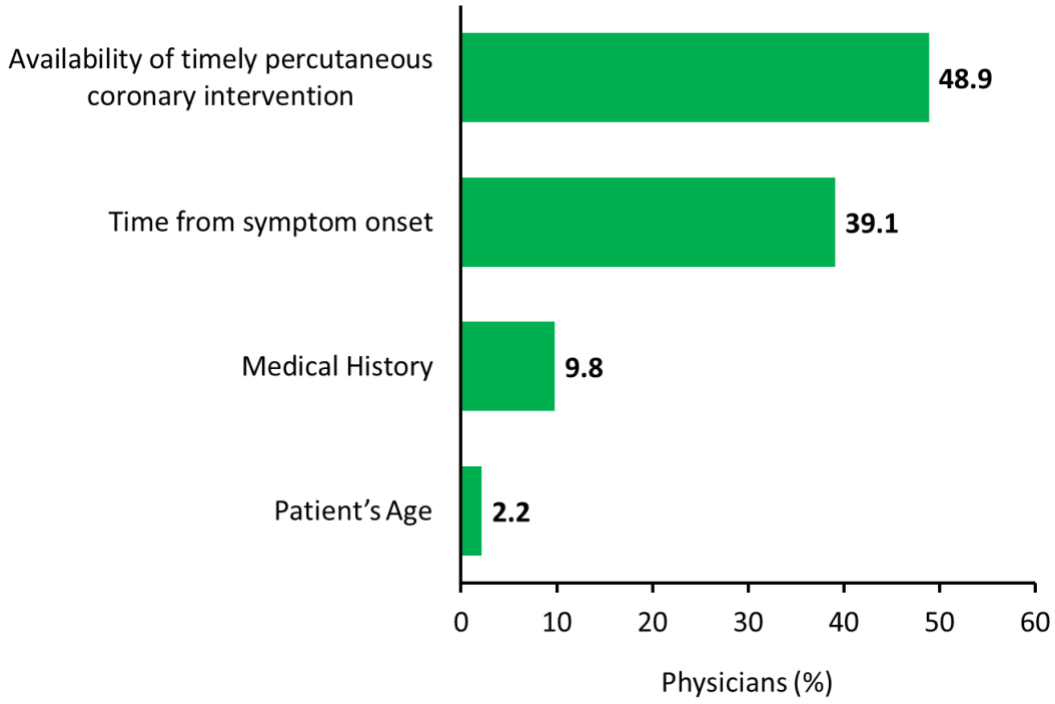
4. What are the primary factors you consider when deciding whether to administer fibrinolytic therapy to an MI patient?

a. Time from symptom onset

b. Patient's Age

c. Medical History

d. Availability of timely percutaneous coronary intervention



- The availability of timely PCI was the primary factor considered by 48.9% of physicians when deciding whether to administer fibrinolytic therapy to an MI patient.
- Time from symptom onset was the primary factor considered by 39.1% of physicians in their decision-making process for fibrinolytic therapy.
- Medical history was considered by 9.8% of physicians, while patient age was considered by only 2.2% of physicians.
- This survey data highlighted that timely access to PCI and the duration of symptoms were pivotal considerations in choosing fibrinolytic therapy for MI patients.

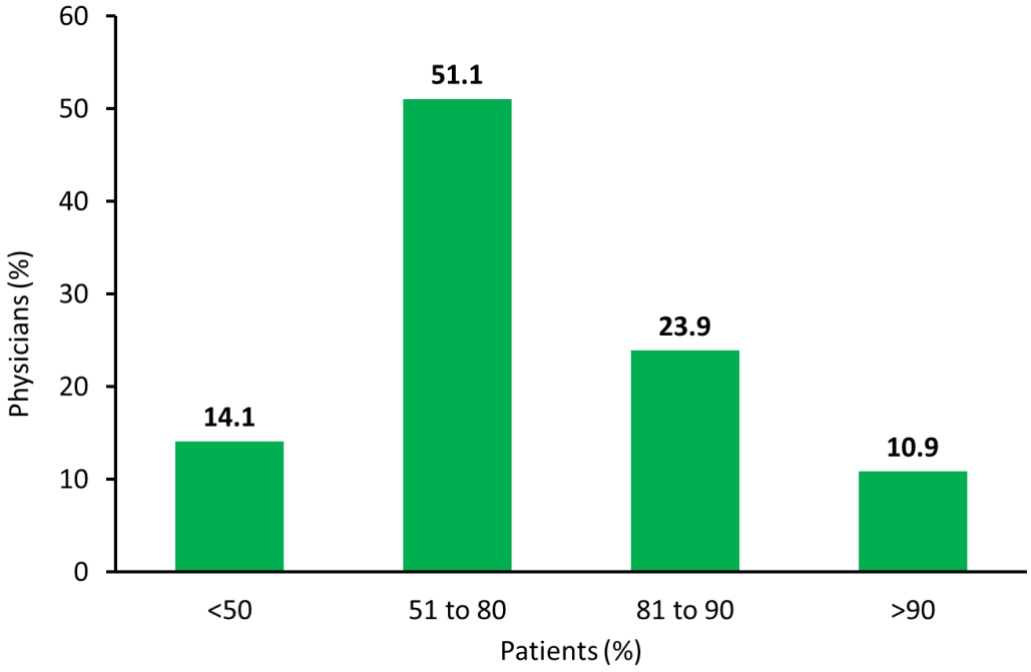
5. In your clinical practise, what percentage of patients on an average achieve clinically significant changes in ECG post thrombolysis in patients with STEMI?

