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Carlos Alberto da Silva Magliano

**Preferências dos pacientes entre angioplastia e cirurgia de revascularização miocárdica:
um experimento de escolha discreta.**

Rio de Janeiro

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Tese apresentada ao Programa de Pós-graduação em Saúde Pública, da Escola Nacional de Saúde Pública Sergio Arouca, na Fundação Oswaldo Cruz, como requisito parcial para obtenção do título de Doutor em Saúde Pública.

Orientadora: Dra. Claudia Cristina de Aguiar Pereira

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Banca Examinadora

Dra Marisa da Silva Santos
Instituto Nacional de Cardiologia

Dr Roberto Magalhães Saraiva
Fundação Oswaldo Cruz - Instituto Nacional de Infectologia Evandro Chagas

Dra Paula Mendes Luz
Fundação Oswaldo Cruz – Instituto Nacional de Infectologia Evandro Chagas

Dr Cosme Marcelo Furtado Passos da Silva
Fundação Oswaldo Cruz – Escola Nacional de Saúde Pública Sergio Arouca

Dra Claudia Cristina de Aguiar Pereira (Orientadora)
Fundação Oswaldo Cruz – Escola Nacional de Saúde Pública Sergio Arouca

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Dedico esta tese a meu pai, Nilton, minha mãe, Lizabeti, irmão Sandro, esposa Adriana e filhas Carolina e Beatriz, que sempre torceram pelo meu sucesso me apoiando nesta fase, cada um à sua maneira.

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RESUMO

A angioplastia coronariana e a cirurgia de revascularização miocárdica representam as atuais formas de manejo para a revascularização miocárdica. Muitos ensaios clínicos compararam estes tratamentos em diferentes condições clínicas e apresentaram recomendações acerca da melhor opção terapêutica com base na redução de desfechos desfavoráveis, principalmente morte, infarto, acidente vascular cerebral e necessidade de repetição do procedimento. Tais estudos exercem papel fundamental guiando a prática médica e o desenvolvimento de diretrizes.

Comumente, os desfechos são analisados de maneira combinada (desfecho composto) em uma categoria chamada MACE (sigla em inglês para *major adverse cardiovascular events*). Porém, a escolha de quais desfechos incluir na análise ou qual a importância relativa (peso) de cada um deles são fatores que permanecem indefinidos. A omissão de desfechos importantes ou conclusões baseadas em desfechos compostos (que admitem pesos iguais para desfechos fatais e não fatais) podem gerar recomendações que não representam a perspectiva dos pacientes.

O objetivo desta tese é identificar quais desfechos são importantes na escolha entre angioplastia e cirurgia aberta, ranqueá-los e determinar o seu peso relativo considerando a perspectiva dos pacientes.

Após revisão sistemática da literatura e entrevistas realizadas no Instituto Nacional de Cardiologia, foram identificados 14 atributos. Estes atributos foram ranqueados e receberam pontos de acordo com sua relevância, onde se observaram diferenças significativas tanto na ordem quanto nos valores quando comparadas as respostas dos médicos e pacientes.

Os quatro atributos selecionados para avaliação do peso relativo através de experimentos de escolha discreta foram: morte perioperatória, morte em cinco anos, infarto em cinco anos e necessidade de repetir o procedimento em cinco anos. A cirurgia aberta foi a escolha da maioria (73%) dos pacientes, julgada como um procedimento mais definitivo. Notadamente, como implicação prática dos achados desta tese, ao considerar a importância relativa dos atributos em combinação com dados nacionais, foi possível estimar que uma parcela significativa dos pacientes passasse a escolher a angioplastia, caso o risco de reintervenção fosse reduzido dos valores atuais, em torno de 25%, para uma taxa inferior a 18%. Esta redução de risco é passível de ser alcançada caso sejam disponibilizados no SUS os *stents* farmacológicos de segunda geração.

Palavras-chave: Preferência do paciente. Isquemia miocárdica. Angioplastia. Revascularização miocárdica. Experimentos de escolha discreta.

ABSTRACT

Percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) represent the current treatment options for myocardial revascularization. Several clinical trials have compared these two treatments in different clinical conditions, and their results were compared based on the capacity of each procedure in reducing unfavorable outcomes, mainly death, myocardial infarction, stroke and the necessity to repeat revascularization. Such clinical trials play a crucial role in guiding medical practice and guidelines.

These outcomes have been often analyzed as a composite outcome called MACE (major adverse cardiovascular events). However, which outcomes should be included or their relative importance (weight) are still not defined. The possible omission of outcomes considered important by patients or conclusions based on composite outcomes that admit equal weights for fatal and non-fatal outcomes may generate recommendations that do not represent patients' preferences.

This thesis aimed to elicit the relevant outcomes, rank them, and identify their relative weights considering patients' perspective.

After a systematic review of the literature and interviews at the Instituto Nacional de Cardiologia (National Institute of Cardiology), 14 attributes were identified. After ranking and rating the attributes, significant differences were found in the relative importance of the outcomes and also between doctors and patients. Among the 14 attributes, four (perioperative death, death within five years, infarction within five years and the necessity to repeat the procedure within five years) were selected to be used in discrete choice experiments. Most patients (73%) chose CABG over PCI, judging it as a more definitive option. Notably, considering the relative importance of the attributes and the Brazilian national database, it is possible to estimate that patients would choose PCI only if their rate of reintervention was reduced from the current values, around 25%, to less than 18%, which could be achieved if the second-generation drug-eluting stents were available in the Brazilian National Health System.

Keywords: patient' preferences (preferências do paciente). Myocardial ischemia (isquemia miocárdica). Angioplasty (angioplastia). Myocardial revascularization (revascularização miocárdica). Discrete Choice Experiment (Experimentos de escolha discreta).

LISTA DE ABREVIATURAS E SIGLAS

AVC	Acidente vascular cerebral
CABG	<i>Coronary Artery Bypass Graft</i>
CAD	<i>Coronary Artery Disease</i>
CRM	Cirurgia de Revascularização Miocárdica
DAC	Doença Arterial Coronariana
DCE	<i>Discrete Choice Experiment</i>
ICP	Intervenção Coronariana Percutânea
INC	Instituto Nacional de Cardiologia
INMETRO	Instituto Nacional de Metrologia, Normalização e Qualidade Industrial
MACE	<i>Major Adverse Cardiovascular Events</i>
PCI	<i>Percutaneous Coronary Intervention</i>
RP	<i>Revealed preference</i>
SP	<i>Stated Preference</i>

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APRESENTAÇÃO

Esta Tese de Doutorado buscou identificar e avaliar as preferências dos pacientes internados no Instituto Nacional de Cardiologia (INC) em relação a dois tratamentos de revascularização miocárdica: intervenção coronariana percutânea (ICP) ou angioplastia versus a cirurgia de revascularização miocárdica (CRM) ou cirurgia aberta.

Os resultados estão apresentados sob o formato de quatro artigos, antecedidos pela contextualização do problema de pesquisa, objetivos, perguntas de pesquisa, métodos e resumo dos achados no texto introdutório.

O primeiro artigo apresentou uma revisão sistemática sobre estudos de preferências declaradas em pacientes enfrentando o *trade-off* entre ICP e CRM, identificando-se atributos, sua relevância de acordo com pacientes e médicos, além dos métodos utilizados para obtenção das preferências. O artigo foi aceito para publicação na *Patient Preference and Adherence* em 2 de dezembro de 2018.

O segundo artigo, já publicado na *Patient Preference and Adherence* em 8 de maio de 2018, avaliou a viabilidade do uso de figuras e cenários hipotéticos com diferentes riscos para a obtenção de respostas economicamente racionais em pacientes internados no INC, método utilizado no quarto trabalho.

O terceiro artigo, também já publicado na *Patient Preference and Adherence*, em 8 de maio de 2018, apresenta como foram evocados os atributos e como estes foram ranqueados para posterior inclusão nos cenários do quarto trabalho.

O quarto trabalho é resultado de entrevistas realizadas com pacientes no INC, utilizando-se como método o experimento de escolhas discretas, onde os pacientes entrevistados fizeram escolhas entre a ICP e a CRM com base em cenários hipotéticos e níveis que refletem a realidade brasileira de mortalidade perioperatória. Tais cenários foram criados com o formato e com os atributos reportados nos trabalhos anteriores. A síntese dos resultados encontrados está contemplada nas considerações finais.

INTRODUÇÃO

As doenças cardiovasculares, compostas pela doença arterial coronariana (DAC) e o acidente vascular cerebral (AVC) representam a maior causa de mortalidade no mundo. O tratamento da DAC envolve além da prevenção, orientação dietética, atividade física e terapêutica medicamentosa, dois procedimentos invasivos: a intervenção coronariana percutânea (ICP) e a cirurgia de revascularização miocárdica (CRM) (1).

