UNIVERSIDADE ESTADUAL DE MARINGÁ
CENTRO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE

LUCIANO DE ANDRADE

Disparidades regionais na mortalidade por doença isquêmica do coração no estado do Paraná e uma avaliação a partir do nível local (municipal) sobre o acesso ao tratamento do infarto agudo do miocárdio com supradesnivelamento do seguimento ST.

Maringá
2014

LUCIANO DE ANDRADE

Disparidades regionais na mortalidade por doença isquêmica do coração no estado do Paraná e uma avaliação a partir do nível local (municipal) sobre o acesso ao tratamento do infarto agudo do miocárdio com supradesnivelamento do seguimento ST.

Tese apresentada ao Programa de Pós-Graduação em Ciências da Saúde do Centro de Ciências da Saúde da Universidade Estadual de Maringá, como requisito parcial para obtenção do título de Doutor em Ciências da Saúde.
Área de concentração: Saúde Humana.

Orientador: Prof.ª Dr.ª Maria Dalva de Barros Carvalho.

Maringá
2014

FICHA CATOLOGRÁFICA

Dados Internacionais de Catalogação na Publicação (CIP)
Biblioteca do Campus de Foz do Iguaçu – Unioeste
Ficha catalográfica elaborada por Miriam Fenner R. Lucas - CRB-9/268

A553 Andrade, Luciano de
Disparidades regionais na mortalidade por doença isquêmica do coração no estado do Paraná e uma avaliação a partir do nível local (municipal) sobre o acesso ao tratamento do infarto agudo do miocárdio com supradesnivelamento do seguimento ST / Luciano de Andrade. – Maringá, 2014.
89 fl. : il. : gráf. : mapas

Orientadora: Profª Drª Maria Dalva de Barros Carvalho.
Tese (Doutorado) – Programa de Pós-Graduação em Ciências da Saúde - Universidade Estadual de Maringá.

1. Isquemia miocárdia. 2. Paraná – Distribuição espacial da população - Fatores socioeconômicos. 3. Epidemiologia. 4. Angioplastia coronária. 5. Acesso aos serviços de saúde. 7. Serviços de saúde – Administração. I. Título.

CDU 616.12-008
614.4(816.2)

FOLHA DE APROVAÇÃO

LUCIANO DE ANDRADE

Disparidades regionais na mortalidade por doença isquêmica do coração no estado do Paraná e uma avaliação a partir do nível local (municipal) sobre o acesso ao tratamento do infarto agudo do miocárdio com supradesnivelamento do seguimento ST.

Tese apresentada ao Programa de Pós-Graduação em Ciências da Saúde do Centro de Ciências da Saúde da Universidade Estadual de Maringá, como requisito parcial para obtenção do título de Doutor em Ciências da Saúde pela Comissão Julgadora composta pelos membros:

COMISSÃO JULGADORA

Prof.ª Dr.ª Eniuce Menezes de Souza
Universidade Estadual de Maringá

Prof. Dr. Reinaldo Antônio Silva-Sobrinho
Universidade Estadual do Oeste do Paraná

Prof. Dr. Rogério Toshiro Passos Okawa
Universidade Estadual de Maringá

Prof.ª Dr.ª Sandra Marisa Pelloso
Universidade Estadual de Maringá

Prof.ª Dr.ª Maria Dalva de Barros Carvalho (Orientadora)
Universidade Estadual de Maringá

Aprovada em: 26/09/2014.

Local de defesa: Sala 01, Bloco 126, campus da Universidade Estadual de Maringá.

DEDICO ESTE TRABALHO

Aos meus filhos Ana Caroline e Bruno, que por tantas vezes, sacrificaram os poucos momentos de convivência comigo, para que eu pudesse me dedicar a este trabalho, obrigado por me acompanharem nesta jornada. E em especial a minha esposa Eliane, por sua tão grande paciência e compreensão comigo durantes estes anos, sempre comigo nos momentos mais difíceis. Só eu sei o tamanho da importância de vocês na minha vida. Amo vocês...

AGRADECIMENTOS

A DEUS, por me proteger nas viagens a Maringá e também ao meu tempo em Durham (Carolina do Norte) nos Estados Unidos, dando força e sabedoria para enfrentar e superar os contratempos na realização dos trabalhos neste período de qualificação.

Ao meu Pai Benedito Luciano (*in memorian*) e a minha mãe Maria Aparecida "Dona Cida" por mostrar o verdadeiro sentido de família em minha vida. Ao meu irmão Lucino "Dedé" (*in memorian*) minha referência de dedicação aos estudos, e às minhas irmãs e meus sobrinhos pelo carinho de sempre.

Ao meu grande amigo Professor Oscar kenji Nihei pela contribuição valiosa que vem dando a mim nestes últimos anos, me ensinando lições de pesquisa, mas principalmente lições de humildade.

Aos professores Sandra Marisa Pelloso, Eniuce Menezes de Souza e Nelson Luiz Batista de Oliveira, por acreditarem na minha determinação.

Aos Professores Adelia Batilana, Catherine Lynch, Elias Carvalho, Clarissa Garcia Rodrigues, Guttenberg Ferreira Passos, João Ricardo N. Vissoci e Ricardo Pietrobon, pelo auxílio e colaboração para o desenvolvimento deste trabalho, quanto aprendizado, e como importante as parcerias nacionais e internacionais.

Aos meus amigos Alberto Acosta Hermida, Vanessa Zanini, Karen Finato, Robson de Castro Viana, Carmen Pertille Ramos, André Castro, Juliana Donini e Janete Guellere, pelo apoio, parceria e motivação de sempre!

Aos meus colegas de profissão Jean Costa e Patricia Mancini, pela disponibilidade para ajudar durante o período da coleta de dados em Maringá.

À Secretaria do Programa de Pós-graduação em Ciências da Saúde, Olívia Abeche, pela sua dedicação e competência.

Aos colegas do Doutorado, em especial a Joseane B. da Silva e a Simone Castanho de Melo, pela amizade e incentivo.

Ao Professor Rogério Toshiro Passos Okawa por ter aceitado a participar da avaliação deste trabalho.

Agradeço as instituições hospitalares - Hospital Ministro Costa Cavalcanti e Unidade de Pronto Atendimento João Samek em Foz do Iguaçu e em Maringá Hospital Santa Rita, pelas autorizações para a coleta de dados.

Aos professores do curso de Enfermagem da Universidade Estadual do Oeste do Paraná - Campus Foz do Iguaçu, em especial aos Professores Marieta Fernandes Santos e

Reinaldo Antonio Silva-Sobrinho, pelo incentivo de sempre.

A Universidade Estadual do Oeste do Paraná – Campus Foz do Iguaçu por ter me liberado para este período de qualificação profissional.

Ao programa Ciências sem Fronteiras do Governo Federal Brasileiro por ter financiado meu Doutorado Sandwich nos Estados Unidos.

A Duke University (*Duke Global Health Institute*) pela oportunidade de realização do Doutorado Sandwich.

E, por fim, obrigado a todos que de alguma forma, direta ou indiretamente, contribuíram para a realização deste trabalho.

AGRADECIMENTO ESPECIAL

À minha orientadora Prof.ª Dr.ª Maria Dalva de Barros Carvalho, por ter acreditado e confiado em mim, pelos sábios conselhos, pela oportunidade de trabalhar ao seu lado, no qual adquiri conhecimentos importantes e preciosos para minha vida profissional e pessoal. A você "Dalvinha", o meu respeito e gratidão por toda a minha vida.

EPIGRAFE

“A educação é a arma mais poderosa que
você pode usar para mudar o mundo.”
Nelson Mandela

RESUMO

A alta tecnologia no campo da cardiologia intervencionista aplicada em hospitais terciários trouxe enormes benefícios no tratamento de doenças isquêmicas do coração (DIC). No entanto, as taxas de mortalidade por DIC, em especial, por Infarto Agudo do Miocárdio com Supradesnivelamento do Seguimento ST (IAMCSST), permanecem elevadas, atingindo notadamente os países desenvolvidos e cada vez mais os países em desenvolvimento. Avaliamos neste trabalho a relação entre a taxa de mortalidade por DIC e as condições socioeconômicas, demográficas e geográficas em 399 cidades do estado do Paraná, Brasil, de 2006 a 2010, como também fatores relacionados com atrasos para o inicio do tratamento de pacientes com IAMCSST em um hospital terciário (Centro de referência em cardiologia intervencionista) para apoiar um plano estratégico para modificações estruturais e de pessoal em um hospital primário alinhando o processo com as diretrizes internacionais. Os dados sobre mortalidade por DIC no estado do Paraná foram obtidos no Sistema de Informações de Mortalidade (SIM) do Ministério da Saúde e as informações populacionais, socioeconômicas e demográficas foram disponibilizadas em formato digital pelo Instituto Brasileiro de Geografia e Estatística (IBGE). Dados complementares para avaliar os atrasos no tratamento de pacientes com IAMCSST em um hospital terciário a partir (originados) de um hospital primário foram obtidos através do prontuário médico e entrevistas. Utilizou-se diferentes métodos: a Análise Exploratória de Dados Espaciais (AEDE); uma análise integrada qualitativa e quantitativa, incluindo observações *in loco*, entrevistas, análise dos registros nos prontuários dos pacientes, Análise Qualitativa Comparativa (QCA) e Dinâmica de Sistemas (SD). Para o tratamento dos dados, foram utilizados os softwares GeoDA™, NVIVO versão 10.0, R statistical versão 2.15.0 e Vensim DSS ® version 5.11. Na Análise Exploratória de Dados Espaciais (AEDE) encontramos uma autocorrelação espacial positiva a respeito de mortalidade por DIC ($I = 0{,}5913$, $p = 0{,}001$) no estado do Paraná. Houve uma associação espacial positiva significante entre três indicadores socioeconômicos e demográficos e as taxas de mortalidade por DIC: Proporção de Idosos na População ($I = 0{,}3436$ $p = 0{,}001$), Taxa de Analfabetismo ($I = 0{,}1873$ $p = 0{,}001$) e Índice de Desenvolvimento Humano Municipal (IDH-M) ($I = 0{,}0900$ $p = 0{,}001$). Além disso, outros dois indicadores apresentaram associação espacial negativa significativa com as taxas de mortalidade por DIC: População ajustada por idade ($I = -0{,}1216$ $p = 0{,}001$) e Produto Interno Bruto ($I = -0{,}0864$ $p = 0{,}001$). Também foi encontrada uma autocorrelação espacial positiva entre as taxas de mortalidade por DIC e as distâncias geográficas entre as cidades de residência dos pacientes e seus correspondentes centros de referência em cardiologia intervencionista (I = 0,3368). Cidades localizadas dentro de Regionais de Saúde com centro referência em cardiologia intervencionista apresentaram uma taxa de mortalidade significativamente mais baixa por DIC. À alta taxa de mortalidade por DIC dentro das Regionais de Saúde não se restringiu a variáveis socioeconômicas e demográficas, mas apresentou correlação positiva com a variável ‘distância entre cada cidade e seu centro de referência de cardiologia intervencionista’. Quando analisado os fatores relacionados com atrasos no tratamento de pacientes com IAMCSST a partir de um hospital primário, as principais causas foram categorizadas em três temas: a) profissional, b) equipamentos e c) logística de transporte. A análise comparativa qualitativa (QCA) confirmou quatro estágios principais de atrasos para o cuidado do paciente com IAMCSST em relação ao tempo '*Door-In to Door-Out*' no hospital primário. Estes estágios e seus atrasos médios em minutos foram: a) Primeiro contato médico (da porta de entrada até o primeiro contato com a enfermeira e/ou médico): 7 minutos; b) Aquisição do eletrocardiograma (ECG) e avaliação por um médico: 28 minutos; c) Transmissão do ECG e *feedback* do hospital terciário (Centro de referência em cardiologia intervencionista): 76 minutos; e d) Tempo de espera para transferência do paciente: 78 minutos. A linha de base do Modelo de Dinâmica de Sistemas confirmou o comportamento do sistema, sobre todos os atrasos que ocorrem e as necessidades de melhorias. Além disso, após a validação de análise de sensibilidade, os resultados sugeriram que uma melhoria global de 40% a 50% em cada uma destas fases identificadas iria reduzir o atraso. Concluímos que fatores geográficos desempenham um papel significativo na mortalidade por DIC dentro dos municípios do estado do Paraná e têm implicações políticas importantes com relação à distribuição geográfica das redes de cuidados de saúde cardiovascular. Avaliação *in loco* do atraso no tratamento do paciente com IAMCSST sugere que o investimento na formação de pessoal de saúde, a diminuição da burocracia e gerenciamento de diretrizes pode levar a melhorias importantes, diminuindo o atraso identificado.

Palavras-chave: Isquemia Miocárdica, Distribuição Espacial da População, Fatores Socioeconômicos, Epidemiologia, Angioplastia Coronária, Acesso aos Serviços de Saúde, Administração de Serviços de Saúde.

ABSTRACT

High technology in the field of interventional cardiology applied in tertiary hospitals has brought enormous benefits in the treatment of ischemic heart disease (IHD). However, for Acute Myocardial Infarction with Elevation of the ST Segment (STEMI) mortality rates from IHD remain high, affecting especially developed countries and becoming increasingly problematic in developing countries. In the present study were evaluated the relationship between the rate of IHD mortality and the socioeconomic, demographic and geographic conditions in 399 cities in the state of Paraná, Brazil from 2006 to 2010. Furthermore, the factors related to delays in treatment of patients with STEMI in a tertiary hospital (Reference Interventional Cardiology Center) were taken into account to support a strategic plan for structural and staff changes in a primary hospital, aligning the process with international guidelines. Data on IHD mortality in the state of Parana were obtained from the Mortality Information System (SIM) of the Ministry of Health. The population, socioeconomic and demographic information were provided in digital format by the Brazilian Institute of Geography and Statistics (IBGE). Additional data to assess the delays in the treatment of STEMI patients in a tertiary hospital transported from a primary hospital were obtained from medical records and interviews. We used different methods: Exploratory Spatial Data Analysis (ESDA); and a qualitative and quantitative integrated analysis, including *on-site* observations, interviews, examination of medical records, Qualitative Comparative Analysis (QCA) and Dynamic Systems Modeling (SD). For the treatment of data, were used the softwares GeoDA^{TM}, NVivo version 10.0, statistical R version 2.15.0 and Vensim DSS ® version 5.11. In Exploratory Spatial Data Analysis (ESDA) was found a positive spatial autocorrelation regarding IHD mortality (I = 0.5913, p = 0.001) in Parana state. There was a significant positive spatial association between each of the three socioeconomic and demographic indicators and the rate of IHD mortality: Elderly Population Index (I = 0.3436 p = 0.001), Illiteracy Rate (I = 0.1873 p = 0.001) and Municipal Human Development Index (HDI-M) (I = 0.0900 p = 0.001). In addition, two other indicators showed significant negative association with IHD mortality rate: Adjusted population (I = -0.1216 p = 0.001) and Gross Domestic Product (I = -0.0864 p = 0.001). A positive spatial association was also found between mortality rates from IHD and the geographic distances between city of residence of the patients and their corresponding reference interventional cardiology center (I = 0.3368 p = 0.001). Cities located within Regional Health with reference interventional cardiology center had a significantly lower rate of IHD mortality. The high rate of IHD mortality within the

Regional Health Services was not restricted to socioeconomic and demographic variables and presented positive correlation with the distance between each city and its reference interventional cardiology center. When the factors associated with delays in treatment of patients with STEMI were analyzed from primary hospital, the main causes were categorized into three themes: a) professional b) equipment c) transportation logistics. Qualitative comparative analysis (QCA) confirmed four main stages of delays for the care of patients with STEMI versus 'Door-In to Door-Out' time at the primary hospital. These stages and their average delays in minutes, were: a) First medical contact (from the gateway to the first contact with the nurse and / or physician): 7 minutes; b) Acquisition of electrocardiogram (ECG) and evaluation by a physician: 28 minutes; c) Transmission of ECG and tertiary hospital feedback (reference interventional cardiology center) time: 76 minutes; d) Waiting times for patient transfer: 78 minutes. The baseline Model of System Dynamics confirmed the system's behavior overall delays that occurred and the need for improvements. Moreover, after the validation of the sensitivity analysis, the results suggested that an overall improvement of 40% to 50% in each of these identified phases would reduce the delay. We conclude that geographic factors play a significant role in IHD mortality within the municipalities of the state of Parana and have important policy implications with regard to heart health care networks' geographic distribution. In loco, evaluation of the delay in STEMI patients' treatment suggests that investment in training of health personnel, the reduction of bureaucracy and management guidelines can lead to important improvements decreasing the detected delay.

Keywords: Myocardial Ischemia, Residence Characteristics, Socioeconomic Factors, Epidemiology, Coronary Angioplasty, Health Services Accessibility, Health Services Administration.

Tese elaborada e formatada conforme as normas da ABNT (Capítulo I) e das publicações científicas (Capítulo II):

Artigos científicos publicados no periódico: PLOS ONE. Fator de Impacto: 3.730.

Qualis A - Medicina II

Artigo 1: Regional Disparities in Mortality after Ischemic Heart Disease in a Brazilian State from 2006 to 2010.

Disponível em:

http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0059363

Artigo 2: System Dynamics modeling in the evaluation of delays of care in ST-segment elevation myocardial infarction patients within a tiered health system.

Disponível em:

http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0103577

SUMÁRIO

APRESENTAÇÃO

Sobre o autor e o interesse pelo tema

Atualmente, eu, Luciano de Andrade sou professor assistente na Universidade Estadual do Oeste do Paraná, Brasil. Possuo graduação em Enfermagem pela Universidade de Taubaté - SP. Especialista nas áreas de Vigilância Sanitária, Formação Pedagógica do Ensino Superior e Unidade de Terapia intensiva. Mestre em Enfermagem. Trabalhei por mais de 13 anos nas áreas de Unidades de Terapia Intensiva Geral, Coronariana e em Laboratório de Hemodinâmica em duas importantes cidades brasileiras, São José dos Campos - SP e Foz do Iguaçu - PR. Fui um dos responsáveis pela implantação da Unidade de Terapia Intensiva Coronariana no Hospital Ministro Costa Cavalcanti em Foz do Iguaçu no ano de 2005, sendo hoje um Centro Regional de Referência no atendimento a pacientes com cardiopatia isquêmica. Este tempo dentro do hospital, sobretudo dentro do laboratório de hemodinâmica foi determinante para a minha decisão de estudar a logística do Infarto Agudo do Miocárdio com Supradesnivelamento do Seguimento ST (IAMCSST), pois a grande maioria dos pacientes que chegava ao nosso centro de intervenção coronariana percutânea estava atrasada em relação ao tempo ideal preconizado pelos *guidelines* internacionais da *American Heart Association* e da Sociedade Europeia de Cardiologia. Eu sempre ficava torcendo para que os pacientes que fossem diagnosticados com IAMCSST inicialmente em hospitais primários fossem encaminhados rapidamente para o procedimento de angioplastia transluminal coronariana (ATC) primária, mas infelizmente isso quase sempre não ocorria, e o que me deixava mais chateado era os pacientes encaminhados com mais de 12 horas do início dos sintomas, quando já não tinha tempo para fazer mais nada para o doente, pois não adiantava desobstruir uma artéria e passar sangue numa área em que já estava necrosada, "morta".

É ponto pacífico para todos que as últimas décadas foram marcadas por grandes avanços tecnológicos dentro da cardiologia e, em especial, no tratamento do IAMCSST, devido ao uso da imaginologia para o diagnóstico precoce e o emprego de novas opções terapêuticas, tais como a reperfusão química através do uso de trombolíticos e da reperfusão mecânica através do emprego da angioplastia transluminal coronariana (ATC), que é o procedimento mais utilizado em todo o mundo, com melhores resultados imediatos para os pacientes.

Entretanto, as taxas de morbimortalidade por IAMCSST permanecem altas, devido ao retardo para o inicio do tratamento. Grande parte dos pacientes que chega aos centros de referência em cardiologia intervencionista, já está atrasada em relação ao tempo ideal para o atendimento inicial, devido a fatores sociodemográficos, comportamentais e geográficos, e ainda podem passar por outro tipo de atraso que é o intra-hospitalar, pela falta de estrutura do serviço, ocorrendo atrasos para a realização da ATC primária, fazendo com que o paciente que sobrevive ao IAMCSST evolua com sérios comprometimentos da função miocárdica. Portanto, esses retardos têm graves consequências quando o tratamento não é realizado precocemente e ou realizado de forma tardia.

Todas estas ponderações foram determinantes para que eu realizasse o doutorado abordando diferentes aspectos do tratamento do IAMCSST em dois hospitais com níveis de atendimento primário e terciário no município de Foz do Iguaçu e da mortalidade por DIC nos municípios do Estado do Paraná, respectivamente, através do Programa de Pós Graduação em Ciências da Saúde pela Universidade Estadual de Maringá - PR. Assim como para um desenvolvimento adicional da pesquisa estive na condição de *Research Fellow* na Duke University, Durham NC, USA, no período de março de 2013 a março de 2014, aprofundando as pesquisas a respeito dessa temática.

Assim, os objetivos dessa tese foram especificamente de verificar a relação entre as taxas de mortalidade por DIC e variáveis socioeconômicas, demográficas e geográficas em 399 cidades do estado do Paraná, Brasil, como também demonstrar através de uma modelagem dinâmica de sistemas uma estratégia de organização dentro um hospital primário, onde se poderia atingir um tempo ideal de atendimento do paciente e encaminhá-lo o mais breve possível para um centro de referencia cardiológico. Dessa forma, nestes anos de doutorado procurei me direcionar para as pesquisas em epidemiologia espacial da morbimortalidade das doenças isquêmicas do coração.

1 CAPÍTULO I

1.1 Introdução

A mortalidade por doenças isquêmicas do coração (DIC) é a principal causa de morte em países desenvolvidos e vem afetando cada vez mais países em desenvolvimento (O'GARA et al., 2013). Em 2011, cerca de 7 milhões de pessoas morreram em todo o mundo por DIC, o que representou cerca de 11,2% de todas as mortes globais, sendo considerada a maior causa de óbitos (WHO, 2013). Esta elevada taxa de mortalidade é causada principalmente pela falta de acessibilidade e do atraso pré-hospitalar no tratamento de pacientes que vivem em áreas sem serviços especializados e ou centros de referência em cardiologia intervencionista próximos (ALTER et al., 2003; DE LUCA et al., 2003; WELSH, 2005; FRANCONE et al., 2009).

O Brasil não tem registros de pacientes que procuram os serviços de saúde depois de sintomas sugestivos de DIC, que dentre estas, se destaca o infarto agudo do miocárdio com supradesnivelamento do seguimento ST (IAMCSST) que é a forma mais letal. No entanto, de acordo com o banco de dados nacional de saúde (DATASUS) em 2010 ocorreram 221.898 internações por DIC, com 99.725 mortes (8,77% do total geral de mortes no país), sendo que 37.688 pessoas morreram antes de chegar a um hospital (BRASIL, 2010). Existem poucos estudos no Brasil que abordam os dados demográficos de pacientes que receberam algum tipo de terapia de reperfusão coronariana. Em uma pesquisa com 158 pacientes com IAMCSST no Rio de Janeiro em 2009, destes 67,7% chegaram ao hospital em 180 minutos, 81,3% em 360 minutos e 8,4% chegaram depois de doze horas. Neste estudo, 26% dos pacientes foram tratados com angioplastia transluminal coronariana (ATC) primária, 32% com trombolíticos e 42% com o tratamento clínico otimizado. É importante ressaltar que cerca de 35% dos pacientes com IAMCSST, que deveriam ter recebido a trombólise não receberam neste estudo (SOARES, et al., 2009).

Pesquisas tem demonstrado que este retardo é influenciado por diferentes fatores, considerando-se as características de cada região estudada e do paciente, tais como: geográficos, sociodemográficos, comportamentais, disponibilidade de transporte, estrutura dos serviços hospitalares primários e terciários (GOLDBERG et al., 2002; FRANCO et al., 2008; GIULIANI et al., 2009; KHRAIM e CAREY, 2009).

Estudos ao redor do mundo tem mostrado claramente que a reperfusão mecânica através da Angioplastia Coronariana Transluminal Percutânea (ACTP ou ATC) primária com implante de *stent* é, na atualidade, a melhor opção terapêutica no tratamento do IAMCSST, sendo superior à terapia fibrinolítica (reperfusão química) (WIDIMSKY *et al*., 2000; MATTOS *et al*., 2002; KEELEY *et al*., 2003; NIELSEN *et al*., 2010). No entanto, agilizar ATC primária continua a ser um desafio constante para os especialistas e sistemas de saúde em todo o mundo (JOLLIS et al., 2012; VICTOR et al., 2012; PARK et al., 2012; HERRIN et al., 2011).

Outras pesquisas tem procurado analisar os fatores que predizem o atraso pré-hospitalar até a admisssão no hospital terciário (tempo sintoma-porta), e o atraso intra-hospitalar (tempo entre o primeiro atendimento na sala de emergência até a primeira insuflação do balão no laboratório de hemodinâmica para a recanalização da artéria coronária obstruída; constituindo o tempo porta-balão), e propor estratégias para reduzir o atraso para o tratamento, tanto na fase pré-hospitalar como na intra-hospitalar (MCGINN *et al*., 2005; DE LUCA *et al*., 2005; BRADLEY *et al*., 2006; PERKINS-PORRAS *et al.,* 2009; SANT'ANNA *et al*., 2010).

Mesmo em países desenvolvidos, a maioria dos pacientes com IAMCSST apresenta-se inicialmente em hospitais primários, e diante disso, o transporte rápido de um hospital primário para um hospital terciário (transporte inter-hospitalar) torna-se um grande obstáculo (MAHMOUD et al., 2013; DE LUCA et al., 2008; CARNEIRO et al. 2005).

Conforme orientações da American Hearth Association (AHA) o tempo porta-balão deve ser menor que 90 minutos (AHA, 2009), na atualidade esse tempo serve como um indicador de qualidade para os hospitais terciários. Segundo dados obtidos por Rathore et al. (2009), há uma relação entre um tempo porta-balão mais longo e um maior risco de mortalidade de pacientes com IAMCSST (30'= 3% de mortalidade; 60'= 3,5%; 90'= 4,3%; 120'= 5,6%; 180'= 8,4%). Além disso, o tempo sintoma-balão > 4 horas é um preditor de mortalidade, decorrido 1 ano após o IAMCSST (DE LUCA *et al.,* 2003).

Ainda referindo se aos guidelines internacionais da American Heart Association e da Sociedade Europeia de Cardiologia recomendam uma meta de tempo do primeiro contato médico (FMC) para insuflação do cateter balão (device) em um Centro de referência em cardiologia intervencionista (FMC-to-device) inferior a 120 minutos para pacientes que chamam serviço médico de emergência (EMS) ou auto-presente para um hospital primário (O'GARA et al., 2013; STEG et al., 2012).

Existe uma correlação positiva entre o tempo FMC-to-device e as taxas de mortalidade de pacientes com IAMCSST que é atribuído à demora no atendimento, o que limita os benefícios do ATC primária (JEPH HERRIN et al., 2011; STEG et al., 2012; NIELSEN et al., 2010; LASSEN et al., 2013).

Outro tempo ideal recomendado por estas sociedades é em relação ao tempo de atendimento dentro de um hospital primário é o tempo *Door-In to Door-Out* (DIDO), que significa da porta de entrada até a saída do hospital primário para ser transferido para o centro de referência em cardiologia intervencionista que deve ser de 30 minutos ou menos (O'GARA et al., 2013; STEG et al., 2012).

Esses 30 minutos seriam divididos entre o tempo de entrada do paciente no hospital primário (*Door-In*) até a aquisição de ECG de 12 derivações e avaliação pelo médico de 10 minutos, e um adicional de 20 minutos recomendados para a transmissão de ECG, Feedback do centro de referência em cardiologia intervencionista dando o aceite, até a saída do paciente para a ambulância que realizará a transferência inter-hospitalar (*Door-Out*).

Por esses motivos, nos últimos anos a transferência rápida desses pacientes de hospitais primários ou de suas residências para os hospitais terciários para a realização precoce da ATC primária tem sido um grande e contínuo desafio (CARNEIRO, 2005).

Uma das abordagens para o estudo mais abrangente e ecológico dos fatores relacionados ao atraso pré-hospitalar para o atendimento de pacientes com IAMCSST, ainda pouco explorada internacionalmente, tem sido a análise espacial, que visa à compreensão da influência do território sobre esse fenômeno (BRUNI *et al.* 2008; VANASSE *et al.* 2005; PEREIRA *et al.* 2007).

Atualmente, sabemos que as condições socioeconômicas e demográficas mais baixas, bem como os pacientes que moram em regiões mais distantes tem maior dificuldade de acesso aos serviços de saúde (GUAGLIARDO, 2004; APPARICIO *et al*., 2008; FRANCO *et al*., 2008; GIULIANI *et al*., 2009, MELO et al., 2006; BAJEKAL et al., 2012; PEDNEKAR et al., 2011; JIANG et al., 2012). Estes trabalhos demonstram a importância da análise espacial para determinar as particularidades e diferenças regionais, pertinentes para o planejamento de um sistema de atendimento que atenda às recomendações internacionais referentes aos tempos sintoma-balão, FMC-to-device e porta-balão.

O Brasil ainda apresenta uma escassez de trabalhos sobre fatores pré e intra-hospitalares determinantes do atraso do atendimento dos pacientes com IAMCSST (SOARES 2009). Fatores que contribuem para a morbidade e mortalidade secundária ao DIC tem sido um tema de debate constante. Também tem sido demonstrado que bairros carentes apresentam taxas mais elevadas de mortalidade por DIC (ZORNOFF et al., 2002; CHAIX et al., (2007); TONNE et al., 2005; PEDIGO et al., 2011).

Neste sentido, esta tese visa analisar os tempos pré e intra-hospitalar do paciente com IAMCSST, e suas variáveis, identificando possíveis disparidades relativas ao território, nos serviços primários e na acessibilidade aos centros de referência em cardiologia intervencionista no estado do Paraná. Uma revisão sistemática revelou que apenas 25% dos hospitais dos Estados Unidos têm laboratórios de hemodinâmica e que o transporte de doentes com IAMCSST para estes hospitais, muitas vezes não está dentro do recomendado do período de tempo que é recomendado de 30 minutos, isso em grande parte das vezes devido às variações geográficas e atrasos de diagnóstico (LARSON, HENRY, 2008).

Outra intenção deste estudo foi de avaliar a demora no atendimento de emergência de pacientes com IAMCSST em um hospital primário. Diversos estudos reconhecem os atrasos de pacientes com IAMCSST em hospitais primários, mas não especificam quais variáveis são responsáveis pelos atrasos (TERKELSEN et al., 2010; RATHORE et al., 2006). A avaliação do sistema de saúde comumente reúne algumas das seguintes informações: tempo de triagem, o tempo para a realização do ECG e tempo para transferir o paciente para um centro de cardiologia intervencionista (KHAN et al., 2007; THILO et al., 2013). No entanto, para o nosso conhecimento nenhum outro estudo analisou essas variáveis usando diferentes métodos ou abordagens tais como observações *in loco*, analise qualitativa comparativa (QCA), modelagem da dinâmica de sistemas (SD) (STERMAN, 2000) e análise de sensibilidade (SALTELLI et al., 2000), a fim de realizar uma profunda avaliação do sistema de saúde e identificar as melhorias necessárias, proporcionando com isto um atendimento adequado de acordo com as orientações recomendadas.

1.2 Objetivos

Geral

- Avaliar a relação entre as taxas de mortalidade por doenças isquêmicas do coração e as condições socioeconômicas, demográficas e geográficas no estado do Paraná, Brasil, de 2006 a 2010, como também demonstrar através de modelagem da dinâmica de sistemas um plano estratégico para diminuir os atrasos no atendimento inicial dos pacientes com infarto agudo do miocárdio com supradesnivelamento do seguimento ST dentro de um hospital primário.

Específicos

- Analisar a distribuição espacial das taxas de mortalidade por doenças isquêmicas do coração em 399 cidades do estado do Paraná no período de 2006 a 2010.

- Compreender melhor o sistema de saúde, as variáveis relacionadas aos atrasos no tratamento dos pacientes com infarto agudo do miocárdio com supradesnivelamento do seguimento ST dentro de um hospital primário e identificar as melhorias necessárias.

1.3 Referências

ALTER, D. A. et al. Geography and service supply do not explain socioeconomic gradients in angiography use after acute myocardial infarction. CMAJ 168: 261–264, 2003.

AMERICAN HEART ASSOCIATION. 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update): A Report of the American College of Cardiology Foundation/American Heart With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients Association Task Force on Practice Guidelines. Circulation, Dallas, v.120, p.2271-2306, 2009.

APPARICIO P. et al. Comparing alternative approaches to measuring the geographical accessibility of urban health services: Distance types and aggregation-error issues. International Journal of Health Geographics, Londres, v.7, n.7, 2008.

BAJEKAL M. et al. Analyzing recent socioeconomic trends in coronary heart disease mortality in England, 2000–2007: A population modelling study. PLoS Med 9: e1001237 doi:10.1371/journal.pmed.1001237, 2012.

BRADLEY E. H. et al. Strategies for Reducing the Door-to-Balloon Time in Acute Myocardial Infarction. n engl j med, Massachusetts, v. 355, n. 22, p.2308-2320, 2006.

BRASIL. Ministério da Saúde. DATASUS: Departamento de Informática do SUS. Brasília, Distrito Federal, 2010. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi. exe?sim/cnv/obt10uf.def. Accesso em: 01 Fevereiro de 2012.

BRUNI, M. L.; NOBILIO, L. and UGOLINI, C. The analysis of a cardiological network in a regulated setting: a spatial interaction approach. Health Econ., Connecticut, v.17, p.221–233, 2008.

CARNEIRO, J. K. R. et al. Fibrinólise Imediata ou Transferência para Angioplastia Primária no Infarto Agudo do Miocárdio com Supradesnivelamento do Segmento ST? Quando e Como Transferir? Rev Bras Cardiol Invas., São Paulo, v. 13, n.1, p.32-36, 2005.

CHAIX, B.; ROSVALL, M.; MERLO J. Recent increase of neighborhood socioeconomic effects on ischemic heart disease mortality: a multilevel survival analysis of two large Swedish cohorts. Am J Epidemiol 165: 22–26, 2007.

DE LUCA, G.; BIONDI-ZOCCAI, G.; MARINO, P. Transferring Patients with ST-Segment Elevation Myocardial Infarction for Mechanical Reperfusion: A Meta-Regression Analysis of Randomized Trials. Ann Emerg Med 52:665-676, 2008.

DE LUCA, G. et al. Relation of Interhospital Delay and Mortality in Patients With ST-Seguiment Elevation Myocardial Infarction Transferred for Primary Coronary Angioplasty. J Am Coll Cardiol, California, v.95, n.11, p.1361-1363, 2005.

DE LUCA, G. et al. Symptom-Onset-to-Balloon Time and Mortality in Patients With Acute Myocardial Infarction Treated by Primary. J Am Coll Cardiol, California, v.42, n.6, p.991-997, 2003.

FRANCO, B. et al. Pacientes com infarto agudo do miocárdio e os fatores que interferem na procura por serviço de emergência: implicações para a educação em saúde. Rev. Latino-Am. Enfermagem; Ribeirão Preto, vol.16, n.3, p.414-418, 2008.

FRANCONE, M. et al. Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and microvascular damage in patients with ST- segment elevation myocardial infarction. J Am Coll Cardiol 54: 2145–2153, 2009.

GIULIANI, E. et al. Acute myocardial infarction – from territory to definitive treatment in an Italian province. Journal of Evaluation in Clinical Practice, Londres, Jul, 2009.

GOLDBERG, R. J.; STEG P. G.; SADIQ I. Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). J Am Coll Cardiol, California, v.89, n.7, p.791–796, 2002.

GUAGLIARDO M. F. Spatial accessibility of primary care: concepts, methods and challenges. International Journal of Health Geographics, Londres, v.3, n.3, 2004.

HERRIN, J. et al. National Performance on Door-In to Door-Out Time Among Patients Transferred for Primary Percutaneous Coronary Intervention. Arch Intern Med 171: 1879-1886, 2011.

JIANG, G. et al. Coronary heart disease mortality in China: age, gender, and urban-rural gaps during epidemiological transition. Rev Panam Salud Publica 31: 317–324, 2012.

JOLLIS, J. G. et al. Systems of care for ST-segment-elevation myocardial infarction: a report From the American Heart Association's Mission: Lifeline. Circ Cardiovasc Qual Outcomes 5: 423-428, 2012.

KHAN, S. A. et al. A day in the life of a clinical research coordinator: observations from community practice settings. Study Health Technol Inform 129: 247-51, 2007.

KEELEY, E. C.; BOURA, J. A.; GRINES, C. L. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomized trials. Lancet, New York, v.361, p.13-20, 2003.

KHRAIM, F. M.; CAREY, M. G. Predictors of pre-hospital delay among patients with acute myocardial infarction. Patient Education and Counseling, New York, v.75, n.2, p.155–161, 2009.

LASSEN, J. F.; HANS, E. B; TERKELSEN, C. J. Timely and optimal treatment of patients with STEMI. Nat Rev Cardiol 10: 41–48, 2013.

LARSON, D. M.; HENRY, T. D. Reperfusion options in ST-elevation myocardial infarction patients with expected delays. Curr Cardiol Rep 10: 415-423, 2008.

MAHMOUD, K.D. et al. Interhospital transfer due to failed prehospital diagnosis for primary percutaneous coronary intervention: an observational study on incidence, predictors, and clinical impact. Eur Heart J Acute Cardiovasc Care 2: 166-175, 2013.

MATTOS, L. A. et al. Primary coronary angioplasty in 9,434 patients during acute myocardial infarction: predictors of major in-hospital adverse events from 1996 to 2000 in Brazil. Arq Bras Cardiol, Rio de Janeiro, v.79, n.4, p. 412-418, 2002.

McGINN, A. P.; ROSAMOND, W. D.; GOFF, D. C. Trends in prehospital delay time and use of emergency medical services for acute myocardial infarction: experience in 4 US communities from 1987–2000. Am Heart J, Durham; v.150, n.3, p.392–400, 2005.

MELO, E. C.; CARVALHO, M. S.; TRAVASSOS, C. Spatial distribution of mortality from acute myocardial infarction in the city of Rio de Janeiro, Brazil. Cad Public Health 22: 1225–1236, 2006.

NIELSEN, P. H. et al. Primary Angioplasty Versus Fibrinolysis in Acute Myocardial Infarction Long-Term Follow-Up in the Danish Acute Myocardial Infarction 2 Trial for the DANAMI-2 Investigators. Circulation, Dallas, v.121, n.13, p.1484-1491, 2010.

O'GARA, P. T. et al. ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 61: e78 –140, 2013.

PARK, Y. H. et al. Factors Related to Prehospital Time Delay in Acute ST- Segment Elevation Myocardial Infarction. J Korean Med Sci 27: 864-869, 2012.

PEDNEKAR, M. S.; GUPTA, R.; GUPTA, P. C. Illiteracy, low educational status, and cardiovascular mortality in India. BMC Public Health 11: 567. doi: 10.1186/1471-2458-11-567, 2011.

PEDIGO, A.; ALDRICH, T.; ODOI, A. Neighborhood disparities in stroke and myocardial infarction mortality: a GIS and spatial scan statistics approach. BMC Public Health 11: 644–656, 2011.

PEREIRA, A. et al. Potential generation of geographical inequities by the introduce of primary percutaneous coronary intervention for the management of ST segment elevation myocardial infarction. International Journal of Health Geographics, Londres, v.6, n.43, 2007.

PERKINS-PORRAS, L. et al. Pre-hospital delay in patients with acute coronary syndrome: Factors associated with patient decision time and home-to-hospital delay. Eur J Cardiovasc Nurs, V.8, N.1, P.26-33, 2009.

RATHORE, S. S. et al. Association of door-to-balloon time and mortality in patients admitted to hospital with ST elevation. BMJ, Londres, V. 338:b1807, 2009.

RATHORE, S. S. et al. Regionalization of ST-segment elevation acute coronary syndromes care: putting a national policy in proper perspective. J Am Coll Cardiol 47: 1346-1349, 2006.

SALTELLI, A.; CHAN, K.; SCOTT, M. (eds) Sensitivity Analysis. Wiley Series in Probability and Statistics. New York: John Wiley and Sons, 2000.

SANT'ANNA, F. M. et al. Desfechos Hospitalares em Pacientes Submetidos a Intervenção Coronária Percutânea na Vigência de Síndromes Coronárias Agudas Atendidos em Unidades de Pronto Atendimento (UPAs) – Resultados de um Centro de Cardiologia Terciário. Rev Bras Cardiol Invas, São Paulo, v.18, n.1, p.30-36, 2010.

SOARES, J. S. et al. Tratamento de uma coorte de pacientes com infarto agudo do miocárdio com supradesnivelamento do segmento ST. Arq Bras Cardiol, Rio de Janeiro, vol.92, n.6, p.464-471, 2009.

STEG, P. G. et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J 33: 2569-2619, 2012.

STERMAN, J. D. Business Dynamics: Systems thinking and modeling for a complex world. Boston: Irwin/McGraw-Hill, 2000.

TERKELSEN, C. J. et al. System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA 304: 763-771, 2010.

THILO, C.; BLUTHGEN, A.; SCHEIDT, W. V. Efficacy and limitations of a STEMI network: 3 years of experience within the myocardial infarction network of the region of Augsburg - HERA. Clin Res Cardiol 102: 905–914, 2013.

TONNE, C. et al. Long-term survival after acute myocardial infarction is lower in more deprived neighborhoods. Circulation 111: 3063–3070, 2005.

VANASSE, A. et al. Spatial variation in the management and outcomes of acute coronary syndrome. BMC Cardiovascular Disorders, Copenhage, 5:21, 2005.

VICTOR, S. M. et al. Door-to-balloon: where do we lose time? Single centre experience in India. Indian Heart J 64: 582-587, 2012.

WELSH, P. W. A. It's a matter of time: contemporary pre-hospital management of acute ST elevation myocardial infarction. BMJ 91: 1524–1526, 2005.

WORLD HEALTH ORGANIZATION. The top 10 causes of death (2013). Disponível em: http://who.int/mediacentre/factsheets/fs310/en/index1.html. Accesso em: 2 Outubro 2013.

WIDIMSKÝ, P. et al. Multicenter randomized trial comparing transport to primary angioplasty vs. mmediate thrombolysis vs. combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE Study. Eur Heart J, Oxford, v.21, n.10, p.823-831, 2000.

ZORNOFF, L. A. M. et al. Perfil clínico, preditores de mortalidade e tratamento de pacientes após infarto agudo do miocárdio, em hospital terciário universitário. Arq Bras Cardiol 78: 396–400, 2002.

2 CAPÍTULO II

2.1 Artigo 1: Regional Disparities in Mortality after Ischemic Heart Disease in a Brazilian State from 2006 to 2010.

Autores: Luciano de Andrade[1,2], Vanessa Zanini[1], Adelia Portero Batilana[2], Elias Cesar Araújo de Carvalho[2], Ricardo Pietrobon[3], Oscar Kenji Nihei[1], **Maria Dalva de Barros Carvalho**[4]

1. Department of Nursing, State University of the West of Parana, Foz do Iguaçu, Parana, Brazil.
2. Research on Research Group, Duke University Health System, Durham, North Carolina, United States of America.
3. Department of Surgery, Duke University Health System, Durham, North Carolina, United States of America.
4. Department of Medicine, State University of Maringa, Maringa, Parana, Brazil.

Periódico: PLoS ONE. Fator de Impacto: 3.730. Qualis A - Medicina II

Status da Publicação: Publicado em 19 de março de 2013. PLoS ONE 8(3): e59363. doi:10.1371/journal.pone.0059363

Abstract

Background - High technology in the field of interventional cardiology applied in tertiary hospitals has brought enormous benefits in the treatment of ischemic heart disease (IHD). However, IHD mortality rates remain high. We analyzed the relationship between IHD mortality rate and the socioeconomic, demographic, and geographic conditions in 399 cities in Parana state, Brazil, from 2006 to 2010.

Methods and Results - Data were obtained from the Mortality Information System and the Brazilian Institute of Geography and Statistics and evaluated through Exploratory Spatial Data Analysis. GeoDa™ was used to analyze 29.351 deaths across 399 cities. We found a positive spatial autocorrelation regarding IHD mortality ($I = 0.5913$, $p = 0.001$). There was a significant positive association between each of three socioeconomic and demographic indicators and IHD mortality rate: Population Elderly Index ($I = 0.3436$), Illiteracy Rate ($I = 0.1873$) and City Development Index ($I = 0.0900$). In addition, two indicators presented significant negative association with IHD mortality rate: Adjusted Population Size ($I = -0.1216$) and Gross Domestic Product ($I = -0.0864$). We also found a positive association between IHD mortality rates and the geographic distances between patients' city of residence and their corresponding regional referral centers in interventional cardiology ($I = 0.3368$). Cities located within Regional Health Units with Reference Interventional Cardiology Center presented a significantly lower average specific mortality rate by IHD. The high mortality rate by IHD within the Regional Health Units was not restricted to socioeconomic and demographic variables, but dependent on the distance between each city and their reference interventional cardiology center.

Conclusions - We conclude that geographic factors play a significant role in IHD mortality within cities. These findings have important policy implications regarding the geographic distribution of cardiac health care networks in Latin America and in other emerging countries.

Introduction

Ischemic Heart Disease (IHD) causes 12.8% of all deaths in both developed and developing countries, making it the most prevalent cause of death in these locations [1]. This high mortality percentage is mainly caused by pre-hospital delays in the treatment of patients living in areas without specialized services or nearby interventional cardiology units [2-5]. Although Brazil does not have exact estimates of individuals seeking health services after symptoms suggestive of IHD, according to a national healthcare database in 2010 there were 221,898 hospital admissions for IHD, with 99,725 deaths (8.77% of the overall total of deaths in the country), with 37,688 people dying before reaching a hospital [6]. In developing countries, patients with IHD rarely receive immediate treatment, and as the prevalence of this disease increases, the mortality rate due to IHD is likely to proportionally increase [7].

In Brazil, since 1988 an Unified Health System (SUS) has been implemented with the aim of providing a universal and equitable access to all levels of health care services to the population [8]. Although different health care indicators have clearly improved since its implementation, an example being an overall decrease in mortality secondary to cardiovascular diseases, several of its organizational features have imposed barriers in delivering adequate healthcare to patients with ischemic heart diseases [8-9]. Some of these current characteristics include a focus on primary and acute care rather than prevention and education, the problematic provision of secondary care, poor supply of cardiologists and diagnostic examinations, underfunded public service system, and socioeconomic inequity between the coverage of public and private healthcare systems [8-9].

We currently know that lower socioeconomic and demographic conditions lead to higher IHD death rates [10-16], as well as that long distances from the IHD event and the reference cardiology center is a risk factor for IHD [3]. Factors contributing to morbidity and mortality secondary to IHD have been a topic of constant debate. Patients who are poor, with low educational level, or residing in geographical locations distant from large urban centers all have problems accessing health care services [3-5,17-21]. It has also been demonstrated that deprived neighborhoods present higher rates of mortality due to IHD [22-25]. Studies have investigated whether making reference cardiology services more accessible would ultimately reduce mortality rates [26-29]. Despite the extensive information about isolated factors, to our knowledge the interplay among distance from a reference cardiology center, socioeconomic/demographic conditions, and IHD-specific mortality rate have not been evaluated in developing countries.

Analyzing the connection among these factors was therefore the main aim of our study, specifically focusing on the socioeconomic, demographic and geographic causes of IHD mortality in 399 cities in Parana state, Brazil.

Methods

Ethics

Our study was approved by the Institutional Review Board (Comitê de Ética em Pesquisa Envolvendo Seres Humanos) of the State University of the West of Parana (UNIOESTE), Brazil.

Study Design and Sample Site

This is an observational, cross-sectional, ecological study using spatial analysis techniques based on mortality data from 2006 to 2010 in Parana state, Brazil.

Parana state is located in Southern Brazil, occupying an area of 199,880 km^2, with latitude coordinates 22°30′58″ and 26°43′00″ and longitude coordinates 48°05′37″ and 54°37′08″ (Figure 1A) [30]. According to the 2010 Brazilian Census, Parana state presented 10,439,601 inhabitants, most of them (85.3%) living in urban area, and making it the 6th most populated in Brazil (5.47% of the total population) [31]. The Elderly Index (population above 65 years old) of Parana state was 7.6% in 2009, and therefore similar to the Brazilian average of 7.4% [31-32]. Parana state presented a Gross Domestic Product (GDP) occupying the 5th rank in the country, representing 5.76% in 2010 [32] and a Human Development Index (HDI) of 0.846 (6th of the country). This value is above the Brazilian average HDI of 0.816 [33].

Parana state has 399 cities administratively grouped into 22 Regional Health Units responsible for health care management (Figure 1B) [34].

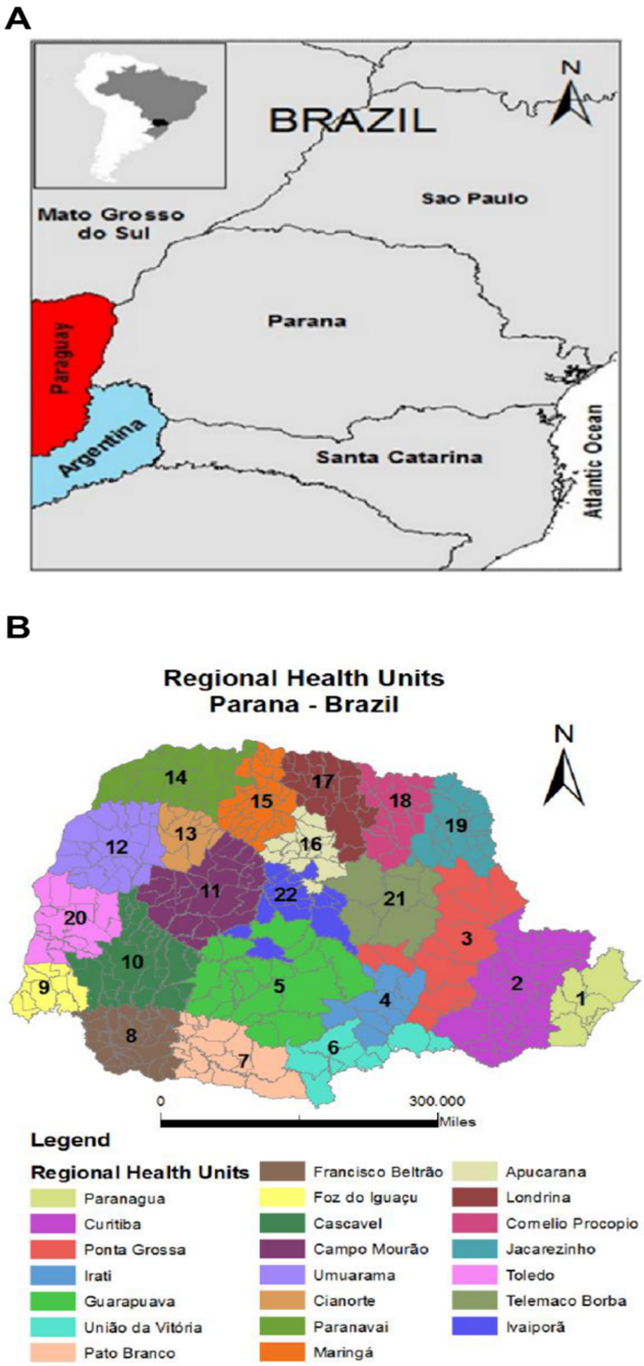

Figure 1. Maps.

A) Map of the Parana state. Source: Geographic Atlas of the Parana state, 2011 [30]. **B)** Regional Health Units in Parana state. Source: Secretary of Health of Parana state (BR), 2012 [34].

Data Sources

We obtained data from the Mortality Information System of the Ministry of Health (SIM/MS) [35] and from the Brazilian Institute of Geography and Statistics (IBGE) [31]. We used population data from the IBGE to calculate the population per city. It was calculated by considering the total number of citizens over age 20 in each city throughout the period and dividing the result by the period of study in years. Hence, we obtained the average number of inhabitants per city for the years 2006 to 2010. The social and economic data of the period of 2009-2010 regarding cities were available online at IBGE and the Parana Institute of Economic and Social Development (IPARDES) [31-32].

The map with the geo-referenced base of Parana state, entitled Political-Administrative Division of Parana State in the Year 2010, was made available for free on the Internet in shapefile (SHP) and online through of the Institute of Cartography and Land Geosciences [36].

To assemble a death profile related to IHD, we evaluated socioeconomic and demographic factors according to patients' city of residence. We analyzed five socioeconomic and demographic indicators for each city: Population Elderly Index (ratio between the population over 65 years old and the population under 15 years of age) [31]; Illiteracy Rate (percentage of illiterate people 15 years of age and older with less than three years of formal education) [31]; Gross Domestic Product per capita [31-32]; City Development Index (measures the performance of management and public actions of the city, considering three areas: employment and income, health, and education) [32]; Adjusted Population Size (city number of individuals over 20 years old - average considering the period of 2006 to 2010) [31]. We selected IHD cases using the International Statistical Classification of Diseases and Related Health Problems -10th Revision (ICD-10) [37], specifically as codes I20 to I25. We used an empirical Bayes spatial estimator to minimize variance in mortality rates by city, due to the variability associated with rates expressing the likelihood of a given event when the rate and population are both small. In other words, this combination might cause random fluctuations. The global empirical Bayes estimator calculates a weighted average of the gross rate of the locality and the region's global rate (ratio between the total number of cases and the total population) [38]. Specific mortality rates per 100,000 inhabitants were obtained for each of the 399 cities in Parana state.

Spatial Analysis

We analyzed spatial data grouped by geographic areas (polygons), to evaluate whether the presence of spatial aggregation was associated with socioeconomic, demographic, and/or geographic variables [39-40]. We used Exploratory Spatial Data Analysis (ESDA) and the software package GeoDa™ version 0.9.5-i (Spatial Analysis Laboratory, University of Illinois, Urbana-Champaign, IL, USA) to determine measures of global spatial autocorrelation and local spatial autocorrelation [41]. To evaluate the existence of spatial autocorrelation, we defined a spatial weight matrix - *W*. This matrix allows for the measurement of non-random association between the value of a variable observed in a given geographical unit with the value of variables observed in neighboring units. Furthermore, we used the binary matrix-type Queen, which attributes a value of one for neighbors in any spatial location within the analyzed region [42].

We calculated spatial autocorrelation evaluating mortality rates, socioeconomic, and demographic indicators for each city using the (I) Global Moran index for univariate and bivariate analysis [42-43]. This index measures both the spatial autocorrelation and the weighted neighborhood matrix, indicating that the IHD mortality rates of a given region might be similar to those of neighboring regions. Values of Moran's I vary between −1 and +1. Values greater or smaller than the expected value of Moran's I [E (I) = −1/(N - 1)] indicate a positive or negative autocorrelation, respectively. If the value of Moran's I is 0 (zero), the region is considered to have spatial independence [42-43].

Moran's I values between 0 and +1 indicate positive spatial association (direct). This indicates that regions with high Moran's I values for the variable in question are surrounded by regions which also have high variable values (high/high). Similarly, regions with low variable values are surrounded by neighbors who also have low variable values (low/low). Negative values of Moran's I (from 0 to −1) represent negative spatial association (reverse). Therefore, regions with high Moran's I values are surrounded by regions with low variable values, while regions with low Moran's I variable values are surrounded by neighbors with high variable values [39,42-43].

A limitation of Global Moran's I is that it can hide local patterns of spatial association since negative values of Moran's I do not necessarily indicate the absence of spatial correlation at the local level [43]. To identify patterns of spatial association that were significant and specific to each analyzed area, we used local indicators of spatial association (LISA). LISA allowed us to identify the existence of spatial clusters, or sites with high or low values for the analyzed variables, ultimately determining regions that can contribute to spatial autocorrelation [42]. Choropleth maps were generated to investigate the presence of mortality rate clusters. These values were divided by class intervals and aggregated into tracks of standard deviation in relation to average. Coefficients of global and local spatial autocorrelation were considered significant at $p<0.05$. These coefficients were analyzed by pseudo significance levels. In other words, they were confirmed through the redistribution of simulated values and examined areas using permutation tests [44].

We used Google Maps [45] featuring satellite images to determine distances between cities and the Reference Interventional Cardiology Centers. We used the Mann Whitney test for independent samples to compare the specific mortality rates of cities belonging to Regional Health Units with reference services to cities with Regional Health Units that lack reference services. For data processing, we used GraphPad Prism v. 5.0. (GraphPad Software, Inc., San Diego, CA, USA).

Results

During the period covered by our study there were 29,351 deaths due to IHD, mainly among men (60.30%), between 60 and 79 years of age (53.07%), white (85.74%), married (53.55%), and with an educational level of up to three years in school (58.29%). Most deaths occurred in the morning (28.79%), followed by the afternoon (26.08%).

Regarding spatial patterns of death distribution from IHD in the 399 cities in Parana state, on average 99.74/100,000 inhabitants over the age of 20 died from IHD. Out of 399 cities, most cities (45.40%) presented IHD mortality rates between 69.04 and 99.74 per 100,000 inhabitants, these cities being located mainly in east, southeast, central south and south-west regions of the Parana state. Rates above 134.43/100,000 inhabitants were identified in 60 cities located mainly in northeast, north, central north, and northwest regions (Figure 2A).

Univariate analysis (Figure 2B) regarding specific mortality rates by IHD indicated the existence of a positive spatial autocorrelation ($I = 0.5913$, $p = 0.001$), demonstrating that cities with high mortality rates by IHD tend to be surrounded by neighboring towns with similar values, so also with high mortality rates by IHD. LISA analysis allowed the detection of clusters based on similarities between cities (Figure 2C). We could therefore classify these groups of cities using the following categories: high-high, i.e., cities with high rates of death from IHD with surrounding neighbors also displaying high rates of death from IHD; low-low, i.e., cities with low death rates from IHD with neighbors with low IHD mortality rates; and low-high, i.e., cities with low death rates from IHD with neighbors with high IHD mortality rates. Our analysis did not demonstrate any significant high-low type of cluster formation, i.e., cities with high rates of death from IHD with neighbors with low IHD mortality rates (Figure 2C).

We identified six high-high type of clusters which involved cities located in the following Regional Health Units: 1) 10th (four cities), 11th (two cities), 12th (eight cities), 20th (three cities); 2) 12th (three cities), 14th (eight cities); 3) 14th (two cities), 15th (five cities), 17th (five cities); 4) 18th (seven cities), 19th (eleven cities); 5) 11th (two cities); 6) 6th (three cities).

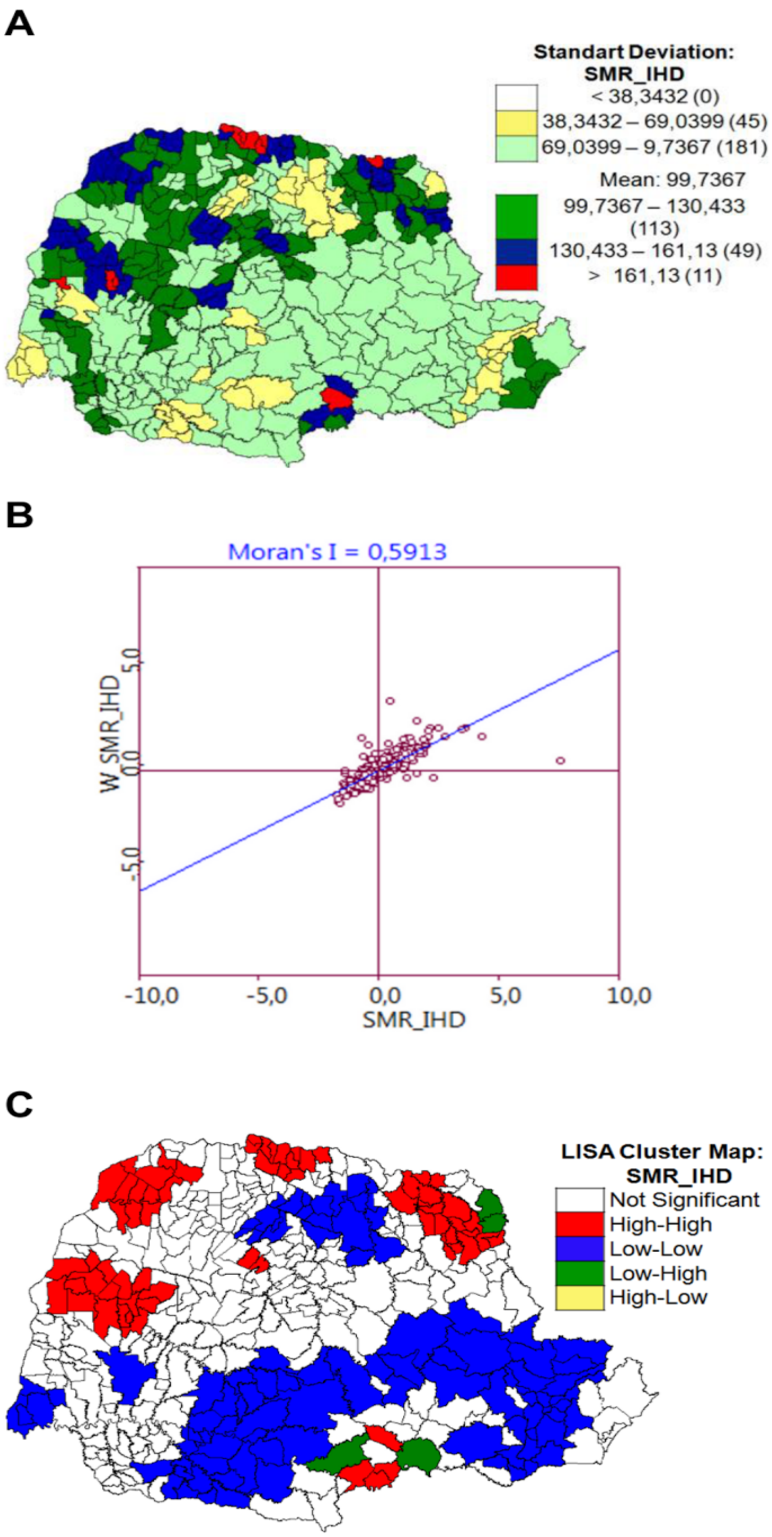

Figure 2. Exploratory spatial analysis of specific mortality rate by IHD in state of Parana, Brazil, 2006–2010.

A) Spatial distribution of cities' specific mortality rate (SMR) by IHD, with ranges of standard deviation from the average for the delimitation of class intervals; the number of cities is in parenthesis. B) Moran's diagram of dispersion (univariate analysis) of specific mortality rate (SMR) by IHD (X axis: city's SMR; Y axis: weighted average SMR of the neighbor cities). C) LISA univariate analysis: cluster formation according to specific mortality rate (SMR) by IHD (Types of cluster: high-high; low-low; low-high, high-low).

Figure 3 demonstrates that all five socioeconomic and demographic indicators used for analysis in this study were significantly associated with the specific mortality rate by IHD ($p<0.05$). The correlation was positive for the Population Elderly Index (I = 0.3436, P = 0.001), Illiteracy Rate (I = 0.1873, p = 0.001) and City Development Index (I = 0.0900, P = 0.001). The positive correlations indicated that cities with a high level of these indicators were surrounded by cities with high specific mortality rates by IHD. However, specific mortality rates by IHD correlated negatively with Gross Domestic Product (I = - 0.0864, P = 0.001) and Adjusted Population Size (I = - 0.1216, P = 0.001), indicating that cities with high values of Gross Domestic Product and/or Population Size were surrounded by cities with low specific rates of mortality by IHD and vice versa. Stated in a different way, socioeconomic and demographic factors significantly influence the number of deaths by IHD in these cities and thus may be related with the observed cities clustering pattern.

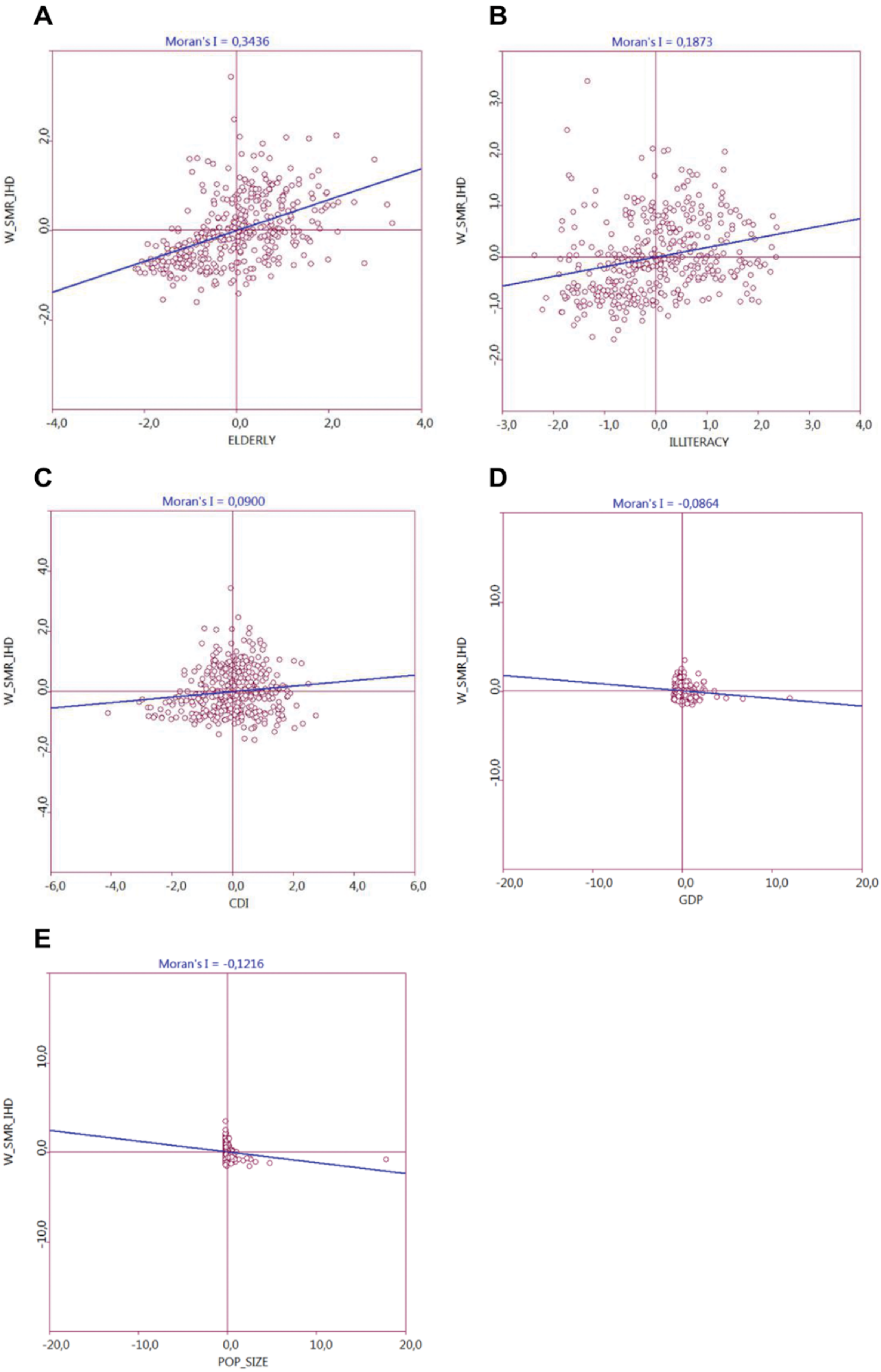
A
Moran's I = 0,3436
W_SMR_IHD
ELDERLY
B
Moran's I = 0,1873
W_SMR_IHD
ILLITERACY
C
Moran's I = 0,0900
W_SMR_IHD
CDI
D
Moran's I = -0,0864
W_SMR_IHD
GDP
E
Moran's I = -0,1216
W_SMR_IHD
POP_SIZE

Figure 3. Moran's diagram of dispersion (bivariate analysis).
Analysis of socioeconomic or demographics variables of the city of residence of the patient (X axis) and the weighted average specific mortality rate by IHD of the neighbor cities (Y axis). A) Population Elderly Index. B) Illiteracy Rate. C) City Development Index (CDI). D) Gross Domestic Product (GDP). E) Adjusted Population Size.

In addition to these parameters, we also investigated the possible influence of the Reference Interventional Cardiology Centers within Regional Health Units in the specific mortality rate by IHD in the cities. We compared the specific mortality rate by IHD of cities located within Regional Health Units with Reference Interventional Cardiology Centers (n = 200) with those from the cities located in Regional Health Units without Reference Interventional Cardiology Centers (n = 199). The cities located within Regional Health Units with Reference Interventional Cardiology Centers presented a significantly lower average specific mortality rate by IHD (90.46±29.92 deaths/100.000 inhabitants) in comparison with the group of cities located in Regional Health Units without Reference Interventional Cardiology Centers (109.1±28.59 deaths/100.000 inhabitants) (Figure 4).

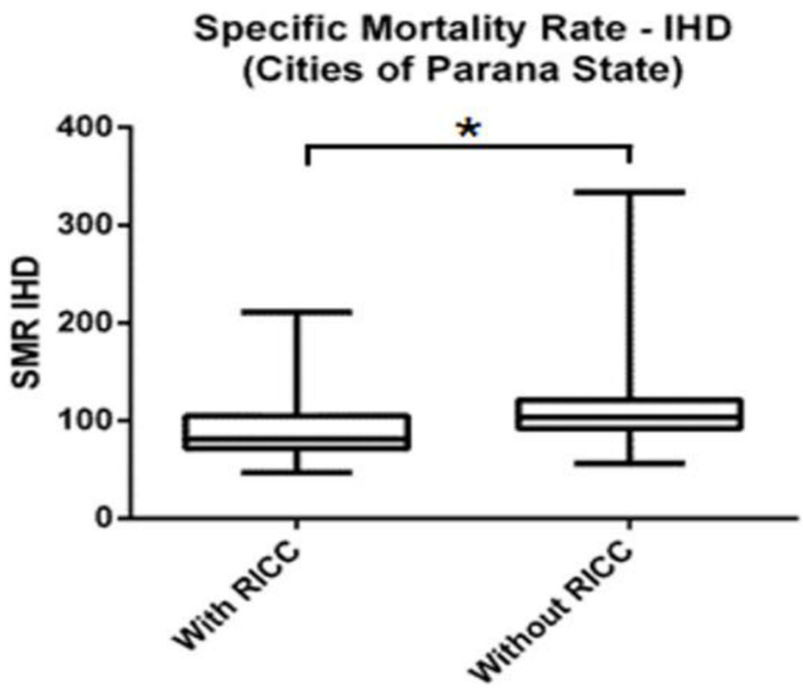

Figure 4. Boxplot comparing specific mortality rate by IHD among cities with and without Reference Interventional Cardiology Centers (RICC).
* p<0.001.

We further analyzed the influence of the existence of Reference Interventional Cardiology Centers on the specific mortality rate by IHD among neighbor cities. Figure 5A presents a map displaying the distribution of Reference Interventional Cardiology Centers in Parana state and their respective area of influence according to the current state's regional master plan. This plan guides the healthcare spatial regionalization process, aiming at the reduction of social and territorial inequalities as well as the improved access to the population at all socioeconomic levels [46]. The univariate global Moran analysis indicated that the geographical distances between the cities of residence to the Reference Interventional Cardiology Centers showed strong positive spatial autocorrelation ($I = 0.7142$; $p = 0.001$), indicating that the cities that are located far from their Reference Interventional Cardiology Center present neighbor cities that also are located far from their Reference Center. Using the bivariate Global Moran analysis, the geographical distance of the patients city of residence to Reference Interventional Cardiology Center also showed a positive spatial autocorrelation with the neighbor cities specific mortality rate by IHD ($I = 0.3368$; $p = 0.001$).

This positive correlation demonstrated that cities far from their respective Reference Interventional Cardiology Center more likely present neighbor cities with higher specific mortality rate by IHD (Figure 5B). The bivariate LISA analysis (Figure 5C) indicated the formation of different types of geographical city clustering according to Reference Interventional Cardiology Center distance and specific mortality rate by IHD. The high-high type of clustering was found mainly involving cities of the 6^{th}, 11^{th}, 14^{th} and 19^{th} Regional Health Units without Reference Interventional Cardiology Center and the 10^{th} and 15^{th} (north region) Regional Health Units with Reference Interventional Cardiology Center.

These data indicated that the cities far from Reference Interventional Cardiology Center were surrounded by cities with high specific mortality rate by IHD. Since our data indicated that these cities are located in high-high type of cluster, these data indicated that the patients that live in cities far from the Reference Interventional Cardiology Center present higher probability to die due to IHD. The cities within 10th and 15^{th} Regional Health Units presented a high-high profile even presenting a Reference Interventional Cardiology Center, possibly due to the fact that these Regional Health Units present great number of cities (25 and 30, respectively), what may increase the distance of the Regional Health Units peripheral cities to the Reference Interventional Cardiology Center. In contrast, the low-low type of clustering involved cities mainly of the 2^{th}, 3^{th}, 5^{th}, 7^{th}, 9^{th}, 15^{th}, 16^{th}, 17^{th} Regional Health Units, all with Reference Interventional Cardiology Center, and the 4^{th} Regional Health Unit, without Reference Interventional Cardiology Center.

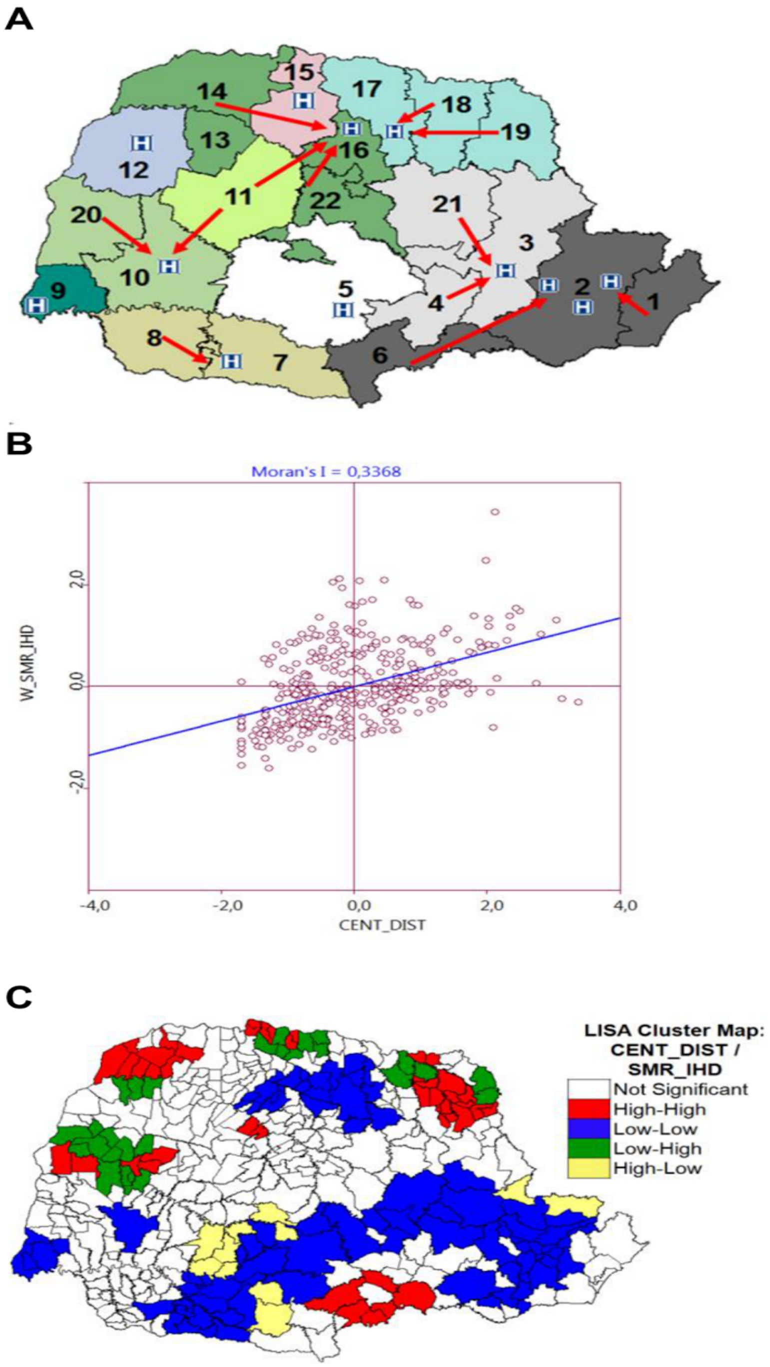

Figure 5. Spatial analysis of distance of the Reference Interventional Cardiology Centers and the mortality by IHD.
A) Map with the approximate localization of the services of high complexity in cardiovascular and interventional surgery in Parana state, Brazil (arrows: indicate the localization of the Reference Interventional Cardiology Centers where the neighbor cities direct the IHD patient [Adapted from: Regional Master Plan/SESA, 2009]) [46]. **B)** Moran's diagram of dispersion showing the relationship between the distance of the Reference Interventional Cardiology Centers to the patients residence city (X axis) and the weighted average of the specific mortality rate (SMR) by IHD of the neighbor cities (Y axis). **C)** LISA bivariate analysis: cluster formation according to the distance of the Reference Interventional Cardiology Center to the patients city of residence and the weighted average specific mortality rate (SMR) by IHD data of the respective neighbor cities (cluster type: high-high; low-low; low-high, high-low).

Since the cities within Regional Health Units with a Reference Interventional Cardiology Center (Group 1) presented a lower average specific mortality rate by IHD when compared with cities of the Group 2 without a Reference Interventional Cardiology Center, we also analyzed the association between socioeconomic and demographic variables of these two groups of cities with their respective mortality rates by IHD (Table 1). This analysis indicated that both the Population Elderly Index and the City Development Index presented a positive association with specific mortality rate by IHD in both groups. However, the cities of Group 1 presented a greater Global Moran's I coefficients in comparison to Group 2. The Illiteracy rate had a positive association in group 1 and a non-significant association in group 2. The Gross Domestic Product and Adjusted Population Size presented significant negative association with specific IHD mortality rate only in the cities of Group 1 but not in group 2. The parameter “Geographical distance to Reference Interventional Cardiology Center” was positively associated with the mortality rates for IHD in both groups. However, the higher Global Moran's I coefficient presented by Group 2 in comparison to Group 1, indicated that when the distance is greater between the cities of residence of the patients that died from IHD and the headquarter city of the Reference Center Interventional Cardiology, higher is the mortality rates for IHD.

Overall, these data indicate a decrease in the impact of socioeconomic and demographic parameters on mortality rates for IHD in group 2 compared with group 1, possibly due to the increased distance between the place of residence of the patient and the respective Reference Interventional Cardiology Center, demonstrating that the absence of these reference centers at a regional level can determine a particular pattern of mortality rates for IHD and greater inequality in access to referral centers for interventional cardiology (Table 1).

Table 1. Global Moran's I coefficient of the IHD specific mortality rate and geographic, demographic and socioeconomic indicators of the cities localized within Regional Health Units with or without Reference Interventional Cardiology Center (RICC).

Indicators	Regional Health Units with a RICC		Regional Health Units without a RICC	
	I	*p value*	*I*	*p value*
Population Elderly Index	0.4779	0.001	0.0872	0.022
Illiteracy Rate	0.3439	0.001	−0.0125	0.434
Gross Domestic Product	−0.1000	0.001	−0.0187	0.388
City Development Index	0.0965	0.025	0.0709	0.048
Adjusted Population Size	−0.1196	0.001	−0.0420	0.217
Geographical distance to RICC	0.1944	0.001	0.2939	0.001

Discussion

To the best of our knowledge, in developing countries, this is the first study to assess the interaction between distance from a center of reference in cardiology, the socioeconomic and demographic conditions and specific mortality rates by IHD. The present study showed a significant univariate positive spatial association for IHD specific mortality rate in the Parana state, i.e., cities with high mortality rates of IHD were surrounded by cities with high mortality rates of IHD, determining a high-high pattern of clustering. Low-low and high-low types of clustering were also observed. Furthermore, there was an association between different socioeconomic, demographic and geographic indicators and higher IHD specific mortality rate; the Population Elderly Index, distance to a Reference Interventional Cardiology Center, City Development Index, and Illiteracy Rate, all were positively associated. In contrast, the Adjusted Population Size and Gross Domestic Product were negatively associated. These data indicate that geographical distribution of Reference Interventional Cardiology Centers as well as socioeconomic and demographic characteristics of the cities influences specific mortality rate by IHD.

Corroborating our findings, other studies have shown that parameters of low levels of socioeconomic development and unfavorable demographic features increase mortality rates by IHD when combined with increased distance from a treatment center [10, 47-51]. These studies highlight the importance of social, environmental and geospatial factors in the mortality rate by IHD, which may interact with other factors such as genetic susceptibility, behavioral variables and other biological attributes.

In our study, the variables related with higher mortality rates by IHD were identified using a bivariate analysis indicated by the Moran's I coefficient. Regression analysis or similar approaches have been performed in other studies evaluating risk factors for IHD in different countries such as Sweden [23], United States of America (USA) [15,25,52] and China [16]. A study performed in India has evaluated the risk factors for IHD mortality utilizing hazard regression modelling [14]. In these studies, risk factors identified as negatively associated with IHD mortality rates included education [14,15,25], income [15,23,25], race (black/hispanic) [15] and urban areas [25] while the variables positively related were sex (male) [15,16] and age [15,16].

Data obtained by these studies corroborate our findings. The associations observed in the our work might therefore be explained as follows: 1) Low Gross Domestic Product and Illiteracy may decrease patients' condition to seek adequate treatment and/or decrease the comprehension of their own health condition [14,53]; 2) High Elderly Index may be associated with improvement in the living conditions of the population. However, the increase in life expectancy leads to increased susceptibility to the development of chronic degenerative diseases, not only determined by aging, but also by environmental factors such as life style, physical inactivity, poor nutrition, housing conditions, labor and difficult access to health service [54]; 3) Low Adjusted Population Size may be related with a city's lower capacity to improve local healthcare system since the municipalities with small population size may present scarcity of resources, lack of investment in transport, equipment and trained professionals [55]; 4) Greater distance to a Reference Interventional Cardiology Center is related with increased time delay and difficulty to access an adequate treatment to the patient; 5) Most of the municipalities of Parana state presents a medium to high City Development Index [32]. Since our results indicate a positive association between IHD specific mortality rate and city development index, city development levels may be related with an increase in the population's susceptibility to develop ischemic heart disease. Factors involved could be a more stressful lifestyle, inadequate nutrition, pollution, unemployment and violence, with the absence of a suitably established tertiary cardiovascular health care system [48,56].

When the regional hospitals with interventional cardiology centers were considered, only 10 of the 22 Regional Health Units have referral centers for interventional cardiology. We found that cities belonging to 12 Regional Health Units without a referral center for interventional cardiology have higher average rates of IHD mortality than cities that belong to Regional Health Units with these centers. These findings can be explained by the long distances that patients had to travel between their city of residence and the Reference

Interventional Cardiology Center [18,49,57,58]. In Parana state, cities located within the Regional Health Units with Reference Interventional Cardiology Center present shorter distances to the respective regional referral hospitals (average of 36.99 miles) while cities located within Regional Health Units without Reference Interventional Cardiology Center present higher distances to the respective regional referral hospitals (average of 86.81 miles).

Our results indicate that the high mortality rate from IHD within the Regional Health Units are not restricted to socioeconomic and demographic variables, but dependent on the distance of each city to the Reference Interventional Cardiology Center. The absence of a Reference Interventional Cardiology Center within the Regional Health Unit may therefore be an important independent predictor of IHD mortality, in tandem with the importance of socioeconomic and demographic variables.

Other studies have shown that higher rates of IHD mortality are frequently associated with greater distances from a patient's place of residence to a major reference interventional cardiology center which may increase the time delay to the specialized treatment initiation or even precluding it [2,13,47-49, 59]. However, one study analyzing the accessibility of cardiac interventional services in Alabama and Mississippi (USA) has demonstrated that the distance factor may not influence IHD mortality rate [52]. To a broader comprehension of these differences it is important to notice that the United States presented on average one Reference Interventional Cardiology Center per 585,135 inhabitants, and Alabama and Mississippi presented one Reference Interventional Cardiology Center per 434,521 and 593,459 inhabitants, respectively [60]. The state of Parana, in Brazil, presents approximately one Reference Interventional Cardiology Center per 855,561 inhabitants, which is comparatively almost half the quantity of Reference Interventional Cardiology Center that Alabama State presents.

Thus, the importance of the distance factor on IHD specific mortality rate may be influenced by the number of Reference Interventional Cardiology Center established regionally, which may also influence the entire health care network organization and the assistance that patients will receive, since both are influenced by the nearby number of available tertiary referral centers. In countries like the United States and Italy, the number of Reference Interventional Cardiology Center per capita is higher than in Brazil, allowing patients to be referred to specialized services closer to their place of residence, increasing survival rates and decreasing the patients' hospitalization duration due to early admission [52,60, 61].

Different studies have indicated that other factors that can decrease the delay time of the treatment of patients with IHD are the pre-hospital diagnosis using established protocols, and the direct referral for primary percutaneous coronary intervention in a Reference Interventional Cardiology Center, reducing the impact of the distance on the mortality rate of such patients[62,63].

In Brazil as a whole and in Parana state, the main health care system prevalent in the country is based on a unified and universal access oriented system which directs the patients to services located in large urban centers when the case demands a more specialized attention [64].

However, as this study indicates, these specialized services are not present in all Regional Health Units. Thus, depending on the geographic location of patients suffering from IHD, which need immediate attention, these patients will be referred to a hospital closer to their primary residence that does not have a specialized service, and from there they will be transferred to a Reference Interventional Cardiology Center. This later scenario increases the distance that the patient must travel and thus delays the adequate treatment initiation.

Previous studies have indicated that the established universal policies of access to health system adopted by different countries does not necessarily lead a real universal access to all groups of the population and equally to all types of specialized services due to difficulties related with distance, availability of general practitioners, among other factors [65-67]. The solution to this problem could be the creation of new tertiary cardiology reference services. The establishment of an efficient network of specialized cardiology centers, however, will require trained nurses and doctors, equipment, supplies, and an adequate emergency service integrated with a pre-hospital diagnosis protocol [62,68].

In the current healthcare scenario in Brazil, problems have been identified regarding the accessibility and equity offered by the different health care levels of assistance [8,9], particularly concerning the care provided to patients with IHD. These problems seem to be related with a lack of adequate attention and orientation for patients with risk factors for IHD in primary health care system and a deficient provision of secondary care, the latter generating lack of access to specialized care. As a consequence, untreated patients may develop an acute heart disorder and are received in primary hospitals without the adequate structure and trained health professionals, ultimately being transferred to tertiary hospitals distant from their residence.

In 2011 the Brazilian government has created the “Emergency Care Network - Acute Myocardial Infarction Line” aiming at integrating a hierarchical and regulated network of different emergency services specifically to serve patients with ischemic heart disease [69].

The availability of an efficient Mobile Emergency Care Service is important in allowing fast dispatch, pre-hospital diagnosis, and ultimately treatment for these patients. In Brazil, a nationwide implementation initiative for an Urgency Mobile Care Service (SAMU) has been in place since 2008 [70]. The success of its implantation in most of the country represents a key element to provide proper care for patients with ischemic heart diseases. However, as our results indicate, the implementation of new Reference Interventional Cardiology Centers in Parana state is fundamental to decrease the distance between patients’ residence and the tertiary hospital. This would likely reduce the delay in treating patients with IHD, also decreasing the corresponding mortality rate secondary to IHD.

One of the possible limitations of the study was the use of secondary data, which may present under-notifications of IHD death. However, the data quality of the Mortality Information System obtained from the website of the Ministry of Health has increased its reliability [71], even so we confirmed our data completeness (number of IHD deaths cases) with the Epidemiological Surveillance System of Health Department of the State of Parana. Another limitation of the study was the fact that we do not considered in our study the existent structure of the Reference Interventional Cardiology Centers, which may be an contributing factor regarding the delay to treatment initiation. These include factors such as the number of available beds in Coronary and Chest Pain Units as well as the number of cardiologists, catheterization laboratory with a team of hemodynamicists and nurses available 24 hours/day.

Our work indicated that the number of Reference Interventional Cardiology Centers in the state of Parana, Brazil, is not sufficient. We therefore suggest that the allocation of new cardiology centers is a priority, especially in the 12 cities constituting Regional Health Units headquarters without Reference Interventional Cardiology Centers. Additionally, there is a need to improve the primary care provided by hospitals in cities where the time between services and transportation to Reference Interventional Cardiology Centers is long, specifically in cities with high rates of specific mortality by IHD.

With the growing global concern about the IHD mortality, we would like to suggest also the creation of an observatory for mapping, monitoring and prevention of IHD mortality using geospatial tools to identify the locations with the highest number of cases and deaths due to IHD, sharing information to be analyzed in the scientific context and also to formulation of local, regional and inter-regional public policy interventions.

In conclusion, our work shows that the high mortality rate by IHD within the Regional Health Units was not restricted to socioeconomic and demographic variables, but dependent on the distance of each municipality to their Reference Interventional Cardiology Center, demonstrating that geographic factors play a significant role in IHD mortality within cities.

Acknowledgments

We would like to thank Ms. Riley Foster for assistance with the final editing of our manuscript.

References

1. World Health Organization (2008) The 10 leading causes of death by broad income group. Available: http://www.who.int/mediacentre/factsheets/fs310/en/index.html. Accessed 18 February 2012.

2. Alter DA, Naylor CD, Austin PC, Chan BT, Tu JV (2003) Geography and service supply do not explain socioeconomic gradients in angiography use after acute myocardial infarction. CMAJ 168: 261–264.

3. De Luca G, Suryapranata H, Zijlstra F, van 't Hof AW, Hoorntje JC, et al. (2003) Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol 42: 991–997. doi: 10.1016/S0735-1097(03)00919-7.

4. Welsh PWA (2005) It's a matter of time: contemporary pre-hospital management of acute ST elevation myocardial infarction. BMJ 91: 1524–1526.

5. Francone M, Bucciarelli-Ducci C, Carbone I, Canali E, Scardala R, et al. (2009) Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and microvascular damage in patients with ST- segment elevation myocardial infarction. J Am Coll Cardiol 54: 2145–2153. doi: 10.1016/j.jacc.2009.08.024.

6. Brazil Ministry of Health (2010) Department of the Unified Health System (Datasus). Health Information System. Available: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sim/cnv/obt10uf.def. Accessed 01 February 2012.

7. Goldberg RJ, Spencer FA, Fox KA, Brieger D, Steg PG, et al. (2009) Prehospital delay in patients with acute coronary syndromes (from the Global Registry of Acute Coronary Events [GRACE]). Am J Cardiol 103: 598–603. doi: 10.1016/j.amjcard.2008.10.038.

8. Paim J, Travassos C, Almeida C, Bahia L, Macinko J (2011) The brazilian health system: history, advances, and challenges. Lancet 377: 1778–1797. doi: 10.1016/S0140-6736(11)60054-8.

9. Schmidt MI, Duncan BB, Silva GA, Menezes AM, Monteiro CA, et al. (2011) Chronic non-communicable diseases in Brazil: burden and current challenges. Lancet 377: 1949–1961. doi: 10.1016/S0140-6736(11)60135-9.

10. Melo EC, Carvalho MS, Travassos C (2006) Spatial distribution of mortality from acute myocardial infarction in the city of Rio de Janeiro, Brazil. Cad Public Health 22: 1225–1236.

11. Sánchez-Barriga JJ (2009) Performance of ischemic heart disease mortality in Mexico in the period 2000–2007. Gac Med Mex 145: 375–82.

12. Ahern RM, Lozano R, Naghavi M, Foreman K, Gakidou E, et al. (2011) Improving the public health utility of global cardiovascular mortality data: the rise of ischemic heart disease. Popul Health Metr 9: 8. doi: 10.1186/1478-7954-9-8.

13. Bajekal M, Scholes S, Love H, Hawkins N, O'Flaherty M, et al. (2012) Analyzing recent socioeconomic trends in coronary heart disease mortality in England, 2000–2007: A population modelling study. PLoS Med 9: e1001237.

14. Pednekar MS, Gupta R, Gupta PC (2011) Illiteracy, low educational status, and cardiovascular mortality in India. BMC Public Health 11: 567.

15. Michimi A (2010) Modeling coronary heart disease prevalence in regional and sociodemographic contexts. Health & Place 16: 147–155. doi: 10.1016/j.healthplace.2009.09.007.

16. Jiang G, Wang D, Li W, Pan Y, Zheng W, Zhang H, et al. (2012) Coronary heart disease mortality in China: age, gender, and urban-rural gaps during epidemiological transition. Rev Panam Salud Publica 31: 317–324. doi: 10.1590/S1020-49892012000400008.

17. Guagliardo MF (2004) Spatial accessibility of primary care: concepts, methods and challenges. Int J Health Geogr 3: 3 doi:10.1186/1476-072X-3-3.

18. Apparicio P, Abdelmajid M, Riva M, Shearmur R (2008) Comparing alternative approaches to measuring the geographical accessibility of urban health services: distance types and aggregation-error issues. Int J Health Geogr 7: 7 doi:10.1186/1476-072X-7-7.

19. Franco B, Rabelo ER, Goldemeyer S, Souza EN (2008) Patients with acute myocardial infarction and interfering factors when seeking emergency care: implications for health education. Rev Lat Am Enfermagem 16: 414–418. doi: 10.1590/S0104-11692008000300013.

20. Bassanesi SL, Azambuja MI, Achutti A (2008) Premature mortality due to cardiovascular disease and social inequalities in Porto Alegre: from evidence to action. Arq Bras Cardiol 90: 370–379. doi: 10.1590/S0066-782X2008000600004.

21. Giuliani E, Lazzerotti S, Fantini G, Guerri E, Serantoni C, et al. (2010) Acute myocardial infarction – from territory to definitive treatment in an Italian province. J Eval Clin Pract 16: 1071–1075. doi: 10.1111/j.1365-2753.2009.01254.x.

22. Zornoff LAM, Paiva SAR, Assalin VM, Pola PMS, Becker LE, et al. (2002) Perfil clínico, preditores de mortalidade e tratamento de pacientes após infarto agudo do miocárdio, em hospital terciário universitário. Arq Bras Cardiol 78: 396–400. doi: 10.1590/S0066-782X2002000400007.

23. Chaix B, Rosvall M, Merlo J (2007) Recent increase of neighborhood socioeconomic effects on ischemic heart disease mortality: a multilevel survival analysis of two large Swedish cohorts. Am J Epidemiol 165: 22–26. doi: 10.1093/aje/kwj322.

24. Tonne C, Schwartz J, Mittleman M, Melly S, Suh H, et al. (2005) Long-term survival after acute myocardial infarction is lower in more deprived neighborhoods. Circulation 111: 3063–3070. doi: 10.1161/CIRCULATIONAHA.104.496174.

25. Pedigo A, Aldrich T, Odoi A (2011) Neighborhood disparities in stroke and myocardial infarction mortality: a GIS and spatial scan statistics approach. BMC Public Health 11: 644–656. doi: 10.1186/1471-2458-11-644.

26. Terkelsen CJ, Sørensen JT, Maeng M, Jensen LO, Tilsted HH, et al. (2010) System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA 304: 763–71. doi: 10.1001/jama.2010.1139.

27. Soares PA, Nascimento LF (2010) Spatial analysis of hospitalization for heart diseases in the Paraíba Valley. Arq Bras Cardiol 94: 747–753. doi: 10.1590/S0066-782X2010005000038.

28. Périssé G, Medronho RA, Escosteguy CC (2010) Urban space and mortality from ischemic heart disease in the elderly in Rio de Janeiro. Arq Bras Cardiol 94: 463–471. doi: 10.1590/S0066-782X2010005000009.

29. Lubovich A, Hamood H, Behar S, Rosenschein U (2011) Bypassing the emergency room to reduce door-to-balloon time and improve outcomes of patients with ST elevation myocardial infarction: the Acute Coronary Syndrome Israeli Survey experience. Isr Med Assoc J 13: 216–219.

30. Espírito Santo Júnior C, Silveira MAT (2007) Atlas Geográfico do Paraná: O uso de novas tecnologias. Available: http://www.diaadiaeducacao.pr.gov.br/portals/pde/arquivos/1127-2.pdf. Accessed 05 Oct 2010.

31. Brazilian Institute of Geography and Statistics (2010) Estados. Available: http://ibge.gov.br/estadosat/perfil.php?sigla=pr#. Accessed 03 May 2012.

32. Parana Institute of Economic and Social Development (2009) Tipologia dos municípios paranaenses segundo indicadores socioeconômico e demográficos. Available: http://www.ipardes.gov.br. Accessed 20 Jan 2012.

33. Brazil. Central Bank of Brazil (2009) Regional Bulletin of the Central Bank of Brazil. Evolution of the Human Development Index of the Major Regions and Federation Units. Available: http://www.bcb.gov.br/pec/boletimregional/port/2009/01/br200901b1p.pdf. Accessed 21 Dec 2012.

34. Brazil. Government of the state of Parana. Secretary of Health of Parana state (2012) Regional Health. Available: http://www.sesa.pr.gov.br/modules/conteudo/conteudo.php?conteudo=2752. Accessed 15 Mar 2012.

35. Brazil. Ministry of Health (2010) Department of the Unified Health System (Datasus) Health Information System. Vital Statistics of the Mortality. Available:http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/obt10pr.def. Accessed: 14 Jun 2011.

36. Institute of Cartography and Land Geosciences (2010) Political-Administrative Division of Parana. Available: http://www.itcg.pr.gov.br. Accessed 20 Oct 2011.

37. World Health Organization (2010) International statistical classification of diseases and related health problems, 10th revision. Available: http://apps.who.int/classifications/icd10/browse/2010/en#/I20-I25. Accessed 28 Jan 2011.

38. Santos AE, Rodrigues AL, Lopes DL (2005) Empirical Bayesian estimators applications for spatial analysis of mortality rates. In: VII Brazilian Symposium on Geoinformatics. Campos do Jordão - SP. Available at:http://www.geoinfo.info/geoinfo2005/papers/P63.PDF. Accessed 30 Nov 2012.

39. Druck S, Carvalho MS, Câmara G, Monteiro AVM (2004) Análise Espacial de Dados Geográficos. Brasília: EMBRAPA. p. 206.

40. Krempi AP (2004) Exploring spatial statistics tools for an accessibility analysis in the city of Bauru. Dissertation - Engineering School of São Carlos, University of São Paulo. 94 f.

41. Anselin L, Syabri I, Kho Y (2006) GeoDa: an introduction to spatial data analysis. Geogr Anal 38: 5–22. doi: 10.1111/j.0016-7363.2005.00671.x.

42. Anselin L (1998) Interactive techniques and exploratory spatial analysis. In: Longley PA, Goodchild MF, Maguire DJ, Rhind DW, editors. Geographical information systems: principles, techniques, management and applications. Wiley: New York. 253–265.

43. Perobelli FS, Haddad EA (2006) Padrões de comércio interestadual no Brasil, 1985 e 1997. Rev Econ Contemp 10: 61–88. doi: 10.1590/s1415-98482006000100003.

44. Campos FG, Barrozo LV, Ruiz T, César CL, Barros MB, et al. (2009) Spatial distribution of elderly individuals in a medium-sized city in São Paulo State, Brazil, according to key socio-demographic and morbidity characteristics. Cad Saude Publica 25: 77–86. doi: 10.1590/S0102-311X2009000100008.

45. Google Maps (2012). Available: www.maps.google.com.Accessed 12 Jul 2012.

46. Brazil. Government of state of Parana. Secretary of State for Health of Parana (2009) Plano Diretor de Regionalização. Available: http://www.sesa.pr.gov.br/arquivos/File/PDR_atualizado__Edson.pdf. Accessed 29 Mar 2012.

47. Shimony A, Zahger D, Ilia R, Shalev A, Cafri C (2010) Impact of the community's socioeconomic status on characteristics and outcomes of patients undergoing percutaneous coronary intervention. Int J Cardiol 144: 379–382.

48. Heslop CL, Miller GE, Hill JS (2009) Neighbourhood socioeconomic status predicts non-cardiovascular mortality in cardiac patients with access to universal health care. PLoS One 4: e4120.

49. Hassan A, Pearce NJ, Mathers J, Veugelers PJ, Hirsch GM, et al. (2009) The effect of place of residence on access to invasive cardiac services following acute myocardial infarction. Can J Cardiol 25: 207–212. doi: 10.1016/S0828-282X(09)70062-5.

50. Awoyemi TT, Obayelu OA, Opaluwa HI (2011) Effect of distance on utilization of health care services in rural Kogi State, Nigeria. J Hum Ecol 35: 1–9.

51. Nogueira MC, Ribeiro LC, Cruz OG (2009) Social inequalities in premature cardiovascular mortality in a medium-size Brazilian city. Cad Saude Publica 25: 2321–2332. doi: 10.1590/S0102-311X2009001100003.

52. Graves BA (2010) Access to cardiac interventional services in Alabama and Mississippi: a geographical information system analysis. Perspect Health Inf Manag 7. pii: 1b.

53. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A (2010) Growing epidemic of coronary heart disease in low- and middle-income countries. Curr Probl Cardiol 35: 72–115. doi: 10.1016/j.cpcardiol.2009.10.002.

54. Gottlie MGV, Carvalho D, Schneider RH, Cruz IBM (2007) Genetics aspects of aging and related diseases: a complex network of interactions between genes and environment. Rev Bras Gerontol Geriatr 10: 273–283.

55. Godoy MF, Lucena JM, Miquelin AR, Paiva FF, Oliveira DLQ, et al. (2007) Cardiovascular mortality and its relation to socioeconomic levels among inhabitants of São José do Rio Preto, São Paulo State, Brazil. Arq Bras Cardiol 88: 200–206. doi: 10.1590/S0066-782X2007000200011.

56. Galea S, Tracy M, Hoggatt KJ, Dimaggio C, Karpati A (2011) Estimated deaths attributable to social factors in the United States. Am J Public Health 101: 1456–1465. doi: 10.2105/AJPH.2010.300086.

57. Pereira A, Niggebrugge A, Powles J, Kanka D, Lyratzopoulos G (2007) Potential generation of geographical inequities by the introduction of primary percutaneous coronary intervention for the management of ST segment elevation myocardial infarction. Int J Health Geogr 6: 43 doi:10.1186/1476-072X-6-43.

58. Vavouranakis I, Fanioudaki A, Lamprogiannakis E, Baltzakis I, Sidiropoulou K, et al. (2010) Delays incurred during acute myocardial infarction: a comparative study of rural and urban populations in Greece. Rural Remote Health 10: 1271.

59. Vanasse A, Niyonsenga T, Courteau J, Grégoire JP, Hemiari A, et al. (2005) Spatial variation in the management and outcomes of acute coronary syndrome. BMC Cardiovasc Disord 5: 21 doi:10.1186/1471-2261-5-21.

60. Wang HE, Yealy DM (2012) Distribution of Specialized Care Centers in the United States. Ann Emerg Med doi:10.1016/j.annemergmed.2012.02.020.

61. Lippi Bruni M, Nobilio L, Ugolini C (2008) The analysis of a cardiological network in a regulated setting: a spatial interaction approach. Health Econ 17: 221–233. doi: 10.1002/hec.1255.

62. American Heart Association (2009) Focused Updates: ACC/AHA Guidelines for the management of patients with ST-elevation myocardial infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on percutaneous coronary intervention (Updating the 2005 Guideline and 2007 Focused Update): A report of the American College of Cardiology Foundation/American Heart with ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2009 Focused Updates: ACC/AHA Guidelines for the management of patients association task force on practice guidelines. Circulation 120: 2271–2306. doi: 10.1161/CIRCULATIONAHA.109.192663.

63. Sorensen JT, Terkelsen CJ, Norgaard BL, Trautner S, Hansen TM, et al. (2011) Urban and rural implementation of pre-hospital diagnosis and direct referral for primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction. Eur Heart J 32: 430–436. doi: 10.1093/eurheartj/ehq437.

64. Brazil. Ministry of Health (2006) Diretrizes para a Implantação de Complexos Reguladores. Available: http://bvsms.saude.gov.br/bvs/publicacoes/DiretrizesImplantComplexosReg2811.pdf. Acessed 23 Mar 2012.

65. Christie S, Fone D (2003) Equity of access to tertiary hospitals in Wales: a travel time analysis. J Public Health Med 25: 344–350. doi: 10.1093/pubmed/fdg090.

66. Diez Roux AV (2005) Persistent social patterning of cardiovascular risk rethinking the familiar. Circulation 111: 3020–3021. doi: 10.1161/CIRCULATIONAHA.105.542845.

67. Soljak M, Samarasundera E, Indulkar T, Walford H, Majeed A (2011) Variations in cardiovascular disease under-diagnosis in England: national cross-sectional spatial analysis. BMC Cardiovasc Disord 11: 12 doi:10.1186/1471-2261-11-12.

68. Kereiakes DJ (2008) Specialized centers and systems for heart attack care. Am Heart Hosp J 6: 14–20. doi: 10.1111/j.1751-7168.2008.07644.x.

69. Brazil. Ministry of Health (2011) Rede de Urgência e Emergência. Linha do cuidado do Infarto Agudo do Miocárdio na rede de atenção às urgências. Available: http://portal.saude.gov.br/portal/arquivos/pdf/linha_cuidado_iam_rede_atencao_urgencia.pdf. Accessed 21 Dec 2012.

70. Machado CV, Salvador FGF, O'dwyer G (2011) Mobile Emergency Care Service: analysis of Brazilian policy. Rev Saude Publica 45: 519–528. doi: 10.1590/S0034-89102011005000022.

71. Jorge MH, Laurenti R, Gotlieb SL (2007) Quality analysis of Brazilian vital statistics: the experience of implementing the SIM and SINASC systems. Cien Saude Colet 12: 643–654.

2.2 Artigo 2: System Dynamics modeling in the evaluation of delays of care in ST-segment elevation myocardial infarction patients within a tiered health system.

Autores: Luciano de Andrade [1,5], Catherine Lynch [2], Elias Carvalho [3,4], Clarissa Garcia Rodrigues [6], João Ricardo Nickenig Vissoci [7], Guttenberg Ferreira Passos [8], Ricardo Pietrobon [9], Oscar Kenji Nihei [5], **Maria Dalva de Barros Carvalho [1].**

1 - Department of Health Sciences, State University of Maringa, Maringa, Parana, Brazil.

2 - Division of Emergency Medicine, Department of Surgery; Duke Global Health Institute, Duke University, Durham, North Carolina, United States of America.

3 - Nucleus of Data Processing, State University of Maringa, Maringa, Parana, Brazil.

4 - Graduate Program in Informatics - PPGIA, Knowledge Discovery and Machine Learning Group, Pontificia Universidade Católica - PUC-PR, Curitiba, Parana, Brazil.

5 - Department of Nursing, State University of the West of Parana, Foz do Iguaçu, Parana, Brazil.

6 - Institute of cardiology of Rio Grande do Sul – University Foundation of Cardiology, Porto Alegre, Rio Grande do Sul, Brazil.

7 - Department of Medicine, Faculdade Inga, Maringa, Brazil.

8 - Department of Informatics, Brasilia University, Brasilia, Brazil.

9 - Department of Surgery, Duke University Health System, Durham, North Carolina, United States of America.

Periódico: PLoS ONE. Fator de Impacto: 3.730. Qualis A - Medicina II

Status da Publicação: Publicado em 31 de julho de 2014. PLoS ONE 9(7): e103577. doi:10.1371/journal.pone.0103577

Abstract

Background: Mortality rates amongst ST segment elevation myocardial infarction (STEMI) patients remain high, especially in developing countries. The aim of this study was to evaluate the factors related with delays in the treatment of STEMI patients to support a strategic plan toward structural and personnel modifications in a primary hospital aligning its process with international guidelines.

Methods and Findings: The study was conducted in a primary hospital localized in Foz do Iguaçu, Brazil. We utilized a qualitative and quantitative integrated analysis including on-site observations, interviews, medical records analysis, Qualitative Comparative Analysis (QCA) and System Dynamics Modeling (SD). Main cause of delays were categorized into three themes: a) professional, b) equipment and c) transportation logistics. QCA analysis confirmed four main stages of delay to STEMI patient's care in relation to the 'Door-in-Door-out' time at the primary hospital. These stages and their average delays in minutes were: a) First Medical Contact (From Door-In to the first contact with the nurse and/or physician): 7 minutes; b) Electrocardiogram acquisition and review by a physician: 28 minutes; c) ECG transmission and Percutaneous Coronary Intervention Center team feedback time: 76 minutes; and d) Patient's Transfer Waiting Time: 78 minutes. SD baseline model confirmed the system's behavior with all occurring delays and the need of improvements. Moreover, after model validation and sensitivity analysis, results suggested that an overall improvement of 40% to 50% in each of these identified stages would reduce the delay.

Conclusions: This evaluation suggests that investment in health personnel training, diminution of bureaucracy, and management of guidelines might lead to important improvements decreasing the delay of STEMI patients' care. In addition, this work provides evidence that SD modeling may highlight areas where health system managers can implement and evaluate the necessary changes in order to improve the process of care.

Introduction

In 2011, approximately 7 million people died worldwide from ischemic heart disease, representing 11.2% of all global deaths. While this issue primarily affects developed countries it is becoming increasingly problematic in developing countries [1-2]. ST-segment elevation myocardial infarction (STEMI) is the most lethal form of acute coronary syndrome (ACS). In addition to high mortality rates, STEMI is also associated with high rates of serious complications that can be avoided with early treatment. Primary percutaneous coronary intervention (PCI), recognized worldwide as the best strategy for myocardial reperfusion in patients with STEMI, improves patients' survival and quality of life. However, expediting PCI continues to be a constant challenge for cardiovascular specialists and health systems worldwide [3-6].

The American College of Cardiology/American Heart Association and European Society of Cardiology recommend a goal time from first medical contact (FMC) to balloon catheter inflation at a PCI center (FMC-to-device) of less than 120 minutes for patients who call requesting emergency medical services or self-present to a non-PCI-capable hospital [2,7]. There is a positive correlation between the FMC-to-device time and mortality rates of STEMI patients that is attributed to delays in care, which limit the benefits of PCI [6-9]. Studies show that multiple factors are responsible for these delays including the regional and patient characteristics, like geographic, demographic, behavioral, transportation availability, and the structure of the referral services [10-15].

Even in developed countries, most patients with STEMI present to a primary hospital without PCI capabilities and it is the rapid transport from a primary hospital to a tertiary hospital with PCI that is a major obstacle [16-18]. The College of Cardiology/American Heart Association and European Society of Cardiology recommend a goal time to proper care of STEMI patients from Door In at a primary hospital to the departure to a PCI Center (Door-in-Door-out time) of 30 minutes or less [2,7]. The ideal time from patient entrance at the primary hospital (Door In) until the acquisition of 12-lead ECG reviewed by physician is 10 minutes, and an additional 20 minutes are recommended for the ECG transmission, decision to transfer a STEMI patient based on PCI center feedback and the patient departure (Door Out). A systematic review revealed that only 25% of United States hospitals have catheterization capacity and transportation of STEMI patients to a catheterization capable hospital is often not within the recommended 30 minutes timeframe. This is often due to geographic variations and diagnosis delays [19]. Other studies acknowledge the delays with

STEMI patients from primary hospitals, but do not speculate which variables at the primary hospital are responsible for delays [20-21].

In Brazil, the proportion of STEMI patients diagnosed by prehospital and hospital triage systems is unclear. There are a few studies in Brazil reporting the demographics of those who received cardiac reperfusion therapies. In a 2009 survey of 158 STEMI patients from Rio de Janeiro, 67.7% arrived at the hospital within 180 minutes, 81.3% within 360 minutes and 8.4% arrived after twelve hours. In this study, 26% of patients were treated with PCI, 32% with thrombolytics, and 42% with optimal medical therapy. Importantly, about 35% of STEMI patients who should have received thrombolysis did not receive it in this study [22].

Health system evaluations commonly gather some of the following information: screening time, time to completion of ECG and time to transfer to an interventional cardiology center [23-24]. However, to our knowledge no other study has analyzed these variables through System Dynamics Modeling [25] and sensitivity analysis [26] to provide a more complete in-depth health system evaluation. As such, the intent of this study is to evaluate delays in routine emergency care of STEMI patients using on-site observations, QCA, system dynamics modeling and sensitivity analysis in order to perform an in depth health system evaluation. This evaluation will enable a better understanding of the variables related to treatment delays in STEMI patients and identify the necessary improvements in order to provide adequate care according to the recommended guidelines.

Methods

Hospital Setting

This research was conducted at João Samek primary hospital located in Foz do Iguaçu, Parana, Brazil. This hospital has an Emergency Care Unit, open 24 hours per day 7 days per week with the capacity to treat 300 to 400 patients per day [27]. Patients diagnosed with STEMI at this hospital are transported by emergency medical services (EMS) to Minister Costa Cavalcanti tertiary hospital and regional interventional cardiology referral center (PCI center), located in Foz do Iguaçu. This regional PCI center attends approximately 170 patients per month, referred from different health care institutions, and on average performs 90 primary percutaneous coronary interventions per year. The distance between the primary hospital and the PCI center is 2.05 miles.

Study Period

The study was conducted from August 2011 to October 2012.

Institutional Review Board

All participants provided a written informed consent to participate in this study. This study was approved by the Institutional Review Board at the State University of Maringa (COPEP / UEM), in Brazil, under the registration number 266/2011.

Qualitative Data Analysis

The qualitative research was conducted and reported based on the 'consolidated criteria for reporting qualitative research' (COREQ) [28].

Data Source

Our qualitative approach included interviews with health professionals regarding their perception of the care of patients admitted with chest pain and diagnosed with a STEMI who required transfer to a PCI center. The study subjects were health professionals who work at the João Samek primary hospital in Foz do Iguaçu. A convenience sampling was used in the selection of participants. The principal investigator (LA) interviewed two physicians, two nurses and two managers. These health professionals were enrolled to participate in this study during the period of September and October 2012. The nurses and physicians had experience providing care in triage and the emergency department while the managers were administrators for the primary hospital. In order to be included in the study, the health professionals had to have worked at the primary hospital for at least two years and have interest in participating in the research project. All participants had more than 10 years of experience in healthcare and 2 with more than 30 years of experience.

Study participants did not know the principal investigator beforehand, and vice versa. The script for the interviews included two open ended questions: *1) In your opinion, what are the causes of delay in care and transfer of patients with STEMI from a primary hospital to the PCI center?; 2) What measures do you think could reduce attendance time and transfer of a patient with STEMI to the PCI center?*

Interview Procedures

All interviews were performed individually and occurred in a private room within the primary hospital facilities. All interviews were recorded and on average lasted 20 minutes.

The speakers were identified by E1, E2 (nurses) and M1, M2 (physicians), and G1, G2 (Managers). Data collection occurred during the months of September and October 2012.

Data Transcription

In order to improve accuracy, all transcriptions were performed by the principal investigator no more than seven days from the original interview. Data saturation was achieved at the conclusion of 6 interviews. All interviews were transcribed verbatim. Notes and impressions obtained during participant interviews were added to the original transcription as comments. All transcripts were reviewed for accuracy and were available to other participating researchers. Physician, nurses and managers identifiers were removed from the transcript to ensure confidentiality. Quotations used for illustration in this report were translated from Portuguese to English and independently back-translated by other bilingual researchers to ensure translation accuracy. Transcripts of the interviews were sent to participants for comments and changes for quality control.

Data Analysis

Interview analysis was completed utilizing content analysis, a research technique used to objectively categorize communication content allowing researchers to identify the essential information behind each participant narrative [29-32]. There are three main phases of content analysis: pre-analysis, material exploration and inference/interpretation of results [30,32]. This study included: a detailed reading of the interview transcript (pre-analysis); data categorization and inclusion of descriptive quotations (material exploration); and interpretation of results (inference/interpretation).

Transcriptions were coded using a combination of manual coding and NVIVO software, version 10.0 (QSR International, Melbourne, Australia) [33]. The data were organized in a spreadsheet Excel ® (Microsoft Office, Microsoft Corporation, USA) and exported to .csv files (comma-separated values). Data were analyzed and the absolute and relative frequencies of the categories that emerged from the interviews of health professionals were presented in Polar Axis graphs (R software, version 2.15.0) [34].

Qualitative Comparative Analysis (QCA)

QCA was performed for a formal analysis of qualitative evidence using Boolean Algebra rather than correlational methods [35]. QCA is a configurational comparative technique that is half-way between the qualitative and quantitative approach [35-36]. QCA has the advantage of being able to analyze samples in small-N situations forming sets of variables based on half verbal/conceptual and half logical/mathematical criteria. The main purpose of QCA is to detect different configurations of the variables that lead to an outcome of interest, allowing a better understanding of a complex multivariable scenario. Thus the QCA focus on the analysis of multivariable conditions necessary and/or sufficient for an outcome of interest unraveling equifinality, multifinality or asymmetric structural causalities [36-39]. Thus, there are three analytic components of QCA: necessity analysis; sufficiency analysis; data set calibration [35,40-41].

For this study, we used crisp-set QCA (csQCA), a conventional and most commonly used technique of QCA, which generates explanatory models containing one or more causal paths to the possible outcomes of interest based on the evidence (variables) [40-42].

In our study, the data for QCA were obtained from medical records of patients initially admitted to the emergency department at the primary hospital with a confirmed STEMI diagnosis who were then transferred to the PCI center in Foz do Iguaçu between August 1st, 2011 and October 30th, 2012. We identified and included the medical records of 29 STEMI patients. The main data obtained from the STEMI patients medical records were four variables: First Medical Contact [FMC] that was defined as the first contact of the STEMI patient with the nurse (in most of the cases) and/or physician (in emergency cases) at the primary hospital; Electrocardiogram acquisition [ECG]; ECG transmission and PCI center team feedback time [TXF]; Patient's Transfer Waiting Time [TWT]; and two outcomes (Ejection Fraction < 50% [EF]; Length of Stay [LOS]).

We constructed a matrix with binary variables, with 'zero' corresponding to 'no delay' and 'one' corresponding to a 'delay in the initial care of patients with STEMI'. We then transformed this array into a truth table, a critical part of a QCA analysis, which evaluates for causal combinations that are sufficient for the outcome and are represented in letters that are linked with Boolean operators [35-38]. The three basic Boolean operators are logical OR (+), logical AND (*), and logical NOT (where the negative is customarily denoted in QCA by replacing an uppercase letter with a lowercase letter). So in the next step, the Boolean minimization was performed which excludes some of these causal combinations, allowing the identifications of the so called 'prime implicants' (PI) related with the regularities in the data [41]. These PI state what combinations of conditions are necessary or sufficient for the outcome to occur or not [35,39,43].

A function within the package QCA in the R software that performs this boolean minimization is the "eqmcc", from which one can derive different solutions from the truth table of the object or a suitable dataset: 1) Complex solutions (Detailed sets); 2) Parsimonious solutions (incorporate logical remainders into the minimization process, generating only the essential simplified sets); 3) Intermediate solutions (middle way path between Complex and Parsimonious solutions) [40-42].

Primary Hospital Process Measures

Different studies have proposed the analysis of additional time intervals within the Door-in Door-out time in order to better understand the processes related with the delay of STEMI patient care within the primary hospital [44-45]. In this work, we proposed to further divide the main two stages (Door-in to ECG acquisition; ECG transmission to patient departure) in four time intervals, considering an optimal time for each process, as follows: 1) Door-to-FMC: 2 minutes; 2) FMC-to-ECG: 8 minutes; 3) ECG transmission-to-PCI center team feedback: 5 minutes; 4) Patient's transfer waiting time until departure to PCI center: 15 minutes. Since these four time intervals totalize the recommended 30 minutes, these intervals were utilized as the ideal times to obtain the delays in each stage.

System Dynamics Modeling

System Dynamics (SD) is an approach to frame, describe and analyze complex systems allowing a better understanding of how their key constitutional elements interact to generate a specific outcome what may help to provide solutions to a problem [25,46-47]. In SD, we create models using diagrams of stocks and flows, whose characteristic is to allow the model to be analyzed quantitatively. Stocks represent the state of the model entities at any point in time, and flows representing the rate of change of stock [25]. A dynamic complex system is characterized mainly by: 1) Interactions between the system's constituents; 2) Dependency on time; 3) An internal complex causal structure subjected to feedbacks, and 4) Delayed behavioral reactions, which are difficult to predict [25]. In addition, the models using SD generally work with continuous time and change of levels of stocks based on instantaneous values.

According to the nature of this study, we build a model based on the concept of "Aging Chains" [48], a structure model that represents the different stages of a maturing process where attributes change as time goes. This structure has information about how long each modeled entity is retained at each stage and based on this a model of the impact on the final outcome of STEMI patients was created.

Model Creation and Mediated Modeling

The model was created to adjust the data based on interviews with the primary hospital professionals and from STEMI patients' medical records. All modeling was conducted using Vensim DSS ® version 5.11 of Ventana Systems, Inc [49]. During model creation, mediated modeling methods were adopted to incorporate researchers and professionals knowledge and experience to produce a coherent, simple but elegant simulation baseline model and create strategies for the solution of a specific problem [50]. Through codification, and converting ideas from qualitative interviews into a SD model these data may indicate a strategic plan to decision makers.

Sensitivity Analysis and Model Calibration

We conducted a sensitivity analysis and a model calibration according to Oliva [51], which relies on Sterman [47]. The sensitivity analysis allow us to identify variation in the behavior of the model when changes are made to certain parameters. In this case the simulation is executed many times with different parameters until the increase of resources does not change the outcome of the model. The model calibration is an interactive process where the modeler, with the knowledge gained from the analysis of sensitivity, adjusts the parameters and re-executed the model and go back to the first step until the behavior of the model reach the best cost-benefits.

Results

Qualitative Data Coding of Delay Causes

A total of six health professionals from a primary hospital were interviewed. The qualitative data were subjected to content analysis and we identified the categories of causes of delay in the care and transfer of STEMI patients from the primary hospital to the PCI center in Foz do Iguaçu, Brazil.

When asked about the causes of delay in the care and transfer of STEMI patients from the primary hospital to the PCI center, the qualitative categories of responses were: a) professional; b) equipment and c) transportation logistics (Figure 1). Professional causes of delay included: professionals' limited capacity to recognize STEMI patients (66.7%), lack communication between the primary hospital medical staff and the staff of the PCI center (66.7%) and lack of specialists in the primary hospital (16.7%). Transportation logistics category of causes of delays include: bureaucracy involved in transferring STEMI patients to the PCI center (66.7%), and incorrect routing of patients by EMS to the primary hospital instead of going straight to the PCI center (33.3%). Equipment causes of delays included: equipment problems sending the ECG result to the PCI center (33.3%). Finally, one participant reported 'failures in all sectors' (16.7%) (Figure 1A).

When the professionals were asked about possible measures to reduce transfer time of the STEMI patient from the primary hospital to the PCI center, the qualitative categories were: a) Professional Development (improve health professionals training and capacity to manage STEMI patients [16.7%], improve communication between the primary hospital and PCI center staff, mainly direct contact with cardiologists [50.1%]); b) Transportation logistics (reduce bureaucracy to transfer process [50.1%] as well as ensuring appropriate EMS disposition of STEMI patients to an PCI center [33.3%]); c) Equipment (acquiring appropriate equipment to improve communication [implementation of electrocardiography connected to internet] [16.7%]) (Figure 1B).

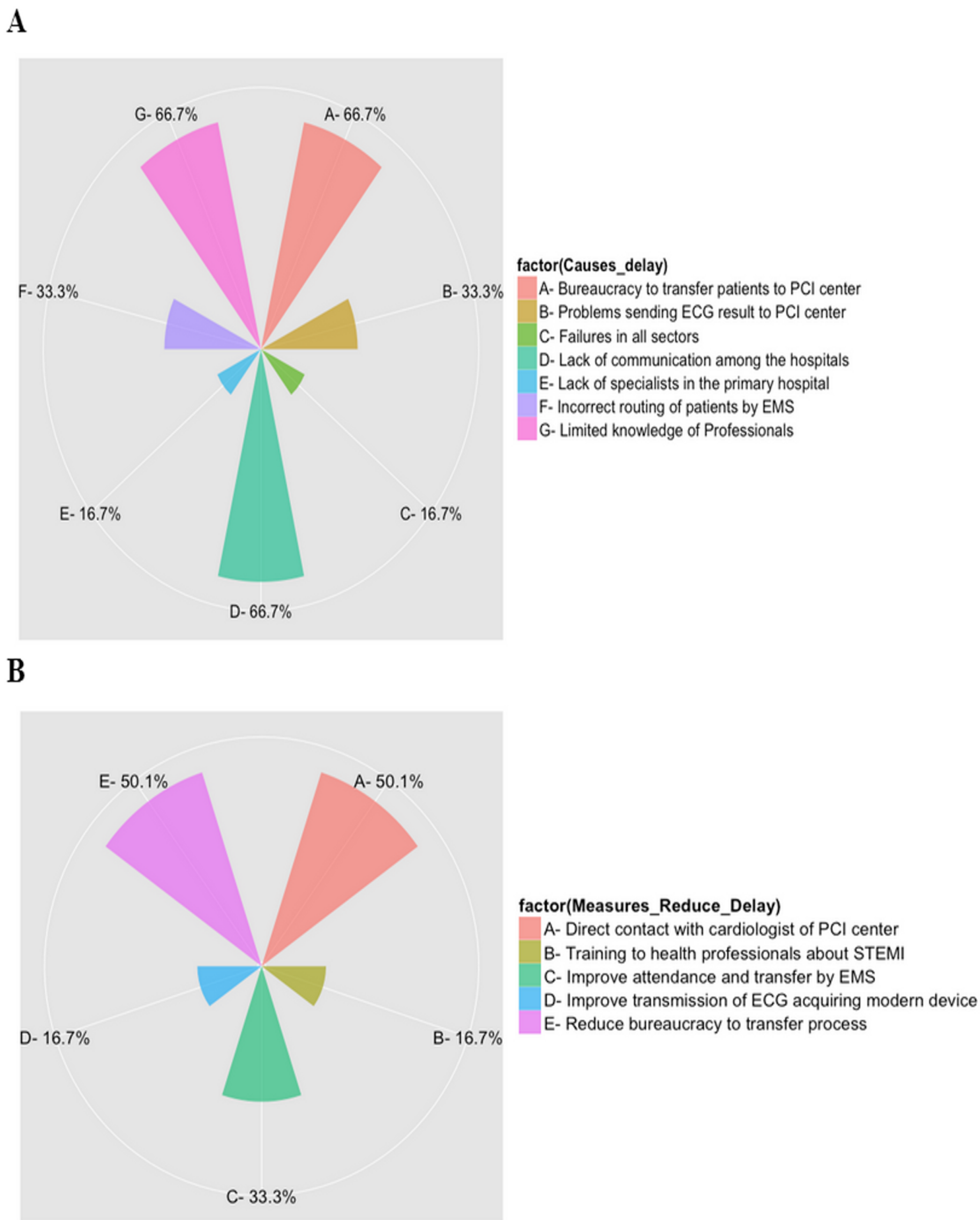

Figure 1. Qualitative data categories obtained from the interviews with primary hospital professionals: A) Causes of Delay; B) Measures to Reduce Delay.

Below are excerpts of key interviews that played a role in defining the categories of causes of delay with reference to the question: *1) In your opinion, what are the causes of* *delay in care and transfer of patients with a STEMI from a primary hospital to the PCI center?*

"We've discussed this a long time, there are flaws in all sectors; we realize that some employees are not prepared to act, difficulties in the initial recognition of patients with myocardial ischemia cause the delay from patient arrival until exit to another hospital" (E1).

"In patients with a diagnosis of STEMI, the physician attendance here is fast, then we fax the ECG, by phone warn the referral hospital that the ECG is being faxed, awaiting their response there is always a delay. When we call for feedback, they said that the fax is unreadable, it has artifact, ask if the ECG cables are placed correctly, and say that we have to repeat another ECG and send it again"(E2) .

"The delay occurs for two reasons, one is that most of the physicians who work here are not qualified as emergency physicians and don't have the required technical knowledge. They are here to get experience. The second reason is difficulty in patient transportation, and the bureaucracy in this process. Sometimes it would be appropriate [for EMS] to directly transport the patient to the Interventional Cardiology Center and it doesn't occur."(G1).

Below are excerpts of key interviews that played a role in defining the categories of measures with reference to the question: *2) What measures do you think could reduce attendance time and transfer of a patient with STEMI to the PCI center?*

"We need an educational refresher course performed by cardiologists from the PCI Center on ECG interpretation. We would be more secure and comfortable transferring patients [with this knowledge…]" (M2).

"The goal is to reduce the bureaucracy and obtain a modern ECG device. In my opinion the adoption of fax to transmit the ECG information increased the delay and decrease the quality of the information that is transmitted, which has hampered the patients' transfer. Many times the complaint is that the ECG is unreadable"(G1).

"When there is an elevation in one or two leads of the ECG, but it is not certain, we talk with the emergency physician of the referral hospital that also most often is not a cardiologist. He

does not trust our word, asks to repeat the ECG that was faxed which increases the delay. If the contact is direct with the interventionist cardiologist this would decrease the delay time in transfer "(M2).

Qualitative Comparative Analysis (QCA)

Our sample consisted of 29 patients transferred from the primary hospital to the PCI center for a STEMI. The sample was mostly made up of men (82.8%) with a mean age of 60 ± 11 years and a body mass index of 27.8 ± 5.9, mostly with incomplete primary education (58.6%), 41.4% had a family history of coronary artery disease, while 10.3% had a prior AMI. Sixty-nine percent had high blood pressure (hypertension), 37.9% had diabetes mellitus, 31.0% dyslipidemia, 41.4% were smokers and only 6.9% practiced physical activity. Most of FMC occurred between 6 pm until 12 am period (41.4%), followed by the afternoon period (24.1%).

To perform QCA we adopted the intermediate solution algorithm, and four variables (FMC, Electrocardiogram [ECG], ECG transmission and PCI center team feedback time [TXF], Transfer Waiting Time [TWT]) and two outcomes (Ejection Fraction < 50% [EF]; Length of Stay [LOS]) were considered. These two outcomes were selected since higher LOS correlate with increasing the hospital expenses and EF loss is related to the infarct type (whether affecting the left [anterior descending artery and circumflex artery] and/or right coronary) and degree of left ventricular damage indicating mainly moderate and major infarcts.

The QCA showed that only one variable and one combination (set) generated by the intermediate solution algorithm, lead to the delay of STEMI initial treatment indirectly increasing the chance of reducing the first outcome analyzed, the ejection fraction (EF) less than 50%. In this case, the QCA generated the following expression: ecg*txf*TWT + FMC*ecg*TWT, which indicated that the reduction of EF are associated with delay in the following time periods: 1) TWT; or 2) FMC and TWT.

In addition, the QCA intermediate solution algorithm showed that two combinations of variables lead to an increase of the length of stay (LOS). In this case, the QCA generated the following expression: FMC*ecg*TXF*TWT + FMC*ECG*txf*TWT. The expression indicated that the increase of LOS may happened when there is a delay in the following combinations of time periods: 1) FMC, TXF and TWT; or 2) FMC, ECG and TWT. When evaluating increased LOS as an outcome, it was associated with a delay in any stages of care at the primary hospital. These data indicated that both LOS and EF are sensitive to TWT and FMC and in the case of LOS it is also affected by ECG and TXF.

System Dynamic Modeling

To start building the system dynamic model, the following time intervals, already described previously, were utilized: FMC, ECG, TXF and TWT. From the collected data a spreadsheet was created (Figure 2) with data from each step. Optimal timing, according to the literature, was inserted and the average delay, the delay retained in each step and the percentage of patients that exceeds the optimal delay was calculated. During the mediated modeling, we described the challenges at each step, the possible solutions and calculated the percentage of potential improvements (Figure 2). According to these data, the 3rd (TXF) and 4th steps (TWT) represented the variables that could, if improved, enable the highest percentage (50%) of overall improvement in order to decrease the delay of treatment of STEMI patients. Accordingly, the results also indicated that the 3rd and 4rd steps presented high percentage of patient exceeding delay, 76% and 86%, respectively, compared to the ideal time (Figure 2).

Data to feed SD Model

Step	Optimal Delay (minutes)	Delay Retained (minutes)	% of patients exceeding optimal delay	Nº	Problem	Solution	% Improvement on timeout	% Overall improvement	Cost	Degree of difficulty
FMC	2	5	52%	1	Lack of knowledge by workers at reception and nursing screening about signs and symptoms of patient with the STEMI.	Training for professionals. Manchester - Risk Classification System.	15	40	Medium	Medium
	Optimal FMC delay	Delay FMC	Portion FMC	2	Lack of interaction between the reception and the nursing sectors. Delay in referring patients for screening sector.	Improving communication between reception and nursing sectors.	10		Low	Low
				3	Delay in the screening and ECG due to delay in the decision on to do ECG by nursing, because some physicians do not like nurses performing ECGs before their request.	Training for Emergency physicians and nurses regarding the guidelines of ACC/AHA for the initial treatment of patients with STEMI.	15		Medium	Medium
ECG	8	20	79%	4	Some professionals of nursing team do not know how to perform ECG or perform the wrong way.	Training nursing staff on the correct techniques to perform ECG.	10	40	Medium	Medium
	Optimal ECG delay	Delay ECG	Portion ECG	5	Lagged Electrocardiogram	ECG equipment with digital output, less artefacts, and faster transfer via internet.	20		Medium	Medium
				6	ECG equipment gets more broken than working.	Do not loan the device for other sectors. A member of staff should be responsible for get 12-lead ECG.	10		Low	Low
TXF Tx ECG Feedback	5	71	76%	7	Lack of knowledge of the physicians about ECG interpretation.	Training for emergency physicians about interpretation of the ECG.	20	50	Medium	Medium
	Optimal TXF delay	Delay TXF	Portion TXF	8	ECG result transmission by fax and delay in obtaining the feedback by PCI center. Low image quality, and often the transmission process need to be repeated.	Acquisition of modern ECG equipment with transmission by internet.	15		Medium	Medium
				9	The delay in the diagnosis definition and discussion of the case with the emergency physician of PCI Center.	ECG transmission straight to the hemodynamicist physician through internet that will determine whether to accept the patient at that moment for primary PCI.	15		Medium	High
TWT Awaiting Transfer	15	63	86%	10	Many patients are brought by EMS of the residence or public road to primary hospital for first diagnosis and after will be transferred to PCI center.	Perform ECG at the ambulance and after confirming the diagnosis of STEMI, direct transfer of the patient to PCI center.	30	50	High	High
	Optimal TWT delay	Delay TWT	Portion TWT	11	Bureaucracy – The primary hospital have to wait a fax with the authorization of the PCI center, that is need after be send by fax to the EMS, to finally, the EMS, authorize the ambulance transport.	Telephone contact and discussion of the case by the emergency physician with the EMS regulator physician, without the need of authorization transmission by fax. Eliminating the bureaucracy at this phase.	20		Medium	High

Figure 2. Data obtained by medical records and mediated modeling to feed SD model.

Based on collected data, we show in Figure 3 the optimal delay (green line), the average delay (red line) and the delay for each patient (blue line), in four different steps: FMC (3A), ECG diagnosis (3B), TXF (3C) and TWT (3D). The X axis present the number of each patient (1 to 29) and the Y axis represents the delay time in minutes. The 3rd step (TXF) presented 76% of the patients exceeding the optimal delay; the 4rd step (TWT) presented 86% and the 2nd step (ECG diagnosis) presented 79%.

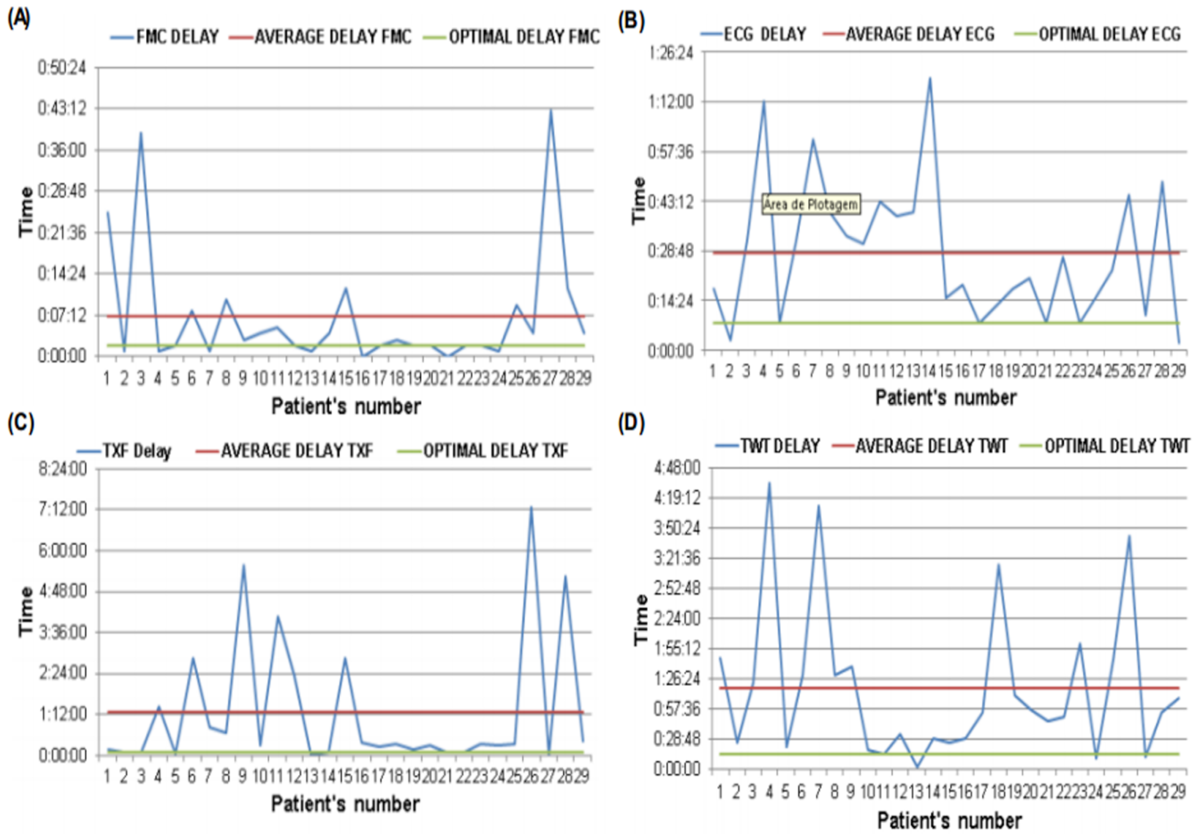

Figure 3. Representation of the Ideal Delay (green line), Average Delay (red line) and Patients Delay (blue line) in four different steps: (A) First Medical Contact (FMC), (B) ECG and diagnostic (ECG), (C) ECG transmission by fax and feedback from PCI center (TXF), (D) Transfer waiting time (TWT). Y axis represent the delay time (hour:minutes:seconds) and the X axis the number of each patient.

We created a baseline simulation model (Figure 4) showing all the steps from the arrival of the patient until the transfer to a PCI center. In this model, the stocks represent the four stages that the STEMI patients need to pass within the primary hospital to be adequately treated namely "FMC", "ECG", "TXF" and "TWT" and flows represents the patients moving through each department while receiving care in the primary hospital. In the proposed model the STEMI patients are retained in each stage for a variable ‘x’ time, increasing their delay time in each stage and consequently increasing the Door in-Door out treatment time. In each stage, the percentage of necessary improvement is calculated in order to obtain a condition where the delay do not occur, what is considered the main goal, in order to reduce the retention of the STEMI patients in each stage. After mediated modeling, we created a diagram over these stocks that represents the actions to implement proposed improvements and reduce the time spent in each phase of patient care. These diagrams have a feedback loop (represented by B1, B2, B3 and B4), which means that if a variable is increased above a certain level it is automatically adjusted and as a result it will return to a desired level and vice versa.

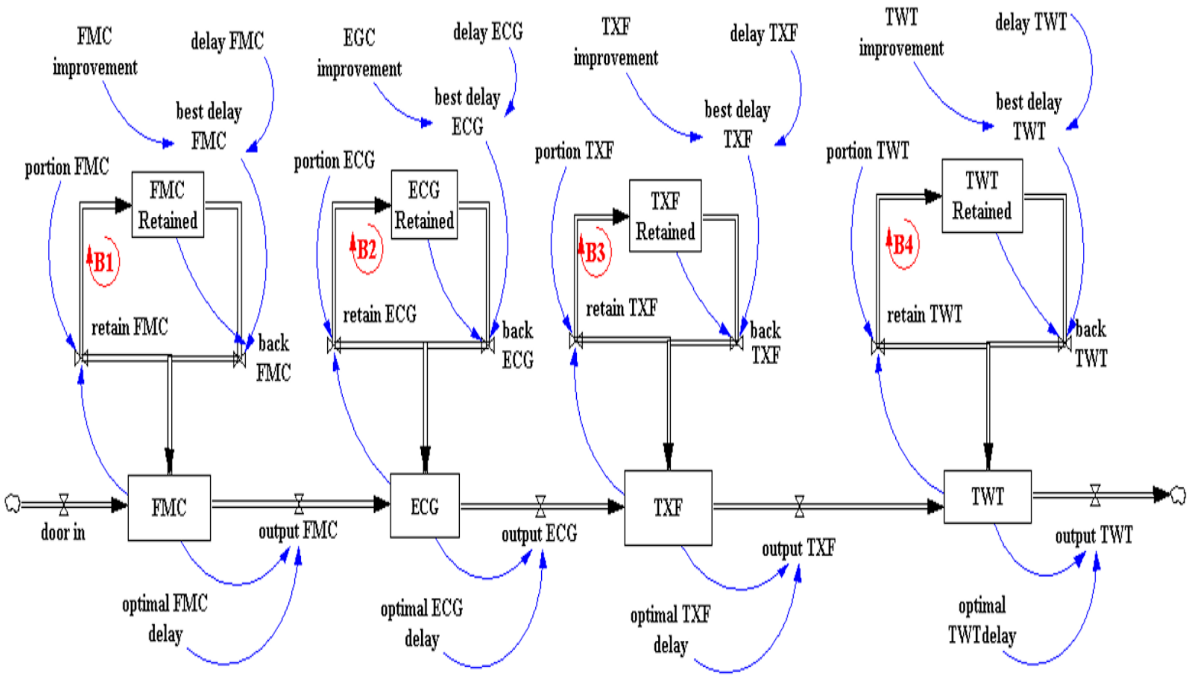

Figure 4. Systems Dynamics Model representing the routine to assist patients inside primary hospital considering the four different steps: First Medical Contact (FMC), ECG and diagnostic (ECG), ECG transmission by fax and feedback from PCI center (TXF) and Transfer waiting time (TWT).

Model Validation and Policy Testing

Based on analysis of collected data, model simulation and calibration it was possible to generate an interval of values that results in no delay (Table 1 and Figure 5). On this table, the data in the column “Value Estimate” is derived from the column "% overall Improvement" presented in the Figure 2, while the column "Interval of Uncertainty" is the variation of improvements obtained during certain number of simulations. This interval is necessary because in the real world there is always the possibility of unexpected events.

Table 1. System Dynamic Model calibration parameters for each step within the primary hospital.

Calibration SD Model - STEMI			
Step	**Parameters**	**Value Estimate**	**Interval "appropriate" Degree of uncertainty**
First Medical Contact (FMC)	FMC improvement	40%	10–50%
ECG and diagnostic (ECG)	ECG improvement	40%	10–50%
ECG Transmission by fax and feedback from PCI center (TXF)	TXF improvement	50%	10–60%
Transfer waiting time (TWF)	TWF improvement	50%	10–60%

In order to adjust the system according to the international guidelines, we tested some policies using different scenarios and values by manipulating variables and model parameters (Figure 5). The objective was to achieve a reasonable match between the observed and the simulated values and detect unacceptable errors, demonstrating expected improvement reducing the delay in care of STEMI patients. The red line represents the number of patients retained in each phase of baseline model and the blue line represents the same values after simulation of the proposed improvements (illustrated in Figure 2).

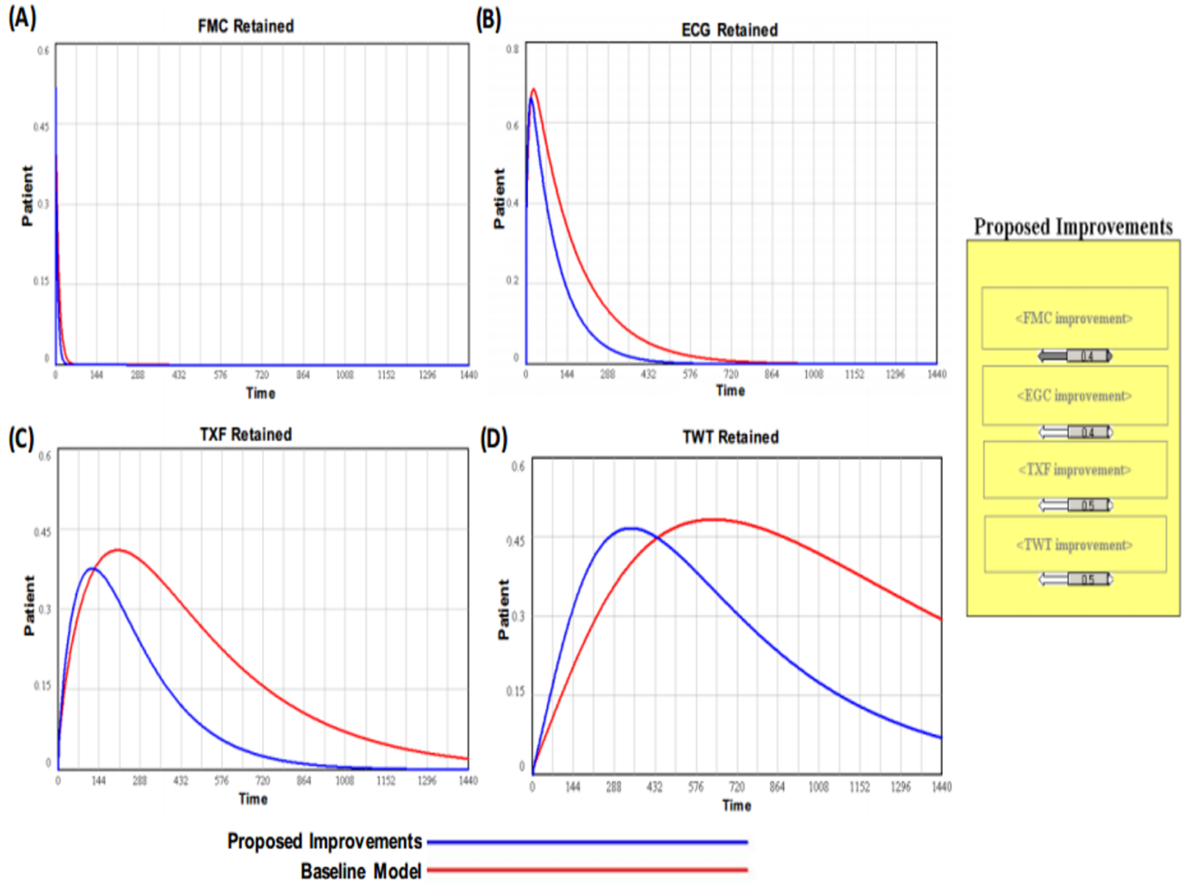

Figure 5. Dashboard to calibrate the model: X axis represents time patients are retained in each process and Y axis represents the percent of patients retained. The right box present the proposed improvement of each variable.

We executed 20,000 simulations where the model parameters changed each time with the aim to understand the behavioral boundaries of a model and test the robustness of policies. The Figure 6, representing the proposed improvements, shows the reduction in the retention time of STEMI patients, by performing these simulations. It is expressed as the probability of occurrence, the range in yellow color indicates that 50% of the results obtained are in this range, 75% of the results are shown in the range yellow plus green, 95% are in the range green plus blue plus yellow band and 100% within the range of the results of all the tracks.

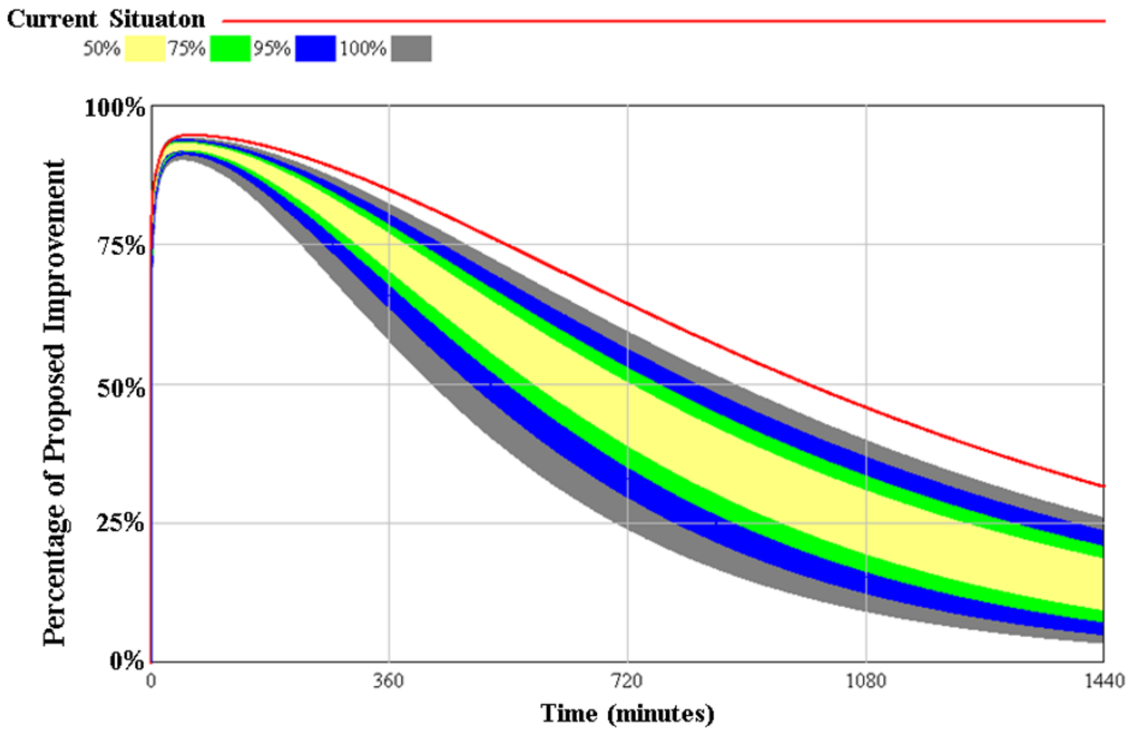

Figure 6. Sensitivity analysis for 20,000 simulations. Total retained means percent of patients (0 to 100%) retained on all processes.

Discussion

This is the first study to analyze the delays associated with care of STEMI patients and the factors behind such delays, using on-site observation, interviews, medical records analysis, qualitative comparative analysis (QCA), system dynamic modeling, mediated modeling and sensitivity analysis. This study identified four primary areas causing delays in treatment of STEMI patients from initial medical attention until their transfer from the primary hospital to the PCI center. These stages and their average delays in minutes were calculated based on the differences considering the gold standards recommended by the American Heart Association and European Cardiology Society [2,7]. According to these recommendations, the ideal time for each of these stages were 10 minutes for FMC and ECG and 20 minutes for TXF and TWT, resulting in the Door-in Door-out time of less than 30 minutes. Based on these criteria, the average delays in each stage at the primary hospital investigated were: a) FMC: 7 min, b) ECG: 28 min, c) TXF: 75 min, d) TWT: 78 min. Through the interviews, we were also able to identify three factors related with these delays: a) professionals, b) equipment and c) the logistics of transporting the patient. Corroborating these findings, other studies also have concluded that delays in the treatment of STEMI patients are caused by many hospitals not having the proper conditions including primary resources of personnel, equipment and good logistical planning to achieve the Door-in Door-out according to the recommended guideline's time of less than 30 minutes [2,6,52].

The qualifications of health professionals and the promotion of health education to the general population depends on the social, technological and economic development of each country [53]. In Brazil, different factors may be related to the unpreparedness of health professionals and lack of medical specialists in the public sector. These include: a) Inconsistent training of health professionals and the existence of gaps between the recommended national curriculum guidelines and the minimum curriculum applied by some universities; b) Disparities in the distribution of medical specialists in Brazil (between rural and urban areas, between rich and poor regions); c) Limited vacancies for specialty residency programs compared to candidates numbers; and d) Financial reasons, owing to the very low residency scholarship many physicians instead choose to have several jobs with salaries generally 3-4 times greater than the scholarship [54-57].

Our results were also consistent with other studies that focused on the relationship between the lack of proper professional training and the delays in care to STEMI patients. In addition, there was also a consensus among researchers about the need for health curriculum reform in Brazil [58-59].

Another issue highlighted by this study was the widespread use of older equipment, specifically electrocardiogram machines. Rapid technological advancement over the past two decades has allowed for almost instant ECG transmission by internet through mobile and wireless technologies. Unfortunately, such technology is not available in most Brazilian hospitals, particularly within primary hospitals where faxing an ECG by phone is the main mode of transmission of an ECG to a PCI center. The quick transmission of an ECG to a PCI center is well known to reduce time from FMC-to-balloon catheter inflation at a PCI center [60-64].

Internationally, the recommended door-to-balloon time has decreased to less than 90 minutes within tertiary hospitals [50]. Now the challenge lies in reducing the time encompassing a patient's presentation to a primary hospital, STEMI diagnosis, and their transfer to the PCI center [52]. Our results were also similar to other studies where it was observed that delays in interhospital transfer of patients was a major predictor of increased ischemic time and higher mortality in the first year [11,16,17]. A study performed in Illinois, USA, analyzed the interhospital transfer time of STEMI patients that needed PCI from a non-PCI-capable hospital to PCI-capable hospital and concluded that approximately two thirds of the delays were due to problems related with patient transport and the logistics associated with this transfer [45].

The rapid transfer of patients from primary hospitals to PCI center has proven to be a great challenge for emergency medical services worldwide [16-18,62,65].

The periodical American Heart Association guidelines publications that have occurred in the past ten years have oriented and improved the health professional practice in the cardiology field [66]. However, the challenge is to overcome the local problems and limitations related with the different factors that may increase the STEMI patient Door-in Door-out delay time in developing countries.

A deeper analysis of these local difficulties is paramount to identify the specific measures to improve the STEMI patients' treatment mainly in the countries and regions with high rates of STEMI morbidity and mortality. These areas include: ECG transmission capabilities, proper training of physician and nurse team to interpret ECG and identify the STEMI cases, improvement of the contact between patient and the cardiologist, proper inter-hospital transfer of STEMI patients, and continuous program of service quality.

In our work, using SD modeling, the main stages identified as the causes of delays for STEMI patients care within a primary hospital were analyzed and it was demonstrated that an improvement of 40 to 50% in each of these stages would reduce the delay, approximating optimal acceptable levels. It is important to note that the SD model only provides results if all participants, especially the hospital managers, are willing to suggest solutions. In the present work, information was obtained from physicians, nurses and managers from primary hospital allowing a broader viewpoint of the service and its potential problems. Thus, the generated SD model is in agreement with the current operation status of the investigated primary hospital. If new guidelines for treatment to STEMI patients arise or if there are changes in the structure of the service, an updated SD model can be easily generated allowing the identification of the main factors related with the delays and defining the measures to reduce it.

The SD model generated in the present work was created to analyze the delays in treatment of STEMI patients at a primary hospital and it took into account the influence of variables encountered at each stage of the care process. The proposed improvements based on such a model will depend heavily on factors such as the organizational structure and proper training of health professionals.

However, the implementation of the necessary modifications in the primary hospital may be hampered by the limited capacity of the managers of the health services to make decisions under internal and external pressures arising from political requests unrelated to the health system. However, the generated SD model can still be used to orientate these decisions.

As limitation of the present study was not to focus on health professionals other than those that work within the primary hospital, such as professionals in the EMS service or within the PCI center in order to identify other possible factors related with the delay of STEMI patients care at the primary hospital. Future studies could investigate these other services related with STEMI patients care.

The present study indicates that integrating qualitative and quantitative data and SD mediated modeling may contribute to a deeper understanding of the different factors related with delay in STEMI patients' treatment. We believe this research model can help the decision makers in providing the best care for STEMI patients, to experiment with new prevention policies, look for improvements in the process and consequently decrease the rate of mortality and complications after a cardiac event.

Acknowledgments

We would like to thank Ms. Sarah Williams for assistance with the final editing of our manuscript.

References

1. World Health Organization (2013) The top 10 causes of death. Available:http://who.int/mediacentre/factsheets/fs310/en/index1.html. Accessed 2013 October 2.

2. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, et al. (2013) ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 61: e78–140.

3. Jollis JG, Granger CB, Henry TD, Antman EM, Berger PB, et al. (2012) Systems of care for ST-segment-elevation myocardial infarction: a report from the American Heart Association's Mission: Lifeline. Circ Cardiovasc Qual Outcomes 5: 423–428.

4. Victor SM, Gnanaraj ASV, Pattabiram S, Mullasari AS (2012) Door-to-balloon: where do we lose time? Single center experience in India. Indian Heart J 64: 582–587.

5. Park YH, Kang GH, Song BG, Chun WJ, Lee JH, et al. (2012) Factors related to prehospital time delay in acute ST-segment elevation myocardial infarction. J Korean Med Sci 27: 864–869.

6. Herrin J, Miller LE, Turkmani D, Nsa W, Drye EE, et al. (2011) National performance on Door-in to Door-out time among patients transferred for primary percutaneous coronary intervention. Arch Intern Med 171: 1879–1886.
7. Steg PG, James SK, Atar D, Badano LP, Blo¨mstrom-Lundqvist C, et al. (2012) ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The task force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J 33: 2569–2619.
8. Nielsen PH, Maeng M, Busk M, Mortensen LS, Kristensen SD, et al. (2010) Primary angioplasty versus fibrinolysis in acute myocardial infarction long-term follow-up in the Danish acute myocardial infarction 2 trial for the DANAMI-2 investigators. Circulation 121: 1484–1491.
9. Lassen JF, Hans EB, Terkelsen CJ (2013) Timely and optimal treatment of patients with STEMI. Nat Rev Cardiol 10: 41–48.
10. de Andrade L, Zanini V, Batilana AP, de Carvalho EC, Pietrobon R, et al. (2013) Regional disparities in mortality after ischemic heart disease in a Brazilian state from 2006 to 2010. PLoS One 8: e59363.
11. Miedema MD, Newell MC, Duval S, Garberich RF, Handran CB, et al. (2011) Causes of delay and associated mortality in patients transferred with ST-segment-elevation myocardial infarction. Circulation 124: 1636–1644.
12. Khraim FM, Carey MG (2009) Predictors of pre-hospital delay among patients with acute myocardial infarction. Patient Education and Counseling 75: 155–161.
13. Giuliani E, Lazzerotti S, Fantini G, Guerri E, Serantoni C, et al. (2010) Acute myocardial infarction – from territory to definitive treatment in an Italian province. J Eval Clin Pract 16: 1071–1075.
14. Franco B, Rabelo ER, Goldemeyer S, Souza EN (2008) Patients with acute myocardial infarction and interfering factors when seeking emergency care: implications for health education. Rev Latino-Am Enfermagem 16: 414–418.
15. Goldberg RJ, Steg PG, Sadiq I (2002) Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). J Am Coll Cardiol 89: 791–796.
16. Mahmoud KD, Gu YL, Nijsten MW, de Vos R, Nieuwland W, et al. (2013) Interhospital transfer due to failed prehospital diagnosis for primary percutaneous coronary intervention: an

observational study on incidence, predictors, and clinical impact. Eur Heart J Acute Cardiovasc Care 2: 166–175.

17. De Luca G, Biondi-Zoccai G, Marino P (2008) Transferring patients with ST-segment elevation myocardial infarction for mechanical reperfusion: A meta-regression analysis of randomized trials. Ann Emerg Med 52: 665–676.

18. Carneiro JKR, Junior LHD, Chaves ALA, Coutinho MMV, Oliveira MDR, et al. (2005) Immediate fibrinolysis or patient transfer for primary angioplasty in acute myocardial infarction with ST segment elevation? When and how to transfer? Rev Bras Cardiol Invas 13: 32–36.

19. Larson DM, Henry TD (2008) Reperfusion options in ST-elevation myocardial infarction patients with expected delays. Curr Cardiol Rep 10: 415–423.

20. Terkelsen CJ, Sørensen JT, Maeng M, Jensen LO, Tilsted HH, et al. (2010) System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA 304: 763–771.

21. Rathore SS, Epstein AJ, Nallamothu BK, Krumholz HM (2006) Regionalization of ST-segment elevation acute coronary syndromes care: putting a national policy in proper perspective. J Am Coll Cardiol 47: 1346–1349. doi: 10.1016/j.jacc.2005.11.053

22. Soares JS, Souza NR, Nogueira Filho J, Cunha CC, Ribeiro GS, et al. (2009) Treatment of a cohort of patients with acute myocardial infarction and ST-segment elevation. Arq Bras Cardiol 92: 464–471.

23. Khan SA, Kukafka R, Payne PR, Bigger JT, Johnson SB (2007) A day in the life of a clinical research coordinator: observations from community practice settings. Study Health Technol Inform 129: 247–251.

24. Thilo C, Bluthgen A, Scheidt WV (2013) Efficacy and limitations of a STEMI network: 3 years of experience within the myocardial infarction network of the region of Augsburg - HERA. Clin Res Cardiol 102: 905–914.

25. Sterman JD (2000) Business Dynamics: Systems thinking and modeling for a complex world. McGraw Hill.

26. Saltelli A, Chan K, Scott M (2000) Sensitivity Analysis. Wiley Series in Probability and Statistics. New York: John Wiley and Sons.

27. Brazil. Ministry of Health (2011) Rede de Urgência e Emergência. Linha do cuidado do Infarto Agudo do Miocárdio na rede de atenção às urgências. Available: http://portal.saude.gov.br/portal/arquivos/pdf/linha_cuidado_iam_rede_atencao_urgencia.pdf. Accessed 2013 October 21.

28. Tong A, Sainsbury P, Craig J (2007) Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 19: 349–57.
29. Bauer MW (2002) Análise de conteúdo clássica: uma revisão. In: M. W. Bauer & G. Gaskell (Orgs.). Pesquisa qualitativa com texto, imagem e som: um manual prático (Tradução de Pedrinho A. Guareschi). Petrópolis: Vozes.
30. Bardin L (1977) Análise de Conteúdo. Lisboa: Edições 70.
31. Minayo MCS (1996) Pesquisa Social: Teoria, Método e Criatividade. 6th Edition. Petrópolis: Editora Vozes.
32. Silverman D (2006) Interpreting qualitative data, methods for analyzing talk, text and interaction. 3rd Edition. London, Thousands Oaks and New Delhi: Sage Publications.
33. NVivo (2012) Qualitative data analysis software; QSR International Pty Ltd. Version 10. Available: http://www.qsrinternational.com/products_nvivo.aspx. Accessed: 2013 Nov 10.
34. Bates D, Chambers J, Dalgaard P, Falcon S, Gentleman R, et al.. (2013) The R Project for Statistical Computing. Available: http://www.r-project.org/. Accessed: 15 September 2013.
35. Ragin CC (1987) The comparative method: Moving beyond qualitative and quantitative strategies. Berkeley: University of California Press.
36. Fiss PC (2007) A set-theoretic approach to organizational configurations. Academy of Management Review 32: 1180–1198.
37. Ragin CC (2008) Redesigning social inquiry: fuzzy sets and beyond. Chicago, University of Chicago Press.
38. Cronqvist L, Berg-Schlosser D (2009) Multi-Value QCA (mvQCA). In Configurational Comparative Methods: Qualitative comparative analysis (QCA) and related techniques, eds. B. Rihoux and C. C. Ragin. London: Sage Publications.
39. Rihoux B (2006) Qualitative comparative analysis (QCA) and related systematic comparative methods: Recent advances and remaining challenges for social science. Research International Sociology 21: 679–706.
40. Marx A, Dusa A (2011) Crisp-set qualitative comparative analysis (csqca), contradictions and consistency benchmarks for model specification. Methodological Innovations 6: 103–148.
41. Thiem A, Dusa A (2013) QCA: A package for qualitative comparative analysis. The R Journal 5/1: 87–97.
42. Dusa A (2010) A mathematical approach to the boolean minimization problem. Quality & Quantity 44: 99–113.

43. Hug S (2013) Qualitative comparative analysis: how inductive use and measurement error lead to problematic inference. Political Analysis 21: 252–265.

44. Wang TY, Nallamothu BK, Krumholz HM, Li S, Roe MT, et al. (2011) Association of Door-In to Door-Out time with reperfusion delays and outcomes among patients transferred for primary percutaneous coronary intervention. JAMA 305: 2540–2547.

45. Aguirre FV, Varghese JJ, Kelley MP, Lam W, Lucore CL, et al. (2008) Rural interhospital transfer of ST-elevation myocardial infarction patients for percutaneous coronary revascularization: The stat heart program. Circulation 117: 1145–1152.

46. Forrester JW (1969) Urban Dynamics. Pegasus Communications. Pegasus Communications, Inc.

47. Sterman J (2004) Appropriate summary statistics for evaluating the historical fit of system dynamics models. Dynamica 10: 51–66.

48. Hines J (2005) Molecules of structure: Building blocks for SD Models. Version 2.02. Available: http://www.systemswiki.org/images/a/a8/Molecule.pdf. Accessed: 2013 Dec 3.

49. Ventana Systems, Inc. (2011) Vensim DSS. Available: http://vensim.com/vensim-software/#vensim-61c. Accessed: 2013 November 5.

50. Van den Belt MJ (2004) Mediated modeling. A system dynamics approach to environmental consensus building. Washington: Island Press.

51. Oliva R (2003) Model calibration as a testing strategy for system dynamics models. European Journal of Operational Research 151: 552–568.

52. Miedema MD, Newell MC, Duval S, Garberich RF, Handran CB, et al. (2011) Causes of delay and associated mortality in patients transferred with ST-segment-elevation myocardial infarction. Circulation 124: 1636–1644.

53. Frigotto G (1996) Citizenship and technical-vocational training: challenges for the end of the century. In: Silva LH, Azevedo JC, Santos ES, organizadores. New cultural maps, new educational perspectives. Porto Alegre: Sulina.

54. Feitosa-Filho GS, Loureiro CMC, Almeida NR, Mascarenhas VN, Camarugy TC, et al. (2012) Reasons alleged by recently graduated physicians at Salvador/BA in 2010 to not attend the residency entrance exam. Rev Bras Clin Med 10: 91–94.

55. Seegmüller EF, Gielon R, Behrens MA, Lima Jr E (2008) Formação Médica: uma proposta diante das demandas da sociedade. Experiência da Pontifícia Universidade Católica do Paraná-PUCPR. Tuiuti: Ciência e Cultura 39: 9–22.

56. Lacerda A, Massignan AG, Vinholi A, Simões JC (2012) Reflexão crítica sobre o mercado de trabalho dos médicos no Brasil. Rev Med Res 14: 193–199.

57. Beltrame RL, Alonso M (2006) A formação do médico: um debate à luz das diretrizes curriculares nacionais. Pontifícia Universidade Católica de São Paulo - PUC-SP. Available: http://www.sapientia.pucsp.br//tde_busca/arquivo.php?codArquivo=2485. Accessed: 2014 March 17.

58. Lino MM, Calil AM (2008) Teaching critical/intensive care in nursing education: a moment of reflexion. Rev Esc Enferm USP 42: 777–783.

59. Loch A, Lwin T, Zakaria IM, Abidin IZ, Wan Ahmad WA, et al. (2013) Failure to improve door-to-needle time by switching to emergency physician-initiated thrombolysis for ST elevation myocardial infarction. Postgrad Med J 89: 335–339.

60. Peacock WF, Bhatt DL, Diercks D, Amsterdam E, Chandra A, et al. (2008) Cardiologists' and emergency physicians' perspectives on and knowledge of reperfusion guidelines pertaining to ST-segment-elevation myocardial infarction. Tex Heart Inst J 35: 152–161.

61. Marcolino MS, Brant LC, Araujo JG, Nascimento BR, Castro LR, et al. (2013) Implementation of the myocardial infarction system of care in city of Belo Horizonte, Brazil. Arq Bras Cardiol 100: 307–314.

62. Hutchison AW, Malaiapan Y, Jarvie I, Barger B, Watkins E, et al. (2009) Prehospital 12-lead ECG to triage ST-elevation myocardial infarction and emergency department activation of the infarct team significantly improves door-to-balloon times: ambulance Victoria and MonashHEART Acute Myocardial Infarction (MonAMI) 12-lead ECG project. Circ Cardiovasc Interv 2: 528–34.

63. Sejersten M, Sillesen M, Hansen PR (2008) Effect on treatment delay of prehospital teletransmission of 12-lead electrocardiogram to a cardiologist for immediate triage and direct referral of patients with ST-segment elevation acute myocardial infarction to primary percutaneous coronary intervention. Am J Cardiol 101: 941–946.

64. Clemmensen P, Sejersten M, Sillesen M, Hampton D, Wagner GS, et al. (2005) Diversion of ST-elevation myocardial infarction patients for primary angioplasty based on wireless prehospital 12-lead electrocardiographic transmission directly to the cardiologist's handheld computer: a progress report. Journal of Electrocardiology 38: 194–198.

65. Thilo C, Bluthgen A, von Scheidt W (2013) Efficacy and limitations of a STEMI network: 3 years of experience within the myocardial infarction network of the region of Augsburg - HERA. Clin Res Cardiol 102: 905–914.

66. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, et al. (2004) ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice

Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). Circulation 110: e82–292.

3 CAPÍTULO III

3.1 Conclusões

As análises realizadas neste trabalho inferiram as seguintes conclusões:

1) Ocorreu presença de autocorrelação espacial positiva para as taxas médias suavizadas de mortalidade por DIC no estado do Paraná, ou seja, cidades com altas taxas de mortalidade de DIC estão rodeadas por cidades com altas taxas de mortalidade de DIC.
2) A alta taxa de mortalidade por DIC dentro das regionais de saúde não se restringiu a variáveis socioeconômicas e demográficas, mas também é dependente da distância de cada município para o centro de referência em cardiologia intervencionista, demonstrando que fatores geográficos desempenham um papel significativo na mortalidade por DIC dentro das cidades.
3) O número de centros de referência em cardiologia intervencionista no estado do Paraná, Brasil, não é suficiente.
4) Há uma necessidade de melhorar a assistência prestada por hospitais primários em cidades onde o tempo entre o serviço e transporte para o centro de referência em cardiologia intervencionista é longo.
5) Identificou-se quatro áreas principais que causam atrasos no tratamento de pacientes com IAMCSST dentro do hospital primário (*Door-In to Door-Out*), ou seja, do atendimento médico inicial até a transferência para o centro de referência em cardiologia intervencionista.
6) Através das entrevistas foram identificados três fatores relacionados com os atrasos: a) conhecimento limitado dos profissionais, b) equipamentos defasados e c) a logística de transporte do paciente (encaminhamento incorreto por parte do serviço de atendimento móvel de urgência).
7) Utilizando o modelo de dinâmica de sistemas (SD) foi demonstrado que pode ocorrer uma melhoria de 40 a 50% em cada etapa onde ocorrem os atrasos.
8) O modelo SD gerado está de acordo com o status de operação atual do hospital primário investigado. Se surgirem novas diretrizes para o tratamento de doentes com IAMCSST ou se houver mudanças na estrutura do serviço, uma atualização do modelo pode ser facilmente gerada.
9) As melhorias propostas com base no modelo vai depender muito de fatores, tais como a estrutura organizacional e formação adequada dos profissionais de saúde.

10) Acreditamos que o modelo de SD possa ajudar os tomadores de decisão a oferecer o melhor atendimento para os pacientes em um menor tempo possível, buscando melhorias no processo e, consequentemente, diminuindo as taxas de mortalidade e de complicações após um evento cardíaco.

3.2 Perspectivas futuras

Acessibilidade plena, equipamentos modernos, associado à uma melhor formação dos profissionais de saúde são os pontos-chave para diminuir a taxa de mortalidade por DIC no Estado do Paraná. Os resultados encontrados neste estudo mostram que fatores pré e intra-hospitalares são determinantes para o atraso no atendimento dos pacientes com IAMCSST e consequentemente elevam significativamente as taxas de mortalidade por DIC dentro das cidades.

Futuros estudos integrando sistemas de informações geográficas, dados qualitativos, quantitativos e modelagem baseada na dinâmica de sistemas, em diferentes regiões do país, podem contribuir para uma compreensão mais profunda das causas e fatores associados com atraso no tratamento de pacientes com IAMCSST, resultando em melhorias adequadas necessárias para reduzir as altas taxas de mortalidade no Brasil.

Alguns desdobramentos possíveis a partir desta tese seriam:

1) Quais seriam as taxas e a distribuição espacial de mortalidade por DIC no estado do Paraná que ocorrem antes do transporte para um centro de referência cardiológica intervencionista?

2) Verificar se ocorrem diferenças significativas nas taxas de mortalidade e no atendimento inicial do IAMCSST entre duas regionais de saúde com dinâmicas distintas no estado do Paraná e com centros de referência em cardiologia intervencionista, em termos de tempo de atendimento em hospitais primários, distâncias médias de viagem para os centros de referência cardiológica intervencionista e características socioeconômicas dos municípios que compõe essa regional de saúde.

3) Investigar sobre o conhecimento acerca das recomendações propostas pela *American Heart Association* para o tratamento inicial do IAMCSST por parte de médicos e enfermeiros que atuam em hospitais primários.

4) Verificar se os pacientes diagnosticados com IAMCSST através do ECG de 12 derivações na ambulância atingiram as recomendações das diretrizes internacionais (tempo ambulância-balão), e além disso verificar se os centros de referência em cardiologia intervencionista diminuíram o seu tempo porta-balão, devido a melhora do atendimento na fase pré-hospitalar.

5) Aplicação de simulação geoespacial para verificar a necessidade de alocação de novos centros de referência em cardiologia intervencionista, como também estações de ambulâncias para agilizar o atendimento e diminuir o tempo de transporte em áreas urbanas e rurais.

6) Integração de sistemas de informação geográfica (SIG) e modelagem baseada em agentes (ABM) para simular atendimento de pacientes que dão entrada em um hospital primário com sintomas sugestivos de infarto agudo do miocárdio.