a. <50%

b. 51 to 80%

c. 81 to 90%

d. >90%



- The majority of physicians (51.1%) observed that 51% to 80 of their patients achieved clinically significant changes in ECG post-thrombolysis for STEMI in their clinical practice.
- About 23.9% of physicians noted that 81% to 90% of their patients achieved clinically significant changes in ECG post-thrombolysis for STEMI in their clinical practice.
- About 14.1% of physicians noted that less than 50% of their patients achieved clinically significant changes in ECG post-thrombolysis for STEMI in their clinical practice.

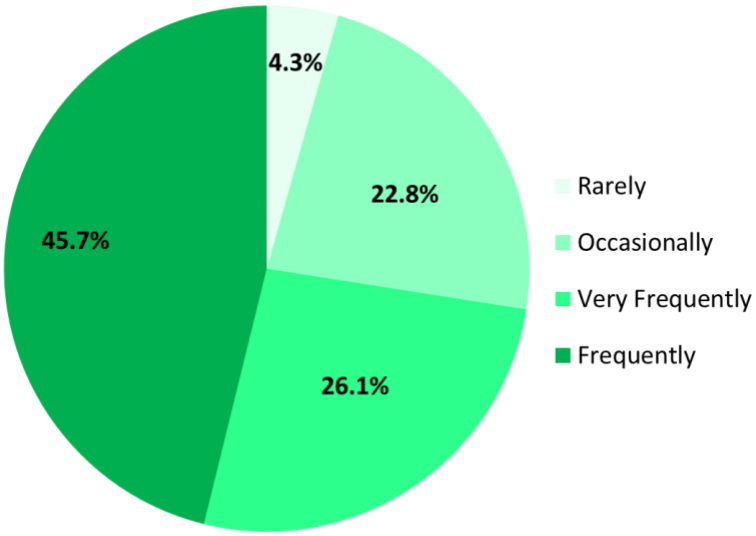
6. In your practice, how often do you consider using Pharmaco-Invasive strategy for patients with suspected MI?

a. Very Frequently

b. Frequently

c. Occasionally

d. Rarely



- About 45.7% of physicians used the pharmaco-invasive strategy frequently for patients with suspected MI in their clinical practice.
- Approximately 26.1% of physicians used the pharmaco-invasive strategy very frequently for patients with suspected MI in their clinical practice.
- Around 22.8% of physicians used the pharmaco-invasive strategy occasionally for patients with suspected MI in their clinical practice.
- However, 4.3% of physicians used the pharmaco-invasive strategy rarely for patients with suspected MI in their clinical practice.

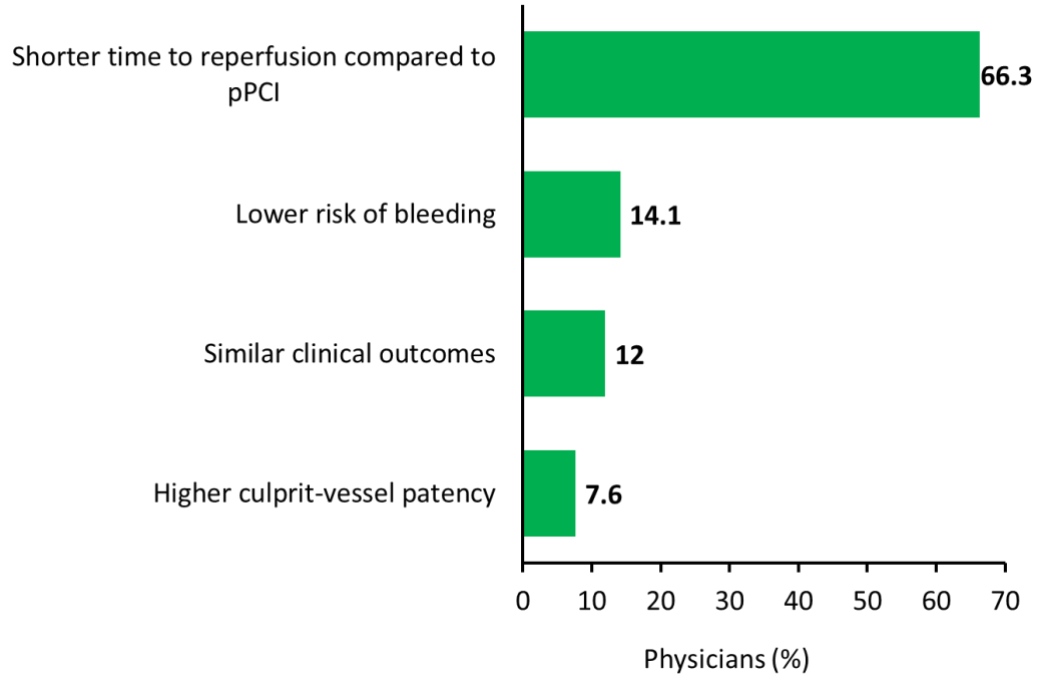
7. What could be the perceived benefits of Pharmaco-invasive therapy as compared to pPCI?

a. Shorter time to reperfusion compared to pPCI

b. Higher culprit-vessel patency

c. Similar clinical outcomes

d. Lower risk of bleeding



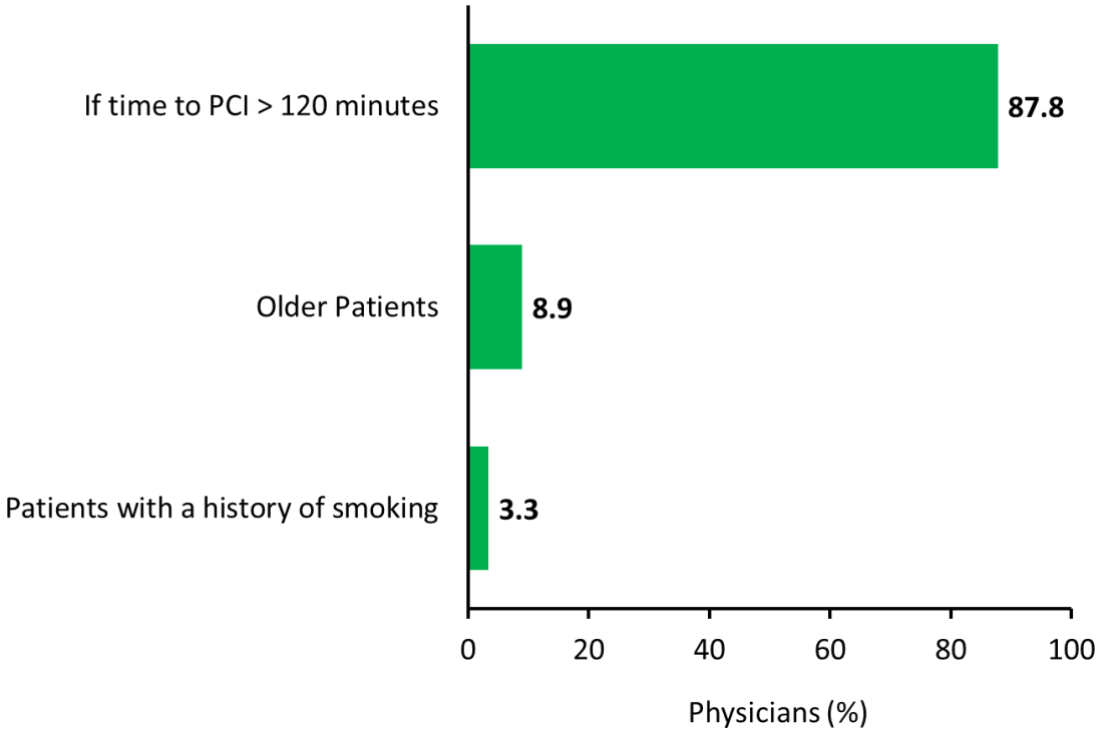
- The majority of physicians (66.3%) believed that pharmaco-invasive therapy offers a shorter time to reperfusion compared to primary PCI (pPCI).
- About 14.1% of physicians considered a lower risk of bleeding as a benefit of pharmaco-invasive therapy compared to pPCI.
- Approximately 12% of physicians believed that pharmaco-invasive therapy provides similar clinical outcomes as pPCI.
- However, 7.6% of physicians believed that pharmaco-invasive therapy offers higher culprit-vessel patency compared to pPCI.

8. Which patient profile(s) could a Pharmaco-Invasive strategy be an alternative to pPCI? (Can mark more than 1 option, if required)

a. If time to PCI >120 minutes

b. Older Patients

c. Patients with a history of smoking



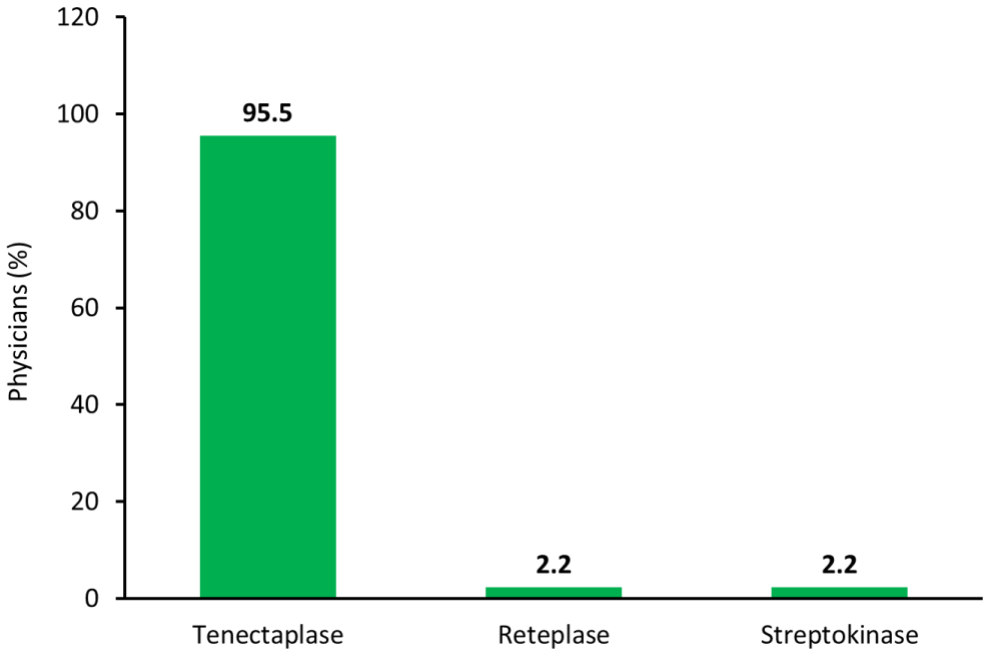
- Majority of physicians (87.8%) observed that pharmaco-Invasive strategy is suitable if the time to PCI exceeds 120 minutes, alternative to pPCI.
- About 8.9% of physicians considered older patients as appropriate candidates for a pharmaco-invasive strategy alternative to pPCI.
- Furthermore, 3.3% of physicians viewed patients with a history of smoking as suitable for a pharmaco-invasive strategy alternative to pPCI

9. Which thrombolytic agent is preferred in your clinical practise?

a. Tenectaplase

b. Reteplase

c. Streptokinase



- The majority of physicians (95.5%) preferred tenecteplase as thrombolytic agent in their clinical practice.
- About 2.2% of physicians preferred reteplase thrombolytic agent in their clinical practice.
- Similarly, About 2.2% of physicians preferred streptokinase thrombolytic agent in their clinical practice.

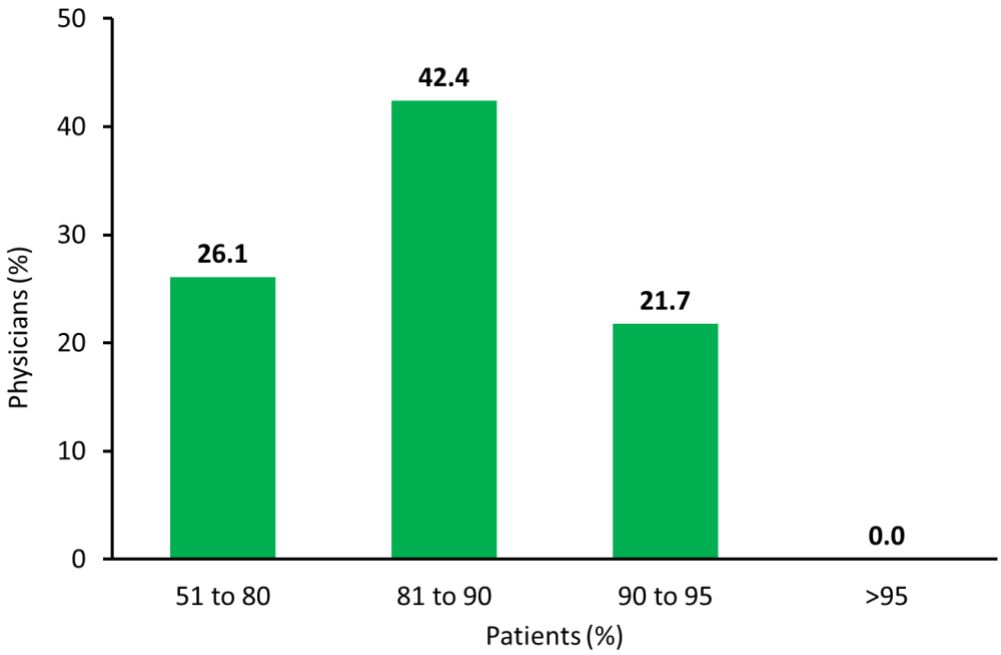
10. In your clinical practice, what percentage of patients achieve a clinically significant change in ST-segment elevation, post thrombolysis with Tenectaplase in patients with STEMI?

a. 51 to 80%

b. 81 to 90%

c. 90 to 95%

d. >95%



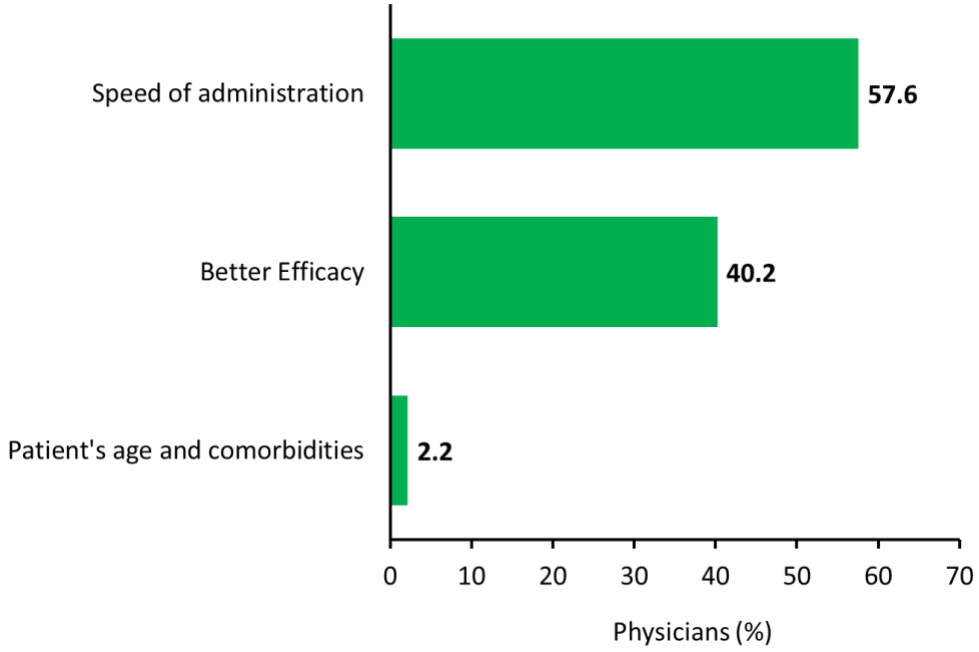
- About 42.4% of physicians reported that 81% to 90% of their patients achieved a clinically significant change in ST-segment elevation post-thrombolysis with Tenecteplase in STEMI patients.
- While 26.1% of physicians reported that 51% to 80% of their patients achieved such changes.
- Approximately 21.7% of physicians reported that 90% to 95% of their patients achieved a clinically significant change in ST-segment elevation post-thrombolysis.
- In contrast, no physicians reported achieving clinically significant changes in more than 95% of their patients.

11. What factors influence your choice between Tenecteplase and other thrombolytic agents for Patients with MI?

a. Speed of administration

b. Patient's age and comorbidities

c. Better Efficacy



- Speed of administration was the factor for majority (57.6%) of physicians influence their choice between tenecteplase and other thrombolytic agents for Patients with MI.
- Better efficacy was the factor for 40.2% of physicians influence their choice between Tenecteplase and other thrombolytic agents for Patients with MI.
- Patient's age and comorbidities was the factor for approximately, 2.2% of physicians influence their choice between Tenecteplase and other thrombolytic agents for Patients with MI.
- Survey data highlights that quick administration and superior efficacy are the main considerations when selecting Tenecteplase over other thrombolytic agents.

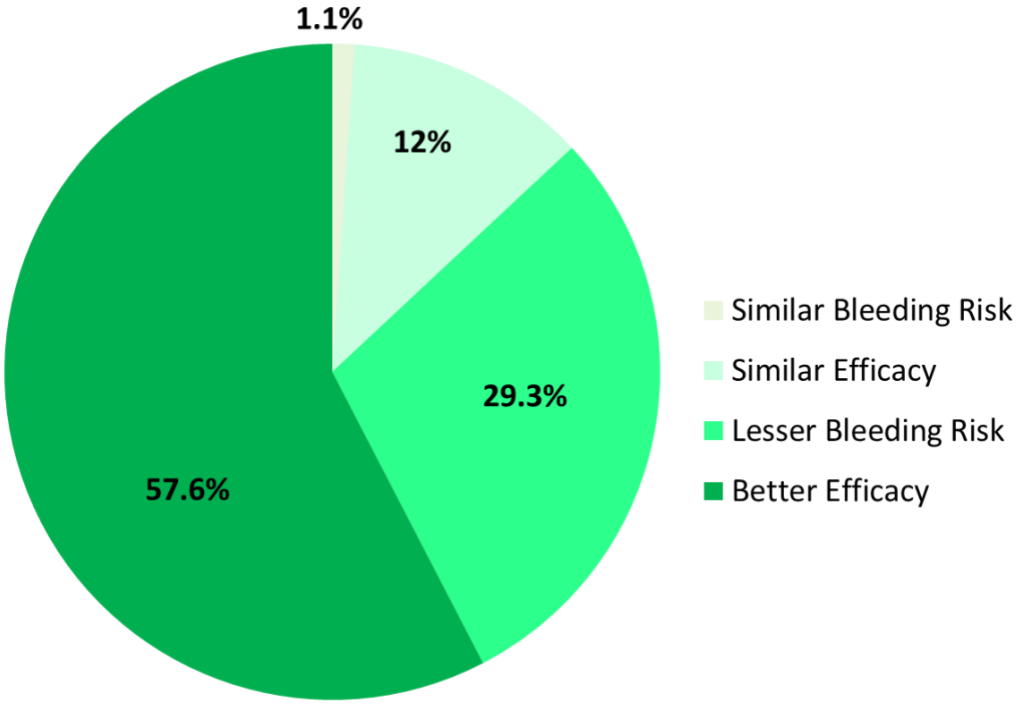
12. How are the clinical outcome(s) with Tenectaplase compared to Reteplase in patients with MI? (Can mark more than 1 option, if required)

a. Better Efficacy

b. Similar Efficacy

c. Lesser Bleeding Risk

d. Similar Bleeding Risk



- Majority of physicians (57.6%) noted that better efficacy was the clinical outcome(s) with tenectaplase compared to reteplase in patients with MI.
- About 29.3% of physicians noted, that lesser bleeding risk was the clinical outcome(s) with tenectaplase compared to reteplase in patients with MI.
- However, 12% of physicians considered the efficacy of the two agent's tenectaplase and reteplase to be similar in patients with MI.
- Only, 1.1% of physicians believed the bleeding risk was similar for both thrombolytic agent's tenectaplase and reteplase in patients with MI.

SUMMARY

The survey conducted among physicians regarding the management of MI, various aspects of treatment approaches and practices were evaluated.

The data revealed that 34.8% of physicians observed that MI patients were admitted to the hospital within less than one hour. Approximately 37% noted admissions occurred within one to three hours, while 22.8% saw admissions within three to four hours. Only 5.4% reported admissions after more than four hours. This highlighted that timely admission was crucial, with most patients arriving within a few hours of symptom onset. When assessing the challenges associated with primary PCI, 46.7% of physicians cited cost as a significant obstacle. Delay in hospital admission was identified as a challenge by 38% of physicians, and 15.2% noted poor infrastructure availability as a concern. These challenges underscored the impact of cost and timely admission on the feasibility of performing primary PCI.

Regarding reperfusion strategies, 34.8% of physicians preferred the pharmaco-invasive approach, while 32.6% favored thrombolysis and the same percentage preferred primary PCI. This indicated a balanced preference among different strategies, with a slight inclination towards pharmaco-invasive methods. The primary factor influencing the decision to administer fibrinolytic therapy was the availability of timely PCI, considered by 48.9% of physicians. Time from symptom onset was the main factor for 39.1% of physicians, while medical history and patient age were considered by 9.8% and 2.2%, respectively. This data highlighted that access to PCI and symptom duration were key considerations in choosing fibrinolytic therapy.

In terms of clinical outcomes, 51.1% of physicians observed that 51% to 80% of their patients achieved clinically significant changes in ECG post-thrombolysis for STEMI. About 23.9% reported that 81% to 90% achieved such changes, and 14.1% noted less than 50% achieved clinically significant changes. Regarding the use of the pharmaco-invasive strategy, 45.7% of physicians applied it frequently, 26.1% very frequently, 22.8% occasionally, and 4.3% rarely. This showed that the strategy was commonly employed, with a majority using it frequently.

The survey found that 66.3% of physicians believed pharmaco-invasive therapy offered a shorter time to reperfusion compared to primary PCI, while 14.1%

considered it had a lower risk of bleeding. About 12% saw similar clinical outcomes, and 7.6% noted higher culprit-vessel patency with pharmaco-invasive therapy. For patients with suspected MI, 87.8% of physicians found the pharmaco-invasive strategy suitable if the time to PCI exceeded 120 minutes. Older patients and those with a history of smoking were considered suitable by 8.9% and 3.3% of physicians, respectively. Tenecteplase was the preferred thrombolytic agent for 95.5% of physicians, with reteplase and streptokinase each preferred by 2.2%. Post-thrombolysis with Tenecteplase, 42.4% of physicians reported 81% to 90% of patients achieved significant changes in ST-segment elevation, while 26.1% noted 51% to 80%, and 21.7% reported 90% to 95%. No physicians observed changes in more than 95% of patients.

Speed of administration and better efficacy were the main factors for 57.6% and 40.2% of physicians, respectively, in choosing Tenecteplase over other agents. Patient age and comorbidities were less influential, considered by only 2.2%. Finally, 57.6% of physicians noted better efficacy of Tenecteplase compared to Reteplase, 29.3% cited a lower bleeding risk, and 12% saw similar efficacy between the two. Only 1.1% believed the bleeding risk was similar for both agents.

DISCUSSION

In the study, 34.8% of physicians reported that MI patients were admitted to the hospital in less than one hour, with the majority being admitted within the first few hours of symptoms. Challenges in performing primary PCI included cost (46.7%) and delays in admission (38%). A balanced preference for reperfusion strategies was noted, with 34.8% favoring the pharmaco-invasive approach. The majority (48.9%) considered timely PCI and symptom duration as key factors in choosing fibrinolytic therapy. Most physicians observed 51% to 80% of patients achieving significant ECG changes post-thrombolysis. Pharmaco-invasive strategy usage varied, with 45.7% using it frequently. Benefits of pharmaco-invasive therapy included shorter reperfusion times (66.3%). Tenecteplase was preferred by 95.5% of physicians, who noted its superior efficacy over reteplase, though some cited similar bleeding risks.

CLINICAL RECOMMENDATIONS

- First- Timely Admission and Reperfusion Strategy: Prioritize swift hospital admission and intervention for MI patients, as a majority are admitted within the first few hours. Given the challenges associated with primary PCI, including cost and delays, consider pharmaco-invasive strategies frequently, especially when PCI availability is limited or delayed.
- Fibrinolytic Therapy Considerations: When deciding on fibrinolytic therapy, the availability of timely PCI and the time from symptom onset should be key factors. With 48.9% of physicians considering timely PCI as critical, ensure that fibrinolytic therapy is administered promptly when PCI cannot be provided within 120 minutes.
- Preferred Thrombolytic Agents: Tenecteplase is overwhelmingly preferred, likely due to its rapid administration and efficacy. It is essential to continue prioritizing Tenecteplase for thrombolysis in STEMI patients, as it achieves significant ST-segment elevation changes in a substantial percentage of cases.
- Pharmaco-Invasive Strategy Suitability: Use pharmaco-invasive strategies particularly when PCI is delayed beyond 120 minutes. This approach can be beneficial in improving reperfusion times and patient outcomes.
- Clinical Outcomes Comparison: Tenecteplase is perceived to offer better efficacy and similar or lower bleeding risks compared to reteplase. Continue utilizing Tenecteplase where feasible, and consider its superior clinical outcomes in decision-making processes.

CONSULTANT OPINION

Based on the survey data, several key insights emerge regarding the management of myocardial infarction (MI) and the use of thrombolytic therapies.

Timely hospital admission for MI patients is a crucial factor, with most physicians noting that patients are admitted within a few hours of symptom onset. This underscores the importance of prompt medical intervention. The primary challenges identified for performing primary PCI include cost and delay in hospital admission, highlighting the need for cost-effective solutions and improved hospital access. In terms of reperfusion strategies, there is a balanced preference among physicians for pharmaco-invasive, thrombolysis, and primary PCI approaches, with a slight inclination towards pharmaco-invasive therapy. Factors influencing the choice of fibrinolytic therapy include the availability of timely PCI and the duration of symptoms, emphasizing the need for rapid access to interventions. The data reveals a strong preference for Tenecteplase over other thrombolytics due to its faster

administration and better efficacy. Additionally, pharmaco-invasive therapy is often preferred when PCI delays exceed 120 minutes. The survey also indicates that Tenecteplase is associated with significant ST-segment elevation changes, though no physicians reported achieving changes in more than 95% of patients.

Overall, these findings highlight the need for strategies that prioritize quick administration of effective treatments and address challenges such as cost and infrastructure to optimize MI management.

MARKET OPPORTUNITIES

The survey data reveals significant market opportunities in the management of myocardial infarction (MI) through thrombolytic therapy and reperfusion strategies. With a clear preference for Tenecteplase (95.5%) and a focus on factors like speed of administration (57.6%) and better efficacy (40.2%), there is a strong market demand for products and solutions that enhance these aspects. Additionally, the majority of physicians (66.3%) believe that pharmaco-invasive therapy offers benefits over primary PCI, especially when PCI times exceed 120 minutes, indicating an opportunity for developing or optimizing pharmaco-invasive protocols. There is also room for innovation in addressing challenges such as cost (46.7%) and infrastructure limitations (15.2%), which impact the adoption of primary PCI. Companies could explore solutions that streamline processes, improve infrastructure, or offer cost-effective options to better serve the evolving needs of healthcare providers managing MI.

MARKET POSITIONING

- The majority of physicians emphasize the importance of timely admission for MI patients, with 34.8% observing admission within less than one hour and 37% within one to three hours. This underscores the need for rapid intervention and highlights the significant role of timely PCI in improving patient outcomes.
- A significant number of physicians (46.7%) identified cost as the primary challenge associated with primary PCI, followed by delay in hospital admission (38%). This suggests a market opportunity for solutions addressing cost-efficiency and improving hospital admission processes.
- The pharmaco-invasive approach was preferred by 34.8% of physicians, with thrombolysis and primary PCI each favored by 32.6%. This indicates a competitive market where each strategy has substantial support, with a slight inclination towards the pharmaco-invasive approach.
- The availability of timely PCI was a critical factor for 48.9% of physicians when choosing fibrinolytic therapy, followed by time from symptom onset (39.1%). These factors are essential for positioning products that optimize PCI access and address symptom duration.
- Tenecteplase is the preferred thrombolytic agent for 95.5% of physicians, with its superior efficacy and speed of administration being key factors (57.6% and 40.2%, respectively). Reteplase and streptokinase are less favored, indicating a strong market position for Tenecteplase.
- A significant percentage of physicians reported that 81% to 90% of patients achieve clinically significant ST-segment changes post-thrombolysis with Tenecteplase. This positions Tenecteplase as a leading choice due to its effectiveness.
- The pharmaco-invasive strategy is seen as suitable when PCI time exceeds 120 minutes (87.8%). This suggests an opportunity for strategies that cater to scenarios with delayed PCI availability.
- Most physicians believe Tenecteplase offers better efficacy (57.6%) compared to Reteplase, with a lower bleeding risk (29.3%). This reinforces Tenecteplase's strong position in the market based on clinical outcomes.

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