A ICP, também denominada como angioplastia, é realizada na sala de hemodinâmica, diferenciando-se da CRM principalmente por não necessitar de toracotomia. A escolha conflitante ou o *trade-off* entre estes dois procedimentos envolve vários aspectos, alguns favoráveis à ICP (ausência de cicatriz cirúrgica da esternotomia, menor tempo de internação, recuperação mais rápida, menor mortalidade perioperatória) outros à CRM, que dependendo do quadro clínico, poderá oferecer menor risco de morte e infarto a médio prazo e principalmente menor necessidade de reintervenção (2).

A ICP foi desenvolvida em 1977, quando a estenose coronariana passou a ser abordada com a técnica de cateter balão, trazendo como principal desvantagem elevados índices de reestenose (retorno da estenose arterial que pode causar piora clínica e necessidade de reintervenção) (3). Em 1986, foram implantados os primeiros dispositivos metálicos (*stents*) no local da placa ateromatosa após o tratamento com o balão. A principal função dos *stents* é a redução da reestenose. Apesar dos *stents*, a taxa de reestenose permaneceu elevada, variando entre 15% a 40% em 6 meses (4), levando à introdução dos *stents* farmacológicos em 1999 (5). Mais recentemente, com a introdução dos *stents* de última geração, as taxas absolutas de reestenose e reintervenção foram reduzidas para valores em torno de 11% (6) a 12% (7).

CARACTERIZAÇÃO DO PROBLEMA E JUSTIFICATIVA DO ESTUDO

O médico possui a obrigação de apresentar ao paciente as opções de tratamento disponíveis, suas vantagens e desvantagens, incluindo possíveis complicações do próprio tratamento. Como apresentar as diferentes probabilidades de sucesso e insucesso aos pacientes é uma tarefa desafiadora. O entendimento de que a falta de informação ou de consentimento sobre procedimentos médico-hospitalares viola direitos do paciente e justifica a condenação de hospitais e médicos ao pagamento de indenização por danos morais e materiais foi consolidado no Informativo de Jurisprudência do Superior Tribunal de Justiça (Informativo nº 0632, publicado em 28/09/2018).

“É uma prestação de serviços especial a relação existente entre médico e paciente, cujo objeto engloba deveres anexos, de suma relevância, para além da intervenção técnica dirigida ao tratamento da enfermidade, entre os quais está o dever de informação. O dever de informação é a obrigação que possui o médico de esclarecer o paciente sobre os riscos do tratamento, suas vantagens e desvantagens, as possíveis técnicas a serem empregadas, bem como a revelação quanto aos prognósticos e aos quadros clínico e cirúrgico, salvo quando tal informação possa afetá-lo psicologicamente, ocasião em que a comunicação será feita a seu representante legal. O princípio da autonomia da vontade, ou autodeterminação, com base constitucional e previsão em diversos documentos internacionais, é fonte do dever de informação e do correlato direito ao consentimento livre e informado do paciente e preconiza a valorização do sujeito de direito por trás do paciente, enfatizando a sua capacidade de se autogovernar, de fazer opções e de agir segundo suas próprias deliberações. Haverá efetivo cumprimento do dever de informação quando os esclarecimentos se relacionarem especificamente ao caso do paciente, não se mostrando suficiente a informação genérica. Da mesma forma, para validar a informação prestada, não pode o consentimento do paciente ser genérico (*blanket consent*), necessitando ser claramente individualizado. O dever de informar é dever de conduta decorrente da boa-fé objetiva e sua simples inobservância caracteriza inadimplemento contratual, fonte de responsabilidade civil per se. A indenização, nesses casos, é devida pela privação sofrida pelo paciente em sua autodeterminação, por lhe ter sido retirada a oportunidade de ponderar os riscos e vantagens de determinado tratamento, que, ao final, lhe causou danos, que poderiam não ter sido causados, caso não fosse realizado o procedimento, por opção do paciente. O ônus da prova quanto ao cumprimento do dever de

informar e obter o consentimento informado do paciente é do médico ou do hospital, orientado pelo princípio da colaboração processual, em que cada parte deve contribuir com os elementos probatórios que mais facilmente lhe possam ser exigidos.”

A decisão da conduta médica deve ser adotada conjuntamente entre o médico e paciente ou seu responsável, após esclarecimento acerca dos possíveis danos e benefícios, incorporando, na medida do possível, suas preferências.

Muitos ensaios compararam a eficácia e segurança da ICP versus a CRM (8-13), porém não foi identificado nestes estudos um levantamento acerca das preferências dos pacientes. Ensaio na área da cardiologia frequentemente apresentam resultados através de desfechos compostos, um agregado de mortalidade, taxa de infarto, AVC e reintervenções. O uso de desfechos compostos é justificado como uma tentativa de expressar o efeito global de um tratamento, além de economizar tempo e recursos (14). Porém, o uso de desfechos compostos envolve premissas questionáveis: 1) importância semelhante de todos os desfechos (por exemplo, o risco de morte e o risco de repetir o procedimento seriam igualmente importantes na escolha dos tratamentos) e 2) médicos e pacientes possuem perspectivas semelhantes quanto ao problema em questão.

Caso os pacientes não considerem estes desfechos como tendo a mesma importância ou caso os pacientes os julguem de maneira diferente dos decisores, as conclusões destes ensaios podem levar a tomadas de decisão que não refletem a escolha de maior utilidade (conceito econômico atribuído ao prazer ou satisfação que os indivíduos sentem pelo consumo de bens ou serviços).

Uma solução potencial seria avaliar adequadamente o peso relativo de cada componente do desfecho composto. Braunwald, na década 90, foi o primeiro autor a apresentar a ideia de criar pesos relativos para cada componente dos desfechos (15). Mais recentemente, Pandit (2), Chow (16), Ahmad (14) e seus colaboradores identificaram resultados semelhantes, confirmando que os pacientes valorizam de forma diferente os atributos utilizados em desfechos compostos e também com pesos diferentes em relação aos médicos.

No estudo de Ahmad et al. os autores entrevistaram 113 pacientes e através de uma escala visual, compararam a importância de vários atributos em relação à morte. Foram avaliados: AVC com e sem sequela, ataque cardíaco sem causar morte, morte pelo procedimento, angina e necessidade de repetir a angioplastia ou a cirurgia. O peso de cada desfecho foi multiplicado por sua incidência e os resultados foram utilizados para reanalisar os dados de uma metanálise de sete estudos derivados de uma revisão

sistemática que compararam a angioplastia com *stents* farmacológicos versus a cirurgia. Antes de aplicar os pesos, a cirurgia era a melhor intervenção, pois a angioplastia apresentava maior risco de eventos adversos combinados, OR 1,44 (IC 1,10 a 1,87). Após aplicar o peso relativo de acordo com a perspectiva dos pacientes a cirurgia perdeu o valor estatístico (OR 1,22, IC 0,97 a 1,53).

Definir o peso relativo de cada desfecho que será utilizado para a tomada de decisão é essencial, por exemplo, quando a análise de ensaios randomizados comparando a ICP com *stents* farmacológicos versus a cirurgia para o desfecho MACE não inclui “repetir a revascularização”, não é identificada diferença entre os tratamentos (OR 0,95, IC 0,73 a 1,24) (14). Identificar o quanto os pacientes valorizam repetir a ICP torna-se então fundamental na tentativa de identificar qual tratamento representaria a opção de sua preferência.

Atualmente, o método de estudo de preferências mais utilizado em saúde para a obtenção dos pesos relativos de cada desfecho é o experimento de escolhas discretas (*discrete choice experiment* - DCE) (17).

EXPERIMENTOS DE ESCOLHAS DISCRETAS

Conceitos relativos à exploração do método de preferências declaradas através da análise conjunta teve início em 1964 com o trabalho de Luce e Tukey (20). Os autores estabeleceram o pressuposto de que a definição do quanto determinado produto ou serviço é desejável é função do valor de suas partes separadas e que inconscientemente criamos sistemas de pontuação para definir a atratividade total de cada oferta. Estes pontos não diretamente observados das partes que compõem a oferta são chamados em inglês de *part-worths*. A soma dos *part-worths* fornece a utilidade total que, quanto maior, torna a opção mais atraente e com maior probabilidade de ser escolhida.

Os experimentos de escolhas discretas representam um método de avaliação de preferências declaradas (18). Entende-se como preferências declaradas a realização de escolhas através de simulações com opções hipotéticas. Duas ou mais alternativas são apresentadas dentro de um cenário criado pelo entrevistador e o entrevistado deve fazer sua escolha levando em consideração as características de cada opção. De maneira divergente, a técnica da preferência revelada baseia-se nas observações das escolhas reais do indivíduo tomadas em um determinado momento e não em cenários hipotéticos (19).

Enquanto a principal crítica aos modelos com preferências declaradas é a natureza hipotética das questões que podem levar a respostas diferentes caso o cenário fosse real, a maior limitação da preferência revelada está na identificação das decisões que os usuários fariam caso se defrontassem com situações que não tenham vivenciado no passado ou na hipótese do lançamento de uma alternativa inovadora (19).

A escolha discreta ocorre quando um indivíduo faz uma escolha entre um conjunto de alternativas finitas, mutuamente exclusivas e que contemplam todas as possibilidades. As alternativas são geralmente apresentadas lado a lado, com recurso a questionários. Cada alternativa é decomposta em função de atributos, e os atributos são apresentados com diferentes níveis. Atributo é o termo utilizado para a característica de um produto, como a cor ou o preço de um veículo. Níveis são as diferentes alternativas que podem ter um atributo, por exemplo: preta ou branca (níveis do atributo cor). Ao variarmos sistematicamente os atributos (e os níveis dos atributos) e observando como os respondentes reagem aos perfis de produtos criados, torna-se possível deduzir estatisticamente os escores (*part-worths*).

De acordo com a teoria maximização da utilidade, um indivíduo irá escolher a alternativa que representa o melhor conjunto de atributos de acordo com seu julgamento

pessoal de valor ou preferência. A alternativa (intervenção, bem ou consumo) com o melhor conjunto de atributos terá maior utilidade.

Por exemplo, na escolha da compra de um imóvel, o comprador iria avaliar diversos atributos como o tamanho do imóvel (os níveis seriam as diferentes áreas), localização (os níveis seriam o bairro ou a rua do imóvel), preço (os níveis seriam os diferentes custos) e etc. Seria improvável supor que o imóvel mais espaçoso e melhor localizado fosse o mais barato então existe um *trade-off* entre os atributos: você estaria disposto a morar distante da localização ideal para ter um imóvel maior? Quanto distante ou quanto maior?

A partir das escolhas dos compradores poderíamos identificar o quanto cada atributo influenciou na escolha, ou seja, o seu peso na preferência. No exemplo do imóvel, como foi considerado também o custo, seria possível ainda avaliar a disposição a pagar pelo acréscimo de 1 metro quadrado de área do imóvel ou para que este esteja localizado em determinada região. Fácil entender a importância da escolha dos atributos para a construção dos cenários, pois os atributos conjuntamente representarão as opções e todo *trade-off* será com base na relação entre os atributos utilizados.

Um serviço médico ambulatorial, segundo o conceito da análise conjunta, poderia ser avaliado de acordo com o nível de atenção da equipe médica, tempo de espera, custos financeiros entre outros aspectos que conjuntamente dariam uma ideia do quanto aquele serviço tem de valor, que será proporcional ao quanto o indivíduo valoriza cada uma destas características. A avaliação de produtos com base em múltiplos elementos (atributos) analisados conjuntamente gerou o termo análise conjunta.

Especificamente na questão entre a angioplastia coronariana versus a cirurgia aberta, seria implausível supor que, se o paciente foi previamente submetido a um dos procedimentos, independentemente se angioplastia ou cirurgia aberta, este representaria sua preferência (revelada). A definição da conduta cirúrgica é multifatorial, considerando-se critérios tais como a extensão da doença coronariana, função ventricular, comorbidades, recursos e preferências da equipe médica. Assim, para avaliar a preferência dos pacientes entre angioplastia e cirurgia aberta, foi escolhido nesta tese como o método ideal as preferências declaradas.

Os níveis dos atributos devem ser apresentados de maneira realística, incluindo os possíveis valores extremos. Por exemplo, no quarto artigo desta tese, o risco de repetir a angioplastia variou de 13 a 35%, incluindo no extremo inferior valores próximos aos resultados recentes com *stents* de última geração (em torno de 12%) e no limite superior as

altas taxas do estudo Syntax no subgrupo de lesão de tronco e escore Syntax > 33, cuja taxa de revascularização em 5 anos foi de 34,1% (6,7). Considerando um comportamento linear, a regressão condicional permitirá estimarmos o quanto o aumento de 1% no risco de repetir o procedimento afetará na probabilidade daquela intervenção ser escolhida.

Em avaliações econômicas, considera-se como um comportamento racional a maximização da utilidade, ou seja, cada vez que um indivíduo escolhe, ele estará atuando racionalmente se escolher a opção de maior utilidade. A utilidade pode ser quantificada numericamente, de maneira que poderemos predizer qual decisão é mais útil e quanto mais útil. Com a obtenção dos pesos relativos de cada atributo tornar-se-ia possível então estimar preferências, representadas pelas alternativas com maior valor final no somatório de valores dos escores.

A escolha dos atributos e de seus níveis e a obtenção dos escores para toda a variedade de atributos que serão incluídos como representativos do bem ou serviço é um desafio. Nesta tese, os atributos e níveis representativos da ICP e da CRM foram selecionados após uma combinação de dados da literatura, elencados através da revisão sistemática, e de entrevistas presenciais com pacientes e especialistas do Instituto Nacional de Cardiologia, no Rio de Janeiro, Brasil.

OBJETIVO GERAL

Avaliar as preferências dos pacientes internados no INC em relação à ICP versus a CRM para o tratamento da doença coronariana estável.

OBJETIVOS ESPECÍFICOS

1. Identificar quais atributos são considerados importantes, na perspectiva dos pacientes, para a escolha entre ICP e CRM.
2. Identificar nos ensaios publicados até o momento, quais métodos (*ranking, rating, DCE e etc.*) foram utilizados para a avaliação das preferências dos pacientes em relação ao tratamento com ICP ou CRM.
3. Identificar se pacientes internados em tratamento cardiológico são capazes de dar respostas economicamente racionais e robustas para cenários hipotéticos envolvendo riscos através de entrevistas presenciais e com o auxílio de figuras.
4. Identificar a importância relativa dos principais atributos que são utilizados no processo de decisão entre a ICP e a CRM na perspectiva dos pacientes internados no INC.

MÉTODOS

Para a evocação dos atributos e descrição dos métodos utilizados até o momento na identificação das preferências dos pacientes em relação ao tratamento da doença coronariana foi realizada uma revisão sistemática da literatura (estudo 1). Para identificar se os pacientes internados em tratamento cardiológico são capazes de dar respostas economicamente racionais para cenários hipotéticos envolvendo riscos foram utilizados os métodos detalhadamente descritos no estudo 2. A definição da importância relativa dos principais atributos e o processo de seleção dos atributos e níveis para servirem de base dos cenários do experimento de escolhas discretas estão detalhados no estudo 3. Por fim, o método utilizado no experimento de escolhas discretas é descrito no estudo 4.

ESCOLHA DO LOCAL DE PESQUISA E PARTICIPANTES

O INC foi escolhido por conveniência, além de ser um hospital federal, público, de caráter terciário, frequentado por pacientes de múltiplas localidades e diferentes níveis sociais.

Os pacientes foram selecionados através da geração randômica de números representativos dos leitos. A escolha de pacientes internados reduz o maior risco de viés dos estudos de preferência, o viés hipotético, causado pela desatenção ou desinteresse em opinar entre escolhas hipotéticas as quais o participante não terá a responsabilidade financeira ou que se submeter aos resultados. Em teoria, pacientes envolvidos com o problema de saúde pesquisado estariam mais atentos e interessados em cooperar com a pesquisa (17).

COMITÊ DE ÉTICA EM PESQUISA

Parecer consubstanciado do CEP da Escola Nacional de Saúde Pública Sergio Arouca aprovando o projeto data de 04 de maio de 2017, CAAE 63684017.0.0005240, parecer número 2.046.648.

APRESENTAÇÃO DA TESE

A apresentação desta tese foi estruturada com base em quatro artigos, quais sejam:

1. *Patient preferences for coronary artery disease: a systematic review.*

Trabalho realizado no intuito de mapear os estudos de preferências declaradas envolvendo ICP e CRM, identificando possíveis divergências entre médicos e pacientes em relação à importância de cada atributo, quais foram os métodos utilizados para definição das preferências e listar quais atributos foram considerados quando avaliado o *trade-off* entre ICP e CABG.

A revisão sistemática foi realizada de acordo com a recomendação PRISMA. As bases Medline, EMBASE e Lilacs foram utilizadas com uma estratégia de busca que combinou termos para a identificação de estudos envolvendo doença coronariana, angioplastia ou cirurgia em estudos de preferências declaradas.

Dentre 735 estudos identificados na busca inicial, seis foram selecionados. Os dados não foram sintetizados em metanálises devido ao caráter qualitativo. Houve uma concordância dos autores em relação a divergência do valor relativo de cada desfecho entre médicos e pacientes. Por exemplo, o AVC foi considerado, apenas pelos pacientes, como um atributo mais importante do que a morte. Um atributo com tal grau de importância deve ser melhor definido em futuros ensaios clínicos, ao menos subdividido entre AVC com e sem sequela neurológica.

Os métodos para avaliação das preferências foram heterogêneos: ranqueamento, graduação (com diferentes escalas), *standard gamble*, *willingness to pay*, escala visual analógica, regressão logística e *discrete choice experiment*. A ausência de um método comum para extração de preferências limita a combinação ou comparação dos resultados.

Por fim, a análise destes estudos possibilitou elencar 14 atributos: angina, AVC, cicatriz da esternotomia, infecção, insuficiência cardíaca, insuficiência renal, fibrilação atrial, infarto do miocárdio, morte a longo prazo, morte perioperatória, pseudoaneurisma, repetir a angioplastia, repetir a cirurgia e tempo de internação.

A identificação dos atributos é uma etapa importante dos estudos de preferência, e a lista de atributos elencada neste trabalho pode servir de base a futuros estudos acerca do tratamento da doença coronariana. Ranqueados com a população de interesse, os atributos identificados podem alicerçar a criação de desfechos combinados, ajudar na definição da

importância relativa de cada desfecho e consequentemente na identificação da superioridade de uma intervenção e no desenho de novos ensaios clínicos, que devem definir e apresentar adequadamente o impacto das intervenções em todos os desfechos importantes. Os 14 atributos identificados serviram ainda de base para o terceiro artigo, onde foram ranqueados com pacientes e cardiologistas do INC.

Outro achado que reforça a importância desta tese é a escassez de estudos de preferências na área da doença coronariana e a sua total ausência na América Latina.

2. Feasibility of visual aids for risk evaluation by hospitalized patients with coronary artery disease: results from face-to-face interviews.

A comunicação sobre riscos e probabilidades entre médicos e pacientes é uma tarefa desafiadora e a utilização de figuras é considerada a melhor forma de apresentação (21, 22). A adequada compreensão dos diferentes percentuais de riscos apresentados em um DCE é essencial para a obtenção de respostas racionais e que reflitam as reais preferências dos participantes. Cientes das possíveis limitações de entendimento, principalmente em uma população com baixo nível educacional, objetivou-se neste estudo avaliar o uso de figuras representando diferentes níveis de risco de mortalidade perioperatória e sobrevida em longo prazo. Escolhas consideradas economicamente racionais e análises qualitativas foram utilizadas para atestar a viabilidade da técnica nesta população.

As entrevistas foram realizadas por um cardiologista (autor desta tese) e duas enfermeiras, treinadas e supervisionadas pelo autor, no Instituto Nacional de Cardiologia (INC), hospital público especializado em cardiologia.

O estudo utilizou uma amostra de conveniência de pacientes hospitalizados com DAC estável, a maioria deles aguardando um procedimento de revascularização coronariana. Os entrevistados foram selecionados aleatoriamente com base no número do leito usando uma lista de números aleatórios gerados pelo Microsoft Excel®. Escolhemos pacientes com DAC porque julgamos que eles estariam mais comprometidos com as entrevistas do que qualquer amostra alternativa da população em geral.

A elegibilidade dos pacientes para participar do estudo foi determinada pelos seguintes critérios de inclusão: diagnóstico de DAC atualmente sendo considerado para um tratamento de revascularização; concordância em participar de uma entrevista e responder perguntas sobre preferências em relação a possíveis complicações do tratamento e permitir que a entrevista fosse gravada. Os participantes foram considerados inelegíveis se já tivessem sido submetidos à cirurgia, angioplastia, ou se acreditassem incapazes de entender o experimento.

Entrevistas individuais e presenciais foram realizadas entre 1 de agosto e 20 de novembro de 2017. Os pacientes foram convidados a imaginar que seu médico estava buscando sua contribuição na decisão sobre qual tratamento representava a melhor opção

para eles. Os recursos visuais foram usados como uma estratégia para apoiar a comunicação.

Como não foram utilizados rótulos de tratamento, os pacientes fizeram suas escolhas entre a opção “A” e a opção “B”, considerando apenas os diferentes benefícios e riscos mostrados em cada cenário. Os riscos e benefícios foram representados pelas diversas proporções de pacientes que morreram durante o período perioperatório e em cinco anos. O principal *trade-off* foi um aumento no risco de morrer durante o tratamento em benefício de uma maior sobrevida a longo prazo (5 anos). Os pacientes eram estimulados a explicar suas escolhas, e as respostas foram gravadas. Cada participante avaliou os mesmos oito cenários.

Os pressupostos básicos foram: 1) morrer na cirurgia é pior (menos utilidade) do que morrer em cinco anos; 2) morrer em cinco anos é pior do que estar vivo em cinco anos; 3) cada indivíduo escolheu de acordo com suas preferências, optando pela alternativa que julgou apresentar maior utilidade; 4) a escolha seria independente do rótulo, A ou B.

De acordo com a teoria econômica (axioma de continuidade), esperávamos que nos dois primeiros cenários, os pacientes escolhessem a opção “A”, devido ao seu menor risco de morte perioperatória e morte em cinco anos. O terceiro e sexto cenários tiveram as mesmas probabilidades, sendo a única diferença os rótulos. As opções foram invertidas; consequentemente, esperávamos que quem escolhesse a opção “A” no terceiro cenário escolheria “B” no sexto e vice-versa. O quarto cenário continha uma opção dominada, apresentada como opção “A” e o oitavo cenário apresentava as mesmas probabilidades porém a opção dominante era a “B”. Esperávamos que os sujeitos escolhessem a opção “A” no quarto e a opção “B” no último cenário.

Todas as entrevistas foram gravadas em áudio no formato digital. Os dados foram transcritos e devidamente comparados com as versões de áudio para detectar erros. Em seguida, os dados foram revisados em busca de ideias ou conceitos repetidos, que foram agrupados em categorias. Uma análise qualitativa foi realizada sobre as respostas transcritas dos pacientes, preservando os termos usados para justificar suas escolhas. Tais termos foram catalogados em grupos com significados semelhantes. Nenhum programa de análise de dados foi usado para executar essa tarefa. O critério utilizado para encerrar a coleta de dados foi a saturação teórica.

Os pacientes, em sua maioria, declararam entender o experimento e forneceram respostas racionais. Os principais fatores limitantes identificados para utilização de cenários hipotéticos foram a heurística (pacientes que focaram apenas em resultados de

curto prazo) e a religiosidade (12% dos pacientes desconsideraram os riscos e benefícios apresentados, creditando à vontade divina seu futuro).

Atestar a possibilidade do uso de figuras e identificar suas limitações para expressar diferentes probabilidades de risco foi essencial para a realização dos experimentos de escolha discreta no quarto trabalho.

3. *Patient and physician preferences for attributes of coronary revascularization.*

Neste trabalho, os objetivos foram: identificar, ranquear e graduar os atributos mais importantes para pacientes e médicos no processo decisório entre ICP e CRM. Além dos atributos identificados na revisão sistemática, foram pesquisados através de entrevistas presenciais com médicos e pacientes do INC, possíveis outros fatores relevantes neste *trade-off*.

A coleta de dados foi realizada por um cardiologista (autor desta tese) e duas enfermeiras, treinadas e supervisionadas pelo autor, no INC. Utilizamos uma amostra de conveniência de pacientes hospitalizados com DAC estável, aguardando por um procedimento de revascularização coronariana. Os entrevistados foram selecionados aleatoriamente com base no número do leito, usando uma lista de números aleatórios gerados no Microsoft Excel®. Escolhemos pacientes com DAC, uma vez que assumimos que eles estariam mais comprometidos com as entrevistas do que qualquer população de amostra alternativa.

A elegibilidade dos pacientes para participar do estudo foi determinada pelos seguintes critérios de inclusão: diagnóstico de DAC atualmente internado para um tratamento de revascularização e concordância em gravar uma entrevista respondendo perguntas sobre possíveis complicações da revascularização. Os participantes foram considerados inelegíveis se já tivessem sido submetidos à cirurgia, angioplastia, ou se o próprio se julgasse incapaz de entender o experimento.

Entrevistas individuais foram realizadas entre 1 de agosto e 20 de novembro de 2017. Os pacientes foram convidados a imaginar que estavam compartilhando o processo de tomada de decisão sobre qual opção de tratamento era melhor para eles entre ICP e CRM e responder um questionário semi-estruturado. As perguntas foram apresentadas na seguinte sequência: 1) O(a) senhor(a) sabe o motivo da sua hospitalização? 2) Quais os benefícios o(a) senhor(a) espera alcançar com o tratamento? 3) Quais riscos ou complicações podem ocorrer com o tratamento? 4) O que mais lhe preocupa em relação ao tratamento? 5) Considerando não haver diferença na mortalidade entre os dois tratamentos (ICP e CRM), qual prefere? 6) Quais são as diferenças entre cirurgia e angioplastia? A última parte do questionário incluiu perguntas sobre informações demográficas (idade, sexo, etnia, renda e nível de educação).

Todas as entrevistas com cardiologistas foram realizadas pelo autor desta tese. A população do estudo foi uma amostra de conveniência de cardiologistas com experiência

em doença coronariana do INC. A elegibilidade do médico foi determinada de acordo com os seguintes critérios: especialista em cardiologia, disposto a participar de uma entrevista presencial e responder perguntas sobre preferências em relação a possíveis complicações da revascularização. Os especialistas foram solicitados a enumerar os riscos e benefícios que geralmente consideram quando exploram os *trade-offs* entre PCI e CABG.

As entrevistas foram gravadas em áudio no formato digital, e os dados coletados foram analisados qualitativamente. Primeiro, os dados foram transcritos integralmente e devidamente contrastados com as versões de áudio para detectar erros. Em seguida, revisamos os dados para identificar qualquer atributo que não tenha sido previamente elencado na revisão sistemática. O critério utilizado para finalizar a coleta de dados foi a saturação teórica.

O segundo objetivo, além da identificação de novos atributos, foi o de avaliar a importância relativa de cada um e buscar diferenças entre as perspectivas dos pacientes e dos médicos.

Os atributos selecionados na etapa anterior foram apresentados aleatoriamente e individualmente a pacientes e médicos. A quantidade de informações explicativas era equivalente para todos os atributos, e essas informações foram apresentadas de acordo com um roteiro.

A seguinte pergunta pré-estabelecida foi apresentada a todos os pacientes: “Considere que você tem angina, uma dor no peito que indica um problema cardíaco. Suas opções de tratamento são: tratamento clínico, angioplastia (cateterização com colocação de *stent*) ou cirurgia. Esses diferentes tratamentos estão relacionados a diferentes benefícios e riscos. Eu tenho uma lista de possíveis complicações resultantes desses tratamentos, e gostaria de saber como você está preocupado em relação a cada um deles. Por favor, coloque em ordem de relevância de um a catorze os riscos que serão apresentados, ou seja, um sendo o mais importante e quatorze o menos importante”.

A seguinte pergunta pré-estabelecida semelhante foi apresentada a todos os médicos: “Imagine que você é responsável por definir o tratamento de um paciente com queixas anginosas. As opções de tratamento disponíveis incluem o ajuste de medicamentos, angioplastia com *stents* ou cirurgia de revascularização miocárdica. Esses diferentes tratamentos estão relacionados a diferentes benefícios e riscos. Eu tenho uma lista de possíveis complicações desses tratamentos e gostaria de saber o quanto o(a) senhor(a) está preocupado com cada um deles. Por favor, coloque em ordem de relevância de uma a catorze os riscos que serão apresentados, ou seja, um sendo o mais importante e

quatorze o menos importante”.

Após o ranqueamento, os participantes foram convidados a distribuir dez pontos de tal maneira que os atributos mais relevantes recebessem proporcionalmente mais pontos. O participante foi solicitado a definir a proporção considerando a importância relativa de cada atributo. Não havia limite para quantos pontos cada atributo poderia receber. Foi possível reordenar os atributos durante esta fase. Este método é conhecido como *dotmocracy*.

As entrevistas duraram cerca de 15 minutos cada. Participaram 76 respondentes, 22 cardiologistas com tempo médio de formado de 15,6 anos e 54 pacientes (32 para elicitación e 22 para classificação).

As entrevistas com cardiologistas e pacientes não acrescentaram novos atributos e os 14 previamente identificados na revisão sistemática foram utilizados. Notavelmente, os pacientes exibiram desconforto quando encorajados a citar possíveis complicações e alegaram que não haviam falado com seus médicos sobre o assunto. As complicações mais citadas pelos pacientes foram morte (68,75%) e acidente vascular cerebral (50%).

Identificamos uma diferença significativa no valor dado pelos pacientes e médicos em relação a quatro desfechos: insuficiência renal, fibrilação atrial, morte a longo prazo e morte perioperatória. Esta foi classificada como o desfecho mais importante pelos cardiologistas, enquanto a insuficiência renal foi a mais importante para os pacientes.

Concluindo, as entrevistas com pacientes e médicos não acrescentaram novos atributos, e os atributos mais citados na revisão sistemática de estudos de preferência coincidiram com aqueles utilizados em ensaios clínicos. Essa informação pode indicar que esses atributos são de fato os mais relevantes, ou pode refletir o impacto de resultados de ensaios publicados anteriormente sobre o racional na decisão.

Nosso estudo tem como importante limitação a ausência de níveis dos atributos. Como premissa, consideramos que apresentar vários atributos com diferentes níveis resultaria em uma demanda cognitiva excessiva, assim, os atributos foram fornecidos sem informações sobre as taxas de incidência. Caso a insuficiência renal tivesse sido apresentada como uma complicação rara, talvez não a tivessem julgado como a mais importante e passassem a valorizar aquelas complicações mais frequentes, como a necessidade de reprocimento.

Uma questão relevante para futuros estudos é saber se os médicos ponderaram em suas decisões todos os atributos relevantes para o paciente ou apenas aqueles apresentados nos ensaios clínicos.

4. *Patients' preferences for coronary revascularization: discrete choice experiments.*

Constatada a escassez de dados referentes às preferências dos pacientes em relação à ICP e CRM (estudo 1), a viabilidade do uso de cenários hipotéticos para obtenção de preferências (estudo 2) e após a identificação dos atributos mais relevantes na perspectiva dos pacientes (estudo 3), no quarto estudo desta tese foi realizado um estudo do tipo experimentos de escolhas discretas.

Para viabilizar cognitivamente a construção dos cenários do DCE, apenas quatro dentre 14 atributos elencados na revisão sistemática foram selecionados. Os critérios para esta seleção foram a relevância sob a perspectiva dos pacientes e ter uma diferença significativa na incidência entre ICP e CRM, pois um atributo de risco com a mesma probabilidade de ocorrer em ambas as opções de tratamento não ajudaria a escolher um deles.

Os quatro atributos selecionados foram: morte perioperatória, mortalidade em cinco anos, taxa de infarto do miocárdio em cinco anos e risco de necessidade de refazer o tratamento em cinco anos. O risco de morte perioperatória foi apresentado em três níveis: 1%, 2% ou 3% para ICP e 4%, 6% e 8% para CRM. Esses níveis foram selecionados com base na média da mortalidade perioperatória da ICP (2,2%) e da revascularização miocárdica (6,2%) de acordo com os dados do DATASUS anos 2016 e 2017. Os demais atributos também foram apresentados em três níveis, com valores selecionados a partir de uma metanálise de estudos comparando a cirurgia de revascularização miocárdica versus angioplastia com *stents* farmacológicos.

A apresentação dos quatro atributos, cada um apresentando três níveis diferentes para cada alternativa foi distribuída em 12 cenários, com todas as combinações de atributos e níveis apresentadas o mesmo número de vezes (balanceado). O desenho experimental foi realizado com o programa Ngene, considerando um desenho ortogonal e eficiente. Cada participante respondeu aos mesmos 12 cenários, apresentados em ordem aleatória e com duas opções de escolha, angioplastia ou cirurgia.

Para testar a compreensão dos entrevistados, foram incluídos dois cenários extras: Uma opção dominada, na qual a opção angioplastia deveria ser a escolhida por representar a opção menos invasiva e associada a menores riscos de morte, infarto do miocárdio ou necessidade de refazer o tratamento e, a segunda verificação foi uma repetição do primeiro cenário, onde buscou-se avaliar se o paciente manteria a escolha realizada entre o primeiro

e o último cenário, caso contrário sua resposta seria considerada irracional, independente se por incompreensão dos riscos, desatenção ou fadiga.

Para serem considerados como tendo apresentado um comportamento racional os entrevistados deveriam ter variado suas escolhas entre os cenários, ter escolhido PCI no cenário dominado e ter mantido sua escolha inicial quando o mesmo cenário fosse reapresentado. Menos da metade dos pacientes (44%) completaram os três passos pré-estabelecidos como critério de racionalidade. Entre os 159 entrevistados, 60 (37,7%) não escolheram a opção dominada e 19 (11,9%) não mantiveram a escolha quando o mesmo cenário foi reavaliado.

A regressão logística condicional foi utilizada para analisar as escolhas dos pacientes. Os quatro atributos de risco entraram no modelo como variáveis contínuas e lineares. Somente as escolhas das 12 tarefas experimentais foram incluídas na análise. As análises foram conduzidas incluindo as respostas em dois subgrupos, uma considerando todos os entrevistados e o outro apenas pacientes com respostas racionais.

Uma vez que as preferências dos pacientes para os atributos de risco são estimadas, é possível calcular taxas marginais de substituição (TMS). A TMS indica o quanto os pacientes estão dispostos a sacrificar de um atributo para obter mais de outro atributo.

Cada alternativa apresenta uma equação de utilidade representada pelo somatório das multiplicações dos níveis dos atributos pelo vetor de valor extraído pela regressão logística. A equação da utilidade da angioplastia pode ser expressa com a seguinte fórmula:

$$\bullet \quad V_{\text{Angioplastia}} = \beta_1 + \beta_2 * \text{morte_periop_a} + \beta_3 * \text{iam_a} + \beta_4 * \text{morte_a} + \beta_5 * \text{repetir_a}.$$

Onde $V_{\text{Angioplastia}}$ é a utilidade obtida com a angioplastia;

β_1 é o intercepto, neste caso representa a média de valor do rótulo angioplastia em relação à cirurgia;

$\beta_2 * \text{morte_periop_a}$ é o valor do peso médio da morte perioperatória com a angioplastia multiplicado pelo nível da mortalidade perioperatória com angioplastia;

$\beta_3 * \text{iam_a}$ é o valor do peso médio do infarto do miocárdio com a angioplastia multiplicado pelo nível do risco de infarto com a angioplastia;

$\beta_4 * \text{morte_a}$ é o valor do peso médio da morte em cinco anos com a angioplastia multiplicado pelo nível da mortalidade em cinco anos com angioplastia;

$\beta_5 * \text{repetir_a}$ é o valor do peso médio de repetir a angioplastia em cinco anos multiplicado pelo nível do risco de repetir a angioplastia em cinco anos.

A equação da utilidade da cirurgia pode ser expressa com a seguinte fórmula:

$$\bullet \quad V_{\text{cirurgia}} = \beta_6 * \text{morte_periop_c} + \beta_7 * \text{iam_c} + \beta_8 * \text{morte_c} + \beta_9 * \text{repetir_c}.$$

Onde V_{cirurgia} é a utilidade obtida com a CRM;

$\beta_6 * \text{morte_periop_c}$ é o valor do peso médio da morte perioperatória com a cirurgia multiplicado pelo nível da mortalidade perioperatória com a cirurgia;

$\beta_7 * \text{iam_c}$ é o valor do peso médio do infarto do miocárdio com a cirurgia multiplicado pelo nível do risco de infarto com a cirurgia;

$\beta_8 * \text{morte_c}$ é o valor do peso médio da morte em cinco anos com a cirurgia multiplicado pelo nível da mortalidade em cinco anos com a cirurgia;

$\beta_9 * \text{repetir_c}$ é o valor do peso médio de repetir a cirurgia em cinco anos multiplicado pelo nível do risco de repetir a cirurgia em cinco anos.

Exponenciando as utilidades, é possível estimar a probabilidade de uma opção ser escolhida dada pela fórmula: $\text{Probabilidade} = \exp(V(\beta, X_i) / \sum \exp(V\beta, X_j))$

Dentre os 160 pacientes abordados, 159 declararam compreender e concordaram em participar do estudo. No geral, os pacientes apresentavam fortes preferências negativas na ICP ($-0,65$). Em outras palavras, independentemente da probabilidade de risco, os pacientes foram 48% menos propensos a escolher ICP (*odds ratio* 0,52; 95% IC, 0,38 – 0,72). Este achado, inicialmente incoerente, é possivelmente explicado pelo elevado número de respondedores (84%) internados devido à falha terapêutica da ICP sendo agora necessária nova intervenção.

Em termos práticos e para facilitar a compreensão vamos explorar a relação de apenas dois parâmetros. O β_5 , peso médio do atributo refazer a angioplastia ($-0,034$) e o β_6 ($-0,153$), peso médio do atributo morte perioperatória na cirurgia. Estes parâmetros foram obtidos no modelo de regressão onde a variável resposta era a alternativa escolhida, PCI ou CRM. Os parâmetros possuem valores negativos, significando que quanto mais morte na cirurgia ou necessidade de refazer a angioplastia, pior (menor utilidade) é o cenário. O valor do β_6 é mais negativo do que o β_5 , ou seja, os pacientes valorizam mais a morte do que a necessidade de refazer o procedimento.

Explorando a relação entre o β_6/β_5 ($-0,153/-0,034$), temos uma TMS de 4,5, ou seja, o aumento em 1% no risco de morte perioperatória na cirurgia equivale a um aumento de 4,5% no risco de refazer a angioplastia. Com base na diferença de 4,0% na mortalidade perioperatória (6,2% na CRM – 2,2% na ICP) e no benefício aceitável marginal de 4,5, poderíamos esperar que nossa amostra de pacientes valorizaria a ICP positivamente em relação à CRM se o risco de refazer o procedimento fosse inferior a 18% (4,0%

multiplicado por 4,5).

Notavelmente, esse nível de aceitação é superior ao identificado em estudos recentes com *stents* de segunda geração, 12% no estudo Best (6) com 4,6 anos de seguimento e 11% no estudo Excel (7) com mediana de três anos de seguimento. Com base nos pesos médios, sugere-se que a incorporação dos *stents* de segunda geração no sistema público brasileiro de saúde possa levar a um maior número de pacientes a optar pela ICP.

CONCLUSÕES

A doença coronariana representa um importante problema de saúde pública no Brasil. O melhor entendimento das preferências dos pacientes em relação aos potenciais riscos e benefícios dos tratamentos pode auxiliar na melhor administração dos recursos, pela previsão de futuras demandas ou ampliando ofertas de maior valor.

Os achados desta tese indicam haver a necessidade de revisão das atuais diretrizes de tratamento da doença coronariana, dado que médicos e pacientes possuem perspectivas dispares em relação à importância relativa dos desfechos, apenas uma parcela dos desfechos pontuados como relevantes foram analisados nos ensaios clínicos e as recomendações acerca do melhor tratamento foram realizadas sem considerar uma hierarquia de valor entre os desfechos combinados.

A principal limitação para uma generalização dos dados e sua utilização como referência para a saúde pública está relacionada à amostra. Os dados representam valores dos pacientes entrevistados no Instituto Nacional de Cardiologia e não podem ser generalizados para a população brasileira. Como os dados foram extraídos de pacientes internados em um hospital especializado, cuja significativa maioria (84%) já havia sido submetida a um dos tratamentos, sua experiência prévia possivelmente enviesou os resultados. A cirurgia, escolhida na maioria dos cenários (73%), embora represente o procedimento mais invasivo, traz a vantagem da menor necessidade de reintervenção, que na linguagem leiga era traduzido como “a cirurgia cura”.

Outras limitações incluem a alta taxa de resposta considerada irracional, tanto no trabalho 2, onde cerca de 30% dos pacientes não mantiveram sua escolha inicial quando o cenário foi reapresentado, quanto no experimento de escolhas discretas, onde a maioria dos participantes (60%) falhou em ao menos uma das três etapas do teste de racionalidade. A melhor maneira de explorar respostas irracionais ainda precisa ser estabelecida.

CONTRIBUIÇÕES À SAÚDE PÚBLICA

Apesar das limitações, esta tese traz significativas contribuições ao campo da saúde pública:

- 1) Identificação da carência de estudos de preferência na área da cardiologia, destacando assim um campo para futuras publicações;
- 2) Resumo das atuais evidências acerca das preferências em doença coronariana, com um levantamento dos métodos utilizados para evocação e hierarquização dos atributos;
- 3) Questionamento acerca da fragilidade da utilização de desfechos compostos devido a diferentes valores dos atributos e da diferença de valores entre médicos e pacientes;
- 4) Levantamento com base em uma revisão sistemática de literatura e entrevistas com especialistas e pacientes hospitalizados de uma lista com 14 diferentes atributos que podem servir de base a futuros estudos de preferências na área da cardiologia;
- 5) Ranqueamento e graduação dos 14 atributos evocados pelos pacientes e uma comparação com a perspectiva dos especialistas;
- 6) Discussão acerca da capacidade de compreensão dos pacientes em relação a atributos envolvendo riscos que pode servir de base a futuros estudos de preferências em diferentes áreas do conhecimento;
- 7) Valoração dos principais atributos sob a perspectiva dos pacientes do INC, realizada através de experimentos de escolha discreta.

REFERÊNCIAS BIBLIOGRÁFICAS

1. Cesar LA AD, Gowdak LH, Mansur AP, Bodanese LC, et al. . Diretriz de doença coronariana estável. Arq Bras Cardiol. 2014;103(2Supl.2):1-59.
2. Pandit J, Gupta V, Boyer N, Yeghiazarians Y, Ports TA, Boyle AJ. Patient and physician perspectives on outcomes weighting in revascularization. The POWR study. International journal of cardiology. 2014;177(2):513-4.
3. P.L. da Luz MCS. Reestenose após angioplastia transluminal coronária: o problema clínico. Rev Assoc Med Bras 1997;43(4).
4. Farb A, Sangiorgi G, Carter AJ, Walley VM, Edwards WD, Schwartz RS, et al. Pathology of acute and chronic coronary stenting in humans. Circulation. 1999;99(1):44-52.
5. Iqbal J, Gunn J, Serruys PW. Coronary stents: historical development, current status and future directions. Br Med Bull. 2013;106:193-211.
6. Stone GW, Sabik JF, Serruys PW, Simonton CA, Genereux P, Puskas J, et al. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. The New England journal of medicine. 2016;375(23):2223-35.
7. Park SJ, Ahn JM, Kim YH, Park DW, Yun SC, Lee JY, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. The New England journal of medicine. 2015;372(13):1204-12.
8. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, et al. Strategies for multivessel revascularization in patients with diabetes. The New England journal of medicine. 2012;367(25):2375-84.
9. Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, et al. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. Journal of the American College of Cardiology. 1995;26(7):1600-5.
10. Rodriguez A, Bernardi V, Navia J, Baldi J, Grinfeld L, Martinez J, et al. Argentine Randomized Study: Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in patients with Multiple-Vessel Disease (ERACI II): 30-day and one-year follow-up results. ERACI II Investigators. Journal of the American College of Cardiology. 2001;37(1):51-8.

11. Morrison DA, Sethi G, Sacks J, Grover F, Sedlis S, Esposito R, et al. A multicenter, randomized trial of percutaneous coronary intervention versus bypass surgery in high-risk unstable angina patients. The AWESOME (Veterans Affairs Cooperative Study #385, angina with extremely serious operative mortality evaluation) investigators from the Cooperative Studies Program of the Department of Veterans Affairs. *Controlled clinical trials*. 1999;20(6):601-19.
12. From AM, Al Badarin FJ, Cha SS, Rihal CS. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis of data from the ARTS II, CARDia, ERACI III, and SYNTAX studies and systematic review of observational data. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology*. 2010;6(2):269-76.
13. Kapur A, Hall RJ, Malik IS, Qureshi AC, Butts J, de Belder M, et al. Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients. 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial. *Journal of the American College of Cardiology*. 2010;55(5):432-40.
14. Ahmad Y, Nijjer S, Cook CM, El-Harasis M, Graby J, Petraco R, et al. A new method of applying randomised control study data to the individual patient: A novel quantitative patient-centred approach to interpreting composite end points. *International journal of cardiology*. 2015;195:216-24.
15. Braunwald E, Cannon CP, McCabe CH. An approach to evaluating thrombolytic therapy in acute myocardial infarction. The 'unsatisfactory outcome' end point. *Circulation*. 1992;86(2):683-7.
16. Chow RD, Wankhedkar KP, Mete M. Patients' preferences for selection of endpoints in cardiovascular clinical trials. *J Community Hosp Intern Med Perspect*. 2014;4.
17. Reed Johnson F, Lancsar E, Marshall D, Kilambi V, Muhlbacher A, Regier DA, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2013;16(1):3-13.
18. Bridges JF, Hauber AB, Marshall D, Lloyd A, Prosser LA, Regier DA, et al. Conjoint analysis applications in health--a checklist: a report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2011;14(4):403-13.

19. Mark TL, Swait J. Using stated preference and revealed preference modeling to evaluate prescribing decisions. *Health economics*. 2004;13(6):563-73.
20. H Krantz D. Conjoint Measurement: The Luce-Tukey Axiomatization and Some Extensions 1964. 248-77 p.
21. Harrison M, Rigby D, Vass C, Flynn T, Louviere J, Payne K. Risk as an attribute in discrete choice experiments: a systematic review of the literature. *Patient*. 2014;7(2):151-70.
22. Vass CM, Payne K. Using Discrete Choice Experiments to Inform the Benefit-Risk Assessment of Medicines: Are We Ready Yet? *PharmacoEconomics*. 2017;35(9):859-66.

PATIENTS' PREFERENCES FOR CORONARY REVASCULARIZATION: A SYSTEMATIC REVIEW

Authors

1. First author (correspondent): Carlos Magliano

Affiliation: Instituto Nacional de Cardiologia, INC, Rio de Janeiro, Brazil.

Address: Rua das Laranjeiras 374, 5º andar. Rio de Janeiro, Brasil. CEP 22240-006.

E-mail of the corresponding author: carlosincnats@gmail.com

Telephone number of the corresponding author: +55(21)996802076

2. Andrea Libório Monteiro

Affiliation: Department of Pharmacy Systems, Outcomes and Policy, College of Pharmacy, University of Illinois at Chicago, Illinois, USA.

3. Amanda Rebelo

Affiliation: Instituto Nacional de Cardiologia, INC, Rio de Janeiro, Brazil.

Address: Rua das Laranjeiras 374, 5º andar, NATS. Rio de Janeiro, Brasil. CEP 22240-006.

4. Claudia Cristina de Aguiar Pereira

Affiliation: Escola Nacional de Saúde Pública, ENSP, FIOCRUZ, Rio de Janeiro, Brazil.

Address: Avenida Brasil 4375, Manguinhos. Rio de Janeiro, Brasil. CEP 21040-900.

ABSTRACT

Aims

Guidelines' current recommendations regarding the best treatment option for coronary revascularization are usually based on composite outcomes that were not selected or weighed with patients thence they may fail in representing patients' preferences adequately. This systematic review aimed to appraise existing literature surrounding stated preferences regarding coronary revascularization.

Methods and results

Studies related to stated preferences regarding coronary revascularization were searched on Medline, EMBASE and Lilacs databases. Two reviewers screened all titles independently, and consensus resolved any disagreements. Of 735 total citations, six studies were included and qualitatively synthesized. Notably, the attributes most often cited in these studies coincided with those already used in clinical trials (death, myocardial infarction, stroke and redo revascularization). Half of the studies analyzed the use of composite endpoints and shown the necessity to review this practice since the attributes are weighed differently, and there is a disagreement between patients and physicians. It was still identified a large variety of methods used to elicitate and value the attributes such as rating, ranking, standard gamble, willingness to pay and discrete choice experiments.

Conclusion

Despite a large number of studies comparing revascularization treatments efficacy, there are just a few focusing on patients' preferences. The selection of outcomes to be considered in the trade-off between treatment options and how to weigh them properly, taking into consideration patients' preferences, need to be explored in future trials.

Key Words: "review, systematic"; "preference, patient"; "angioplasty, transluminal, percutaneous coronary"; "bypass surgery", "coronary revascularization".

Patients' Preferences for Coronary Revascularization: A Systematic Review

1. INTRODUCTION

Coronary artery disease (CAD) is the leading cause of mortality worldwide. For patients with symptomatic CAD refractory to medical therapy, there are two revascularization options: percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). The least invasive option is PCI, as it does not require open-heart surgery. On the other hand, CABG is the gold standard approach for some patients, mainly for those with multivessel disease, diabetes, left main coronary disease or left ventricular dysfunction.¹

While cardiologists and surgeons debate on the optimal revascularization method, little is known about the viewpoint of patients. Decision making in illnesses with more than one viable treatment option may involve trade-offs that are valued differently by patients and physicians. Regarding CAD, to elicit patients' preferences may be particularly relevant for the approximately 12% of patients needing coronary revascularization who are eligible for either PCI or CABG.² Patients' preferences can be evaluated according to patient's choice among treatment options, reflecting the importance they place on each treatment attributes.³

There are two methods to measure preferences: 1) Stated-preference (SP), that elicit subjects' preferences for hypothetical options in an experimental framework and 2) Revealed-preference (RP), that are based on individuals' actual behavior in real decision contexts.⁴ In health care, RP data is often unavailable or unfit to characterize patients' preferences, since the consumption of goods is not exclusively determined by their choices, being hard to determine who (patient, caregiver or physician) and why (preferences, patient's clinical characteristics, coronary disease anatomy or the availability of treatments) one option was chosen. In SP, which is experimental, it is possible to control the survey design and to estimate the trade-off between attributes considering the respondents' preferences. The application of SP techniques, such as discrete choice experiments, has become increasingly popular in outcomes researches.

This systematic review aimed to identify stated preferences studies that appraised the trade-off between PCI and CABG for CAD and to survey the attributes identified as important in the choice between treatments, how they were valued; the methods used to elicit preferences; possible differences between patients and physicians regarding the

attributes' importance and to highlight potential areas for further exploration.

2. METHODS

We performed a systematic review of published studies to investigate patient and physician preferences for PCI or CABG. Medline, Embase, and Lilacs databases were searched for studies published in or before 10 January 2017.

Our search terms consisted of keywords for coronary revascularization, as well as methods used to assess patient preferences (e.g., “patient reported outcome”, “patient satisfaction”, “best-worst scaling”, Maxdiff, “discrete choice experiment”, preference, “conjoint studies”, “conjoint choice experiment”, vignette, choice, willingness-to-pay and “conjoint analysis”).

The detailed strategies are included in the supplementary material (Supplementary Table 1). A written study protocol was prepared following the PRISMA statement,⁵ and the review was registered in PROSPERO (systematic review record CRD42016048664) in September 2016.

2.1 Study Selection and data extraction

Inclusion criteria were: stated preference studies regarding CAD treatments. Both patients and physicians' preferences were surveyed. There were no restrictions regarding language. Exclusion criteria: articles with no original data (e.g., review, commentary, editorial, or meeting abstract).

Two reviewers (CM, AL) screened all titles and summaries independently. Articles were excluded at this stage if both reviewers determined that they did not meet the inclusion criteria. Disagreements were resolved by consensus. The same two researchers then reviewed the full text of all remaining articles and extracted data, including information on study design, locations, sample size, participant characteristics, preference elicitation methods, funding sources, and treatment-related attributes associated with patient preferences.

2.2 Data Synthesis and Analysis

We decided a priori not to statistically combine results in a meta-analysis since we expected studies to be methodologically and clinically diverse. Therefore, the results were qualitatively synthesized. The points prioritized were: 1) primary objectives; 2) sample size; 3) preference elicitation methods; 4) sources of financing; 5) attributes evaluated, and 6) differences between physicians and patients' perspectives.

3. RESULTS

3.1 Study Characteristics

Of 735 total citations (436 from Medline, 299 from Embase), 44 articles were eligible for full-text review. We included six studies^{2,6-10} that met our inclusion criteria in the final report (figure 1). Eligible studies were conducted from 1999 to 2015. All studies were cross-sectional, and sample sizes ranged from 53 to 616 participants. Four (67%) studies were performed in the U.S.,^{2, 6, 7, 9} two (33%) in the UK.^{8, 10} None of these studies were funded by pharmaceutical companies.

3.2 Methods Used to Assess Patient Preferences

Methods to evaluate patient preferences for revascularization included the following: rating,^{2, 6-8, 10} ranking,^{2, 10} standard gamble,² willingness to pay,² conjoint analysis,² and discrete choice experiments⁹ (table 1).

3.3 Attributes associated with patient treatment preferences

The attributes most often cited in these studies coincided with those already used in clinical trials: death,⁶⁻⁹ stroke,⁶⁻⁹ myocardial infarction^{6,8} and repeat revascularization.^{2, 7-9} Other attributes examined within studies included: heart attack,⁷ hospitalization,⁷ repeat PCI,⁶ repeat CABG,⁶ atrial fibrillation,⁶ mediastinitis,⁶ postoperative chronic pain,^{2, 6} post-procedural angina,^{6,7} length of stay,^{2,6} duration of recovery,^{2,6} depression,⁶ procedural cost,⁶ incision scar,^{2,6,10} pseudoaneurysm,⁶ pneumonia,⁶ long-term use of clopidogrel,⁶ renal failure,⁶ acute respiratory distress syndrome,⁶ bleeding,⁶ symptom control,¹⁰ medication side effects,¹⁰ comfort in taking medication,¹⁰ well-being,¹⁰ ability to do things,¹⁰ prolong life,¹⁰ and cure.¹⁰

3.4 Main findings

Death, stroke, myocardial infarction, and repeat revascularization are frequently grouped into a category called major adverse cardiovascular events (MACE). The use of MACE has been justified as an attempt to capture the overall treatment effect and it represents a possible way to reduce the duration, sample size and costs of a clinical trial.^{6,7} In this review, from the six studies that evaluated preferences between PCI and CABG, three focused on the utilization of composite endpoints.⁶⁻⁸

In the first one, Pandit et al.⁶ recruited physicians by emailing and patients directly from a cardiac catheterization laboratory. They rated on a scale of 0 to 10, the relative weight each group placed on potential adverse outcomes from either PCI and CABG. The

outcomes selected were: stroke, death, peri-procedural myocardial infarction, acute respiratory distress syndrome, renal failure, repeat CABG, repeat PCI, major bleed, atrial fibrillation, mediastinitis, postoperative chronic pain, post-procedural angina, long-term clopidogrel, pneumonia, length of stay, length of recovery, depression, procedural cost incision scar and pseudoaneurysm (table 1). Patients weighted stroke the heaviest (8.83 out of 10), physicians weighted death the heaviest (8.63), and both groups considered the incision scar as the lightest. There was a statistically significant difference in weighting most outcomes between groups. Notably, patients weighted repeat percutaneous coronary revascularization, a common outcome in MACE, lower than most others (15th out of 20). Based on Pandit's survey, future studies of PCI versus CABG should report more than just MACE.

In the second study,⁷ patients from a primary care practice were asked about the use of single versus composite endpoints in cardiovascular trials and they also should score, on a scale of 1 to 6, the following outcomes: heart attack, death related to heart disease, death from other causes, stroke and hospitalization with chest pain. Participants expressed a preference for composite endpoints. The authors hypothesized that patients must have considered easier to deal with one composite endpoint than to analyze many single endpoints. Importantly, participants did not value the endpoints as being equivalent, most of them indicated that death from heart disease (4.73), heart attack (4.53), death (3.69) and stroke (3.15) were the most relevant endpoints to be included in a trial.

Ahmad et al.⁸ surveyed the relative importance of the components of MACE using a visual analog scale in hospitalized patients and cardiologists. Neither patients nor physicians considered all clinical end points equal. Stroke was found to be worse than death for patients and comparable for doctors. Interestingly, Ahmad et al.⁸ re-analyzed a meta-analysis with seven randomized clinical trials which had compared CABG to PCI. When clinician-weighted event rate was used, CABG was found to be superior, but when the patient-weighted event rate was considered, there was no statistically significant difference.

Composite endpoint was identified as frequently used in clinical trials and even preferable by most patients, supposedly because it is easier to deal with one than to jointly analyze many single endpoints, but since the outcomes have different values, they should be analyzed considering the attributes' weights.

Hornberger et al.² used various techniques of preference assessment (rating, ranking, conjoint analysis, standard gamble, willingness to pay) to evaluate the importance

patients attach to the consequences of coronary revascularization. The outcomes evaluated, in order from the most to the least relevant were: “3-year risk of repeat revascularization”, “50% reduction in post procedure pain”, “time spent in hospital”, “6-week reduction in time needed to resume normal activities” and “body appearance (scar)”. When assessed the extent respondents preferred to avoid repeat revascularization with a standard gamble technique, they became indifferent between PCI and CABG when the risk of repeat PCI was reduced from 50% to 28% (95% CI 25% to 31%). Bowling et al.¹⁰ applied the Coronary Revascularization Outcome Questionnaire (CROQ) among a convenience sample of patients admitted with acute coronary syndrome. PCI was the preferred treatment for 80% of respondents but 83% of patients would accept “any treatment, no matter how extreme, to return their health to what it was.”

Kipp et al.⁹ hypothesized that patients would choose PCI over CABG even if quoted 1-year PCI risks were higher than those observed in the SYNTAX trial. CABG risk estimates remained fixed across all hypothetical risk scenarios, a 1-year risk of death, stroke, and need for a repeat procedure of 3%, 2%, and 5%, respectively, and the PCI risks was randomly generated between death (2%, 4%, or 6%), stroke (1% or 2%), and repeat procedures (7%, 11%, 15%, or 17%). Patients preferred PCI over CABG even if the risk of repeat procedure was three times higher and the risk of death was twofold the CABG risks. Although stroke presented a similar trend, the difference was not statistically significant.

4. DISCUSSION

In this systematic review, we opted to include exclusively stated preferences studies. The rationale for this decision can be broken down as follows: 1) The application of stated preferences studies to elicit patient’s preferences is becoming increasingly popular in the field of health care and medical decision-making,¹¹ so we believe that this work contributes as a roadmap to the evidence that has been generated in regards to current patients preferