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A Tale of Two Cities: STEMI Interventions in Developed and Developing Countries and the Potential of Telemedicine to Reduce Disparities in Care

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Objectives: *To utilize telemedicine as a foundation platform for creating population-based STEMI networks.*
Background: *Disparate acute myocardial infarction (AMI) management occurs in developed and developing countries on account of differences in infrastructure resources. As a result, developed countries utilize primary percutaneous coronary intervention (PCI) and second- and third-generation thrombolytic therapy, in contrast to developing countries, which primarily rely on earlier-generation thrombolytic therapy and basic medical management. Reducing the vast gap in AMI care between developed and developing countries is an abysmally slow process.*
Methods: *Remote access, telemedicine IT platforms, expert EKG interpretation, teleconsultation, and a strict quality assurance process are incorporated into a population-based AMI network.*
Results: *Lumen Americas Telemedicine Infarct Network (LATIN) is an applied hub-and-spoke strategy, which creates a telemedicine-based STEMI management network across large populations. Primary PCI with targeted door-to-balloon times is the preferred strategy for the hub sites. Telemedicine-guided accurate EKG interpretation and teleconsultation are applied at the spoke sites. An integrated IT platform is used to navigate an effective prehospital triage system. The pilot phase has created 100 LATIN sites in Brazil and Colombia.*
Conclusion: *Telemedicine provides an attractive strategy to reduce the gaps that presently exist in managing AMI in developed and developing countries.* (J Interven Cardiol 2014;27:155–166)

Introduction

Charles Dickens' observations in *A Tale of Two Cities* are exemplified in the disparate nature of acute myocardial infarction (AMI) management in developed and developing countries. Developed countries have access to sophisticated ambulance networks, prehospital management, 24/7 cardiac catheterization suites, a large group of skilled cardiologists, nurses, and technicians, thrombectomy devices and drug-eluting stents, and a host of financial and infrastructural resources.[1,2] Management of AMI under such infrastructure results in reliably low mortality and good long-term outcomes. In striking contrast developing countries lack appropriately recognized or managed AMI care. Ambulance services are often nonexistent; doctors and nurses are lacking; basic thrombolytic therapy is not available; and primary percutaneous coronary intervention (PCI) is unthinkable.[3] As a result of these drawbacks, AMI mortality and long-term outcomes are abysmal.

Health economists analyzing such disparities will confidently conclude that it will be decades of sustained

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Table 1. Relevant Statistics Comparison between Developed and Developing Countries

Indicator	Year		United States of America	Brazil	Colombia	Mexico
Population (Thousands)	2012		315,791	198,361	47,551	116,147
Urban population (%)	2012		82.6	84.9	75.6	78.4
Annual death average (thousands)	2012		2,647	1,270.75	2G4	557.6
General mortality rate (per 1,000 Pop.)	2010		a. 7.96	6.5	5.5	5.1
			b. 4.9	7.1	6.9	6.0
Ischemic heart disease mortality rate (per 100,000 Pop.)	2009/2010	General	a. 125.6	56.1	72.9	60.7
			b. 70.8	62.0	101.7	74.0
		Male	a. 130.8	65.5	80.1	68.7
			b. 96.0	79.5	125.9	93.1
		Female	a. 113.0	47.0	65.9	53.0
			b. 50.3	47.2	82.3	57.6
Estimated mortality rate for ischemic heart disease	2009/2010	45–64 y/o	85.38	102.40	103.01	70.96
		>65 y/o	749.55	518.77	1,008.30	726.94
Proportion of certified deaths due to ill-defined and unknown conditions (%)	2009/2010		1.5S	6.97	2.16	2.05
Poverty headcount ratio at $1.25 a day PPP (%)	2008–2010		—	6.14	8.16	1.15
Annual national health expenditure as a proportion of GPD (%)	2011	Public	9.9	3.1	3.5	3.0
		Private	5.6	4.1	1.5	3.1
Physicians ratio (per 10,000 Pop.)	2009		26.0	15.1	16.6	22.0
Hospital beds ratio (per 1,000 Pop.)	2010/2011		3.0	2.3	1.39	1.7
Number of outpatient care facilities	2001/2010		4,815	67,901	33,029	18,815

a. Corrected rate. b. Adjusted rate.

growth and development for developing countries to match economic, scientific, structural, and logistical parity in AMI care in developed countries. As the world awaits these changes, millions of AMI sufferers in developing countries will be denied access to advanced AMI care.[4] Telemedicine offers a novel platform to dramatically narrow the disparities in AMI care in developed and developing countries. Telemedicine can drastically increase access to AMI care, and it may do so in a cost-effective manner.[5] Diagnostic interpretation of a STEMI electrocardiogram (EKG) may increase.[6] Even more importantly, telemedicine affords an attractive possibility of comprehensively managing AMI and triaging patients into thrombolytic therapy, pharmacoinvasive management, and primary PCI.

In order to demonstrate the feasibility of telemedicine in flattening inequalities in AMI care in developed and developing countries, Lumen America Telemedicine Infarct Network (LATIN) has been developed and its pilot phase has begun in 100 LATIN sites in Brazil and Colombia. Table 1[7,8] reveals some recent statistics comparing the United States, Brazil, Colombia, and Mexico in areas relevant to AMI care. The developing countries such as Colombia and Mexico are less urbanized and have a significant proportion of their population living in poverty. Furthermore, while the mortality of heart disease is high, healthcare expenditure in general is much lower in those countries. Expectedly, access to physician and hospital beds is also considerably lower than in the United States. With most well-equipped medical facilities in the cities, access to quality healthcare and reliable ambulance is problematic for rural residents, which places a large reliance on rural outpatient care facilities. These differences occur from several factors—financial, infrastructure, logistical, and cultural. Several of these elements are interrelated. As an example, the vital factor of ambulance services appears to correlate with economic development of the region.[1,2] This observation is glaring in regions where well-developed ambulance services are entirely absent.[3]

AMI and Ambulance Networks. AMI management remains fundamentally dependent upon existing networks of ambulance services that provide the initial,

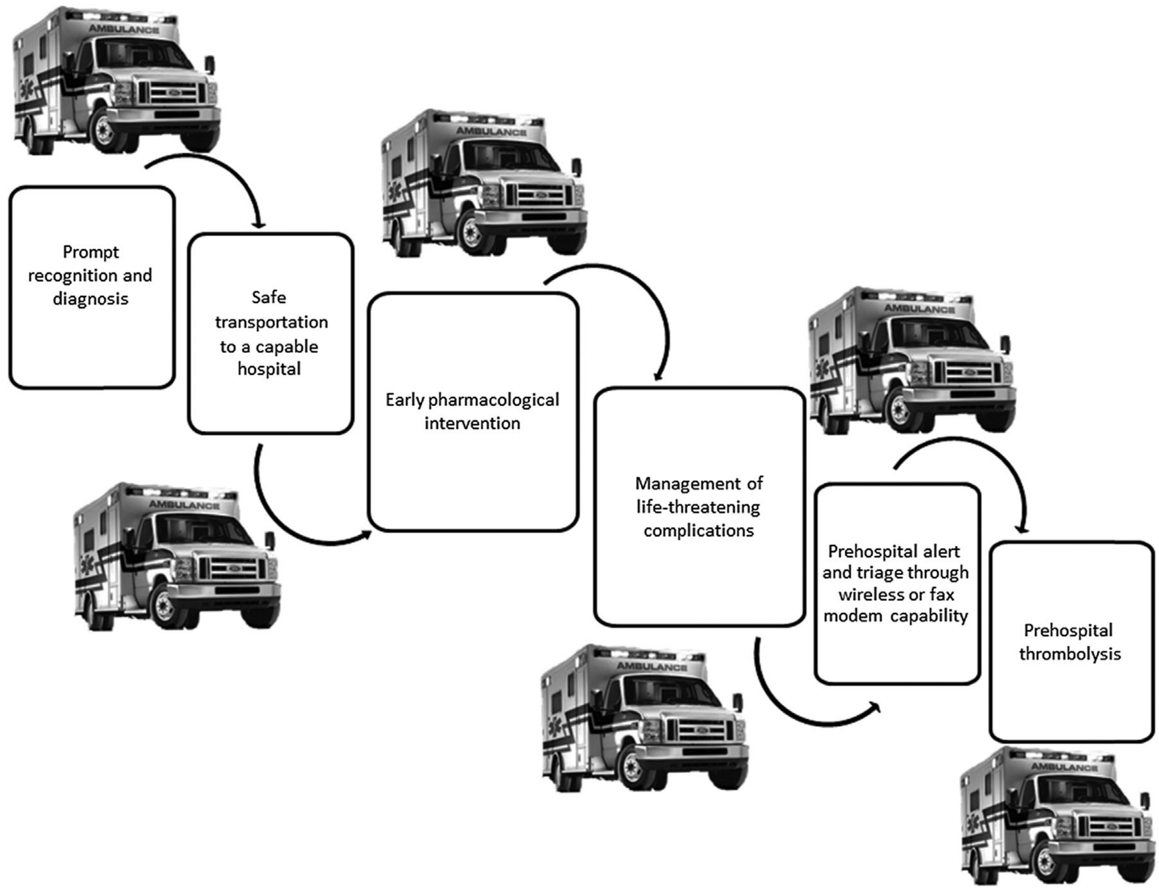

Figure 1. Roles of ambulance in STEMI interventions.

but critical, first step of managing a patient with an AMI.[9] An ambulance provides the following distinct purposes for AMI management,[10] as illustrated in Figure 1. Availability and capability of ambulance resources and networks vary widely, from a complete lack of reliable ambulance to mobile units that provide prehospital thrombolysis.[9] Yet, despite the vast abilities of the ambulance service, even in developed countries, ambulance care for an AMI patient merely represents transportation to a hospital.[11] It is tragic that many patients are being transported *without a definite diagnosis of AMI*.[12] This glaring omission makes it impossible for the ambulance to have an accurate assessment of the patient, let alone the correct management. In some situations, this type of unguided service is dangerous as poorly equipped ambulances provide a deceptive sense of security for an AMI patient.[13] The major difference between AMI care in Europe and the United States emanates from this specific dissimilarity—in Europe, the vast majority of AMI patients are transported to a hospital in an ambulance, whereas in the United States, the larger percentage of patients are still self-transporting.[14] In various Asian nations, there is a blend of such services; in some poor African countries, ambulance services for AMI are unavailable and/or unreliable.

Telemedicine. What should patients do if there is no reliable ambulance network to transport them to a hospital?

In such situations, patients lean on transporting themselves to the hospital, which greatly delays the treatment of an AMI. Management of AMI, either by thrombolysis or by primary PCI, is critically time-dependent. For thrombolytic therapy, a door to needle time of less than 30 minutes, and for primary PCI, a door to balloon time of less than 90 minutes, are the advocated guidelines.[5,15,16] *With a qualitative and quantitative absence of ambulances, achieving these*

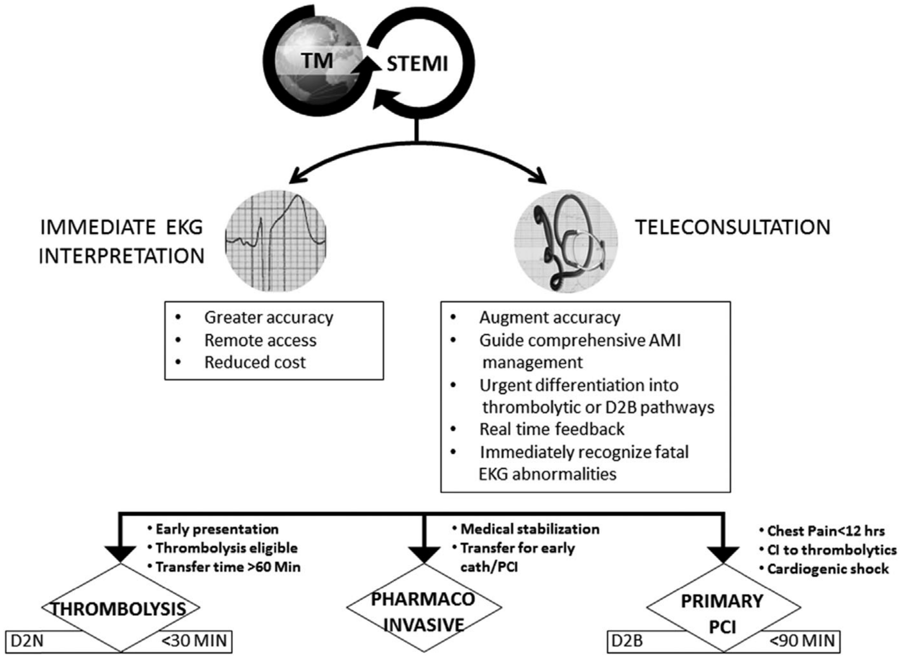

Figure 2. Roles of telemedicine in STEMI intervention.

mandated treatment times is simply not possible. As a result, both thrombolytic therapy and primary PCI will be suboptimal. Unfortunately, this situation is the norm rather than the exception.

Telemedicine effectively reduces these shortcomings.[6,17] It can even improve upon the results of thrombolytic therapy and primary PCI through its unique ability to initiate too early management, both within and outside an ambulance.[18] With thoughtful integration into a regional STEMI network,[19] telemedicine uses the best of today's technology to advance 3 pathways of treatment in the comprehensive management of AMI. Figure 2 introduces the roles of telemedicine when applied to locations with or without ambulance.

Telemedicine is founded on 4 distinct attributes: increased *access*, greater *accuracy*, a *comprehensive* AMI management strategy, and *cost-effectiveness*. Telemedicine support comprises 2 components: (1) accurate EKG interpretation and (2) teleconsultation. Not every EKG interpretation will require a teleconsultation. The role of teleconsultation is to guide triage of patients with a confirmed myocardial infarction. Considering the characteristics of developing countries and their urgent need for improved AMI care, effective use of telemedicine may offer a pragmatic solution to increase access and accuracy of treatment in a cost-effective manner while taking advantage of telemedicine platforms.

Lumen Americas Telemedicine Infarct Network (LATIN). Integration of telemedicine into current global infrastructure is paramount to ensuring its success. Telemedicine is used as a foundation pillar to initiate an optimal strategy for global AMI management. As shown in Table 1, developing countries rely largely on rural outpatient facilities to provide healthcare. An integrated approach that incorporates these facilities in AMI care is essential.

LATIN is structured as a hub-and-spoke strategy for comprehensive AMI management. The primary responsibility of the hubs is to deliver and expedite primary PCI for STEMI interventions with door-to-balloon times of less than 90 minutes. The spokes, up to 5 sites located between 5 and 250 miles from each hub, may provide thrombolytic therapy or pharmaco-invasive management strategy or expedite transfer for primary PCI. Spoke sites lack the ability to provide primary PCI. To carry out this strategy, LATIN has 3 partners with distinct roles. The telemedicine device is be provided by ITMS Inc., which is also providing a wireless software platform—Platform Integrated Telemedicine (PIT). Medtronic, Inc. provides logistical support for both the pilot and the main phase of LATIN. Lumen provides educational training for LATIN sites. Telemedicine devices are strategically placed in the ambulance, remote and inaccessible locations, and in places where AMI patients traditionally present (primary clinics, private nursing homes, and offices of general practitioners).[19] This strategy eliminates huge barriers caused by inadequacies of the ambulance systems to enable the administration of too early, prehospital AMI therapy.[18]

Methods

Most LATIN methods and protocol are based upon established guidelines; some additionally rely on the vast experience gained with the Single Individual Community Experience Registry (SINCERE) that has accumulated vast experience in performing short D2B STEMI interventions. LATIN begins when a patient with clinical suspicion and established coronary artery diseases risk factors presents to a LATIN site. Great clinical prudence is required at this critical juncture. Good clinical decision-making optimally and cost-effectively employs telemedicine and eliminates false positive responses.

Step 1: The Electrocardiogram (EKG) and Prehospital Management. Patients presenting with chest pain obtain a 12-lead EKG within 10 minutes of presentation as per clinical guidelines. Neither a clear STEMI presentation nor a case with atypical history and normal EKG would require assistance from the telemedicine strategy and would not be sent for telemedicine consultation. Uncertainty arises when the EKG includes early repolarization pattern, pericarditis, LAHB and LBBB, LVH with strain, and LV aneurysm. A clinical AMI presentation and suspicious EKG immediately utilizes the telemedicine protocol. While seeking an accurate EKG diagnosis, numerous critical tasks are performed in an ambulance, as described in Figure 1. Early pharmacology is initiated in the ambulance and includes aspirin (325 mg), Clopidogrel (300 mg; Prasugrel and Ticagrelor are even better options), sublingual nitroglycerine, supplemental oxygen, statins, beta blockers, and an anticoagulant. The latter may include a bolus of unfractionated heparin (60 μg/kg) or a bolus of Bivalirudin. Low-molecular-weight heparin may also be used but is less ideal.

Step 2: Teleconsultation-based LATIN Triage. Two documents are required to initiate teleconsultation: the presenting EKG and the LATIN clinical short form. Remotely located (in-hospital, at telemedicine centers or at home), expert cardiologists access these documents from the PIT platform and provide immediate EKG diagnosis based upon a true vector analysis. Prenotification of STEMI to hub sites is performed after accurate EKG diagnosis (as described above) primarily by telemedicine transmission and, if needed, by verbal communication or fax/modem. Telemedicine simultaneously delivers the STEMI EKG and the LATIN clinical short form to all 3 LATIN locations: hub, spoke, and in the ambulance. The teleconsultation cardiologist will communicate with the on-route ambulance EMS to provide prehospital AMI management. Once the patient arrives at a hub site, EMS will have a record of the prehospital intervention and contact information of the teleconsulation cardiologist who diagnosed the STEMI and facilitated prehospital STEMI care.

Step 3: Prehospital/Early Thrombolysis. The hubs initiate the STEMI protocol immediately upon confirmation of a STEMI diagnosis. Each LATIN site has advanced directives for either primary PCI or thrombolytic strategies based upon their location. As a general strategy, thrombolytic therapy is recommended for too early presentation (<2 hours from onset of pain), while PCI is recommended when transfer to a hub is readily available and for patients with cardiogenic shock.

The choice of lytic agents is left to the discretion of the physician seeking telemedicine consultation. These agents include Streptokinase, Alteplase, or Tenecteplase; adjunctive treatment includes antiplatelet and anticoagulants. Analgesics, narcotics, supplemental oxygen, and intravenous access are mandatory. Beta blockers are often used. Spoke sites are encouraged to develop their individual thrombolytic protocols. Successful lysis is marked by relief of chest pain and ST-segment resolution (>60% ST-segment lowering). Failed lysis provides an absolute indication for transfer to a PCI institution for rescue PCI. All patients with successful thrombolysis are transferred to a PCI institution within a reasonable period of time (4–24 hours). Figure 2 is a more detailed description of the thrombolytic pathway where specific roles of telemedicine are highlighted. Two specific roles for telemedicine can be appreciated. First, an electrocardiogram (EKG) is accurately interpreted by an accredited cardiologist,[20] who uses a vector tracing for quick and comprehensive diagnosis and reports it in a secure, HIPAA-compatible

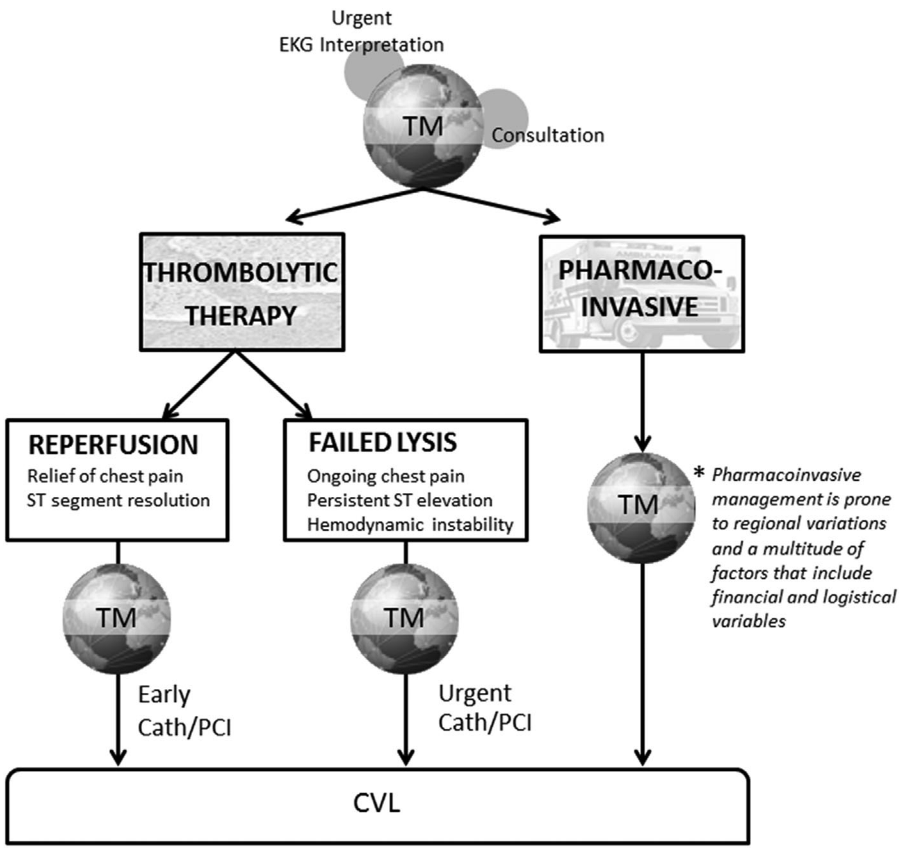

Figure 3. Enhancement of thrombolysis and pharmacoinvasive management with telemedicine.

format. With the electrocardiogram automatically converted to a standardized format, it is directly incorporated into the electronic medical record (EMR) and it serves as a historical template to be used for clinical management and research. The second specific role of telemedicine during thrombolytic therapy is the immediate availability to obtain a consultation for expert guidance during triage and treatment.

Step 4: Pharmacoinvasive Pathway. A pharmacoinvasive pathway mandates early transfer of thrombolytic therapy patients for a PCI strategy. As a result, every patient who receives thrombolytic therapy is expedited for adjunctive PCI. The cardiovascular laboratory at the PCI institution is immediately notified and catheterization laboratory/STEMI activation expedited. Again, choice of thrombolytic therapy is left to the discretion of the operator. Adjunctive therapy is as described for thrombolytic therapy. Figure 3 demonstrates a pharmacoinvasive strategy as compared with the thrombolysis pathway with the use of telemedicine. The role of teleconsultation is foremost in this pathway for the remote expert to guide the consulting physicians regarding the timing of transfer for PCI and the interim clinical management of the patient. Guideline recommendations are followed during this process and decisions such as use of antiplatelets, antithrombotics, and Gp2b/3a therapy are discussed.

Step 5: STEMI Intervention Pathway—Door-to-Balloon (D2B) Interventions. The essence of the STEMI Intervention pathway is the mandated door-to-balloon time of less than 90 minutes. Accurate STEMI diagnosis, intelligent ambulance transport, prehospital activation, and ED bypass are the 4 tenets of this strategy. False activation is considerably minimized through an accurate LATIN short form and remote EKG interpretation by expert cardiologists of the telemedicine network. Telemedicine further accomplishes intelligent EMS transport and prehospital activation. Advanced directives between LATIN hubs and spokes determine a unidirectional or bidirectional

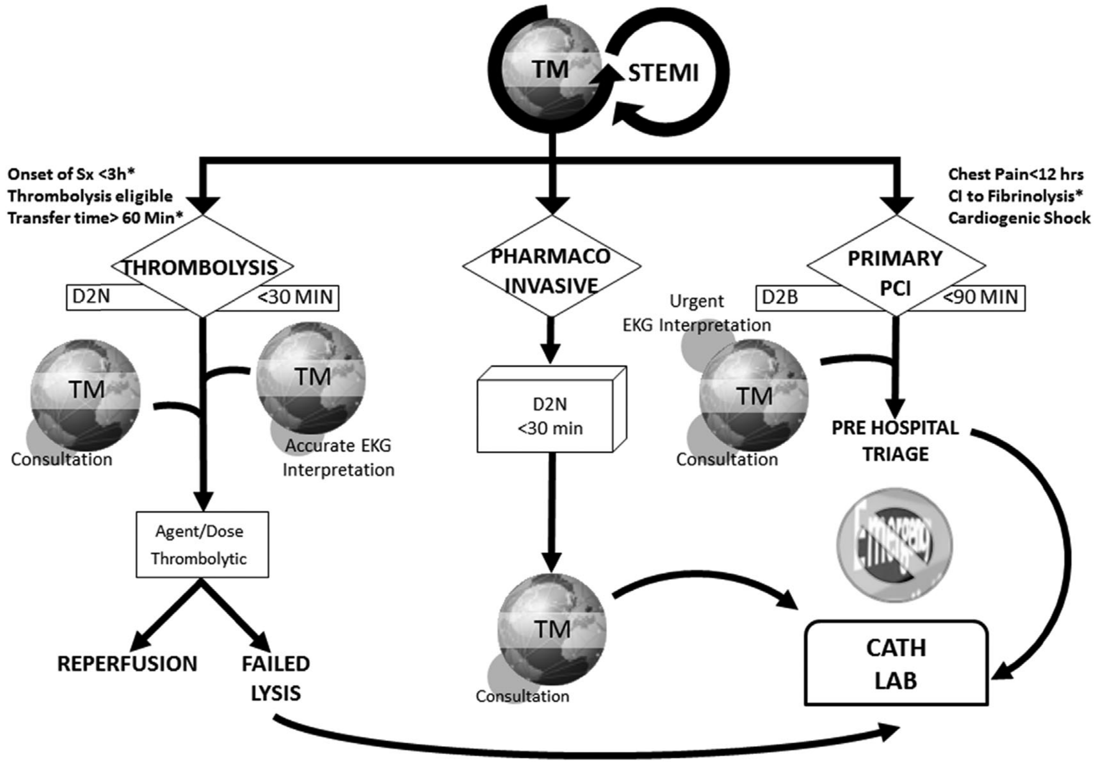

Figure 4. Comprehensive AMI management with telemedicine.

ambulance strategy. Certain LATIN sites have a centralized ambulance network, in addition. An accurate diagnosis triggers prompt ambulance transfer if the patient presents at a spoke site that has quick PCI access. For patients presenting at the hub sites, remote EKG diagnosis automatically triggers a STEMI alert. Optimal response time for cardiac cath lab personnel is less than 30 minutes. With early prehospital activation, the desirable strategy is either complete or partial ED bypass. In a complete ED bypass, the patient is wheeled from the ambulance to the cardiac catheterization laboratory without stopping at the emergency room. In a partial strategy, an emergency physician quickly assesses the patient and confirms availability of the cardiac catheterization laboratory. There is scientific evidence that ED bypass in suitable cases with accurate and early prehospital triage greatly contributes to reducing door-to-balloon times. Figure 4 combines the 3 previous LATIN figures in a master blueprint, demonstrating the novel and comprehensive algorithm that uses a telemedicine platform to facilitate any of the 3 AMI management pathways—thrombolytic therapy, pharmacoinvasive management, and primary PCI.

Results

(Systems Set-Up and Pilot Phase). From the above analysis, telemedicine shows great potential in the facilitation of comprehensive AMI management. It plays a role in diagnosis and consultation, to ensure timeliness, accuracy, and broad access in developing countries. It circumvents infrastructural and financial hurdles and possibly surpassing the performance of current modalities of diagnosis and transmission.[21,22] The LATIN system has begun testing the above hypothesis in a prospective, multicenter demonstration that includes a 1-year pilot study involving 100 STEMI centers (20 hubs, each with 5 spokes) and a 5-year main study involving 250 STEMI centers (50 hubs, each with 5 spokes). Selected sites are located in Brazil and Colombia during the pilot phase. These countries were chosen on account of the prevalence of AMI, inaccessibility to modern care, and existing experience with telemedicine protocols. Site selection has been meticulously performed. Criteria include presence of a catheterization laboratory (hub) and numerous satellites, non-PCI facilities (spokes) that greatly expand the

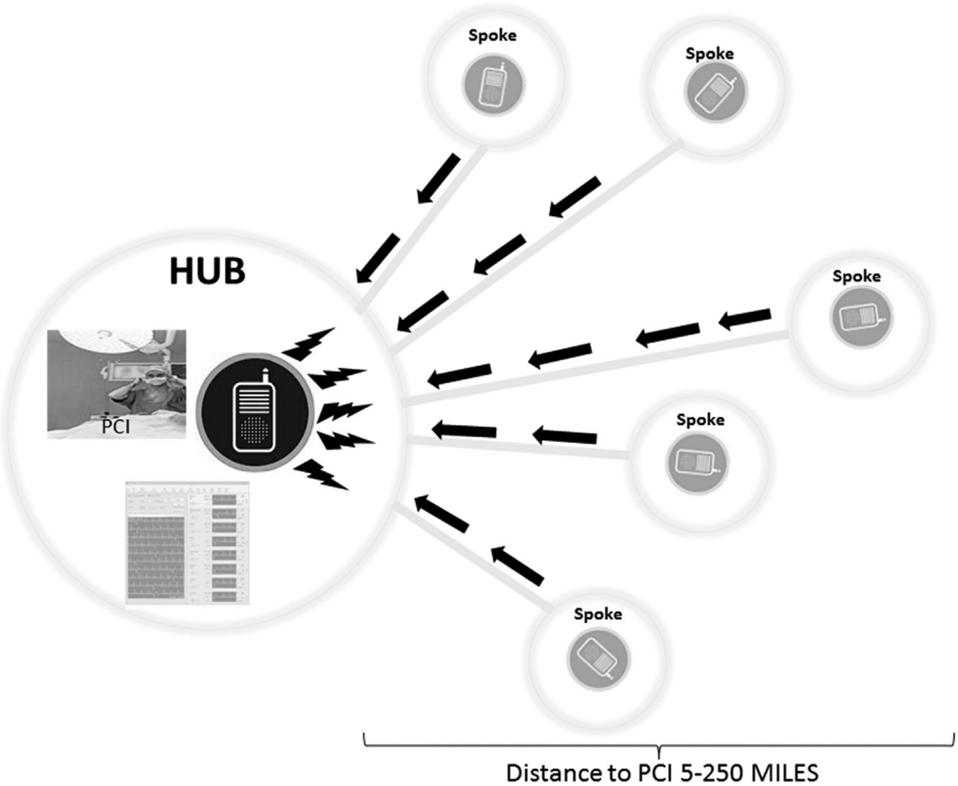

Figure 5. The LATIN Hub and spokes model.

catchment area of the PCI hospital. Figure 5 lays out the spokes and hub system. In the hub facility, selection of a STEMI Champion is mandatory. The STEMI Champions are designated to provide leadership over their respective primary PCI program and ensure quality, teamwork, feedback, and data collection. Selection of STEMI coordinators is encouraged to supplement the work of the STEMI Champions and to coordinate activities of the satellite sites. The hub site employs uniform LATIN protocol for D2B interventions with guideline-based pharmacological management and D2B mandate. All presenting patients with AMI at the hub site will proceed to receive primary PCI unless patients refuse consent for the invasive strategy. Hub sites are encouraged to have an on-call roster with a strict mandate for the catheterization laboratory personnel to reach the catheterization laboratory within 30 minutes. Selection of the spokes has been performed by the hub facility, with transporting distances between 5 and 250 miles. Referring spoke facilities range from being small, primary clinics to larger non-PCI hospitals. Several smaller clinics have no onsite physicians, no primary care physician, no ER physicians, or no cardiologist.

Telemedicine consultation is being provided by 3 facilities, managed by ITMS, Inc. and located remotely in Santiago, Chile, São Paolo, Brazil, and Bogota, Colombia. Network requirement for EKG transmission include broadband connection and cellular network. Accredited cardiologists who have completed a strict quality control program perform all EKG interpretation. Each EKG is vectorized and standardized prior to transmission and it is supplemented by relevant patient history. A comprehensive database of patient demographics and treatment-related parameters is being collected. Several system-related statistics are able being collected: mean time of EKG interpretation; mean age of the interpreting cardiologists and their mean period of telemedicine experience; proportion of remote consultations that occur between a cardiologist and primary care physician, a cardiologist and ED physician, and 2 cardiologists; and the amount of AMI care provided at facilities without cardiologists.

Wireless Transmission	Advanced Paramedics/ Physicians in Ambulance	Telemedicine
✓ Fast ✓ Reliable ✓ Secure	✓ Accurate	✓ Greater accuracy ✓ Less expensive
⊖ Expensive ⊖ Moderate accuracy	⊖ Impractical to equip with skilled personnel ⊖ Possible in few countries	⊖ Lacks supporting evidence ⊖ Network of remote cardiologists required

Figure 6. Comparison of 3 methods of prehospital diagnosis and triage.

Discussion

Current methods for ambulance prehospital triage and transfer of primary PCI with a mandated D2B time of less than 90 minutes are hampered by several drawbacks.[22] Prehospital triage with in-ambulance personnel, either advanced paramedics (Ottawa, Canada) or physicians (France), is clearly an inefficient and expensive method that has not gained greater acceptance globally.[23,24] The current wireless transmission models use a software-only diagnosis of AMI, heavily hampered by both false positive and false negative results.[25] The telemedicine model, in contrast, obtains a 12-lead EKG for real-time interpretation by a cardiologist, avoiding delays and ensuring accuracy.[26,30] The carefully designed platforms and network of dedicated cardiologists on the other end of the transmission make telemedicine an attractive option.[26] Figure 6 compares the 3 pathways of triage. Telemedicine (ITMS, Inc.) has developed an EKG device with multiport transmission capabilities, a patented telemedicine-integrated platform with its own network, and server support. Each EKG received is vectorized into a standard format with correct dimensions, crucial for accurately reading QT interval. The standardization of an EKG makes it ready for EMR and coding compatible with the billing system and ICD 10. This vectorization, if performed on mobile phones with third-party software, is much more time-consuming. The telemedicine platform also takes painstaking measures to be HIPPA compliant while ensuring security of transmission and including time stamps and confirmation of receipt for record keeping. A massive staff of accredited cardiologists is scheduled on shifts to maintain 24/7 availability for immediate EKG interpretation. Trained personnel perform a preliminary filter based on urgency of the received EKGs to further streamline the process. Figure 7 highlights the advantages of the ITMS telemedicine platform, where each EKG is interpreted with maximum accuracy, stored in a robust database, and immediately compatible with other healthcare facilities' medical records. Finally, the cost of telemedicine devices (ITMS, Inc.) is considerably less than the cost of standard wireless transmission devices. Understanding the prevalent modes of telecommunication as they pertain to AMI management is imperative to evaluate telemedicine as an effective strategy for global AMI management. Present modes of interphysician and interfacility transportation include telephone conversation, facismile, wireless communication, and telemedicine. Telemedicine ensures rapid and clear communication on the status of AMI patient, who may require careful management of his or her life-

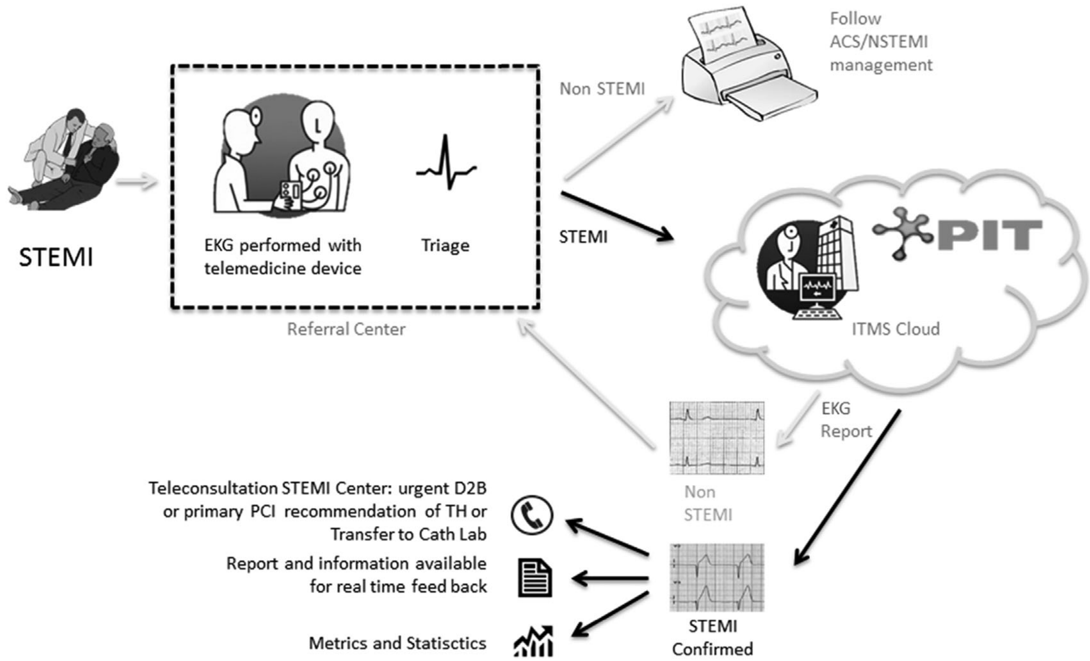

Figure 7. Schematic of ITMS telemedicine STEMI diagnosis and triage.

threatening complications or critical condition during the lengthy transport from emergency rooms to catheterization laboratories. From our present understanding of the various modalities, telemedicine affords distinct advantages as a comprehensive strategy for facilitating AMI communications for seamless navigating through a STEMI process and the STEMI procedure.

Telemedicine provides comprehensive management of AMI by facilitating thrombolytic therapy, pharmacoinvasive management, and primary PCI with mandated D2B times. In the thrombolytic pathway, the critical function of teleconsultation provides the less appreciated and cost-effective benefits of remote consultation.[28] The reviewer/remote consultant obtains a clearer history from the recipient physician and guides the latter through an urgent triage into a thrombolytic or a primary PCI pathway,[27,31] the current bottleneck in STEMI care. As timeliness is of critical importance in STEMI intervention, it is immensely valuable to triage the patient scientifically, cost-effectively, and rapidly through either a mandated door-to-needle time or a door-to-balloon time with this remote, but prompt, discussion.[28,29] The consultation primarily uses the following criteria: (a) thrombolysis is indicated by a too early presentation (<3 hours from symptom onset), long transfer times (>90 minutes to reach PCI facility) for primary PCI, unavailability of primary PCI, and no contraindications for thrombolytic therapy; (b) primary PCI is guided by presentation within 12 hours from the onset of chest pain, contraindication to thrombolytic therapy, presentation with cardiogenic shock, and transfer times of less than 90 minutes.

Limitations. The potential of teleconsultation for advancing the pharmacoinvasive management is not as prominent as local cardiologists are often involved with the management of the case by this stage under less time constraint. Yet discussions are likely to contribute to better clinical management and more efficient transfer. Often repeat EKGs are also compared during this process, where having consultative options may aid the decision process. While the proposed LATIN study will test the practicality and effectiveness of a STEMI network with deep integration of telemedicine and make observations on its most useful features, applying such a controlled system to the Latin American region at large will be challenging. In areas with severely lacking ambulance service, the transfer of patients for PCI still requires fundamental improvements in infrastructure. Public health mandates will be essential to ensure that scientifically proven guidelines are being followed uniformly. Finally, financial inadequacy will still preclude patients from accessing proper treatment without increased insurance coverage and public healthcare expenditure.

Conclusions

Major inequalities exist in the care of AMI in developed and developing countries. Telemedicine provides a strong rationale for reducing these differences. LATIN provides the world's first and comprehensive population-based AMI strategy that uses telemedicine to provide global AMI care and it may be the revolutionary start to bridging the gap between the disparate levels of AMI care.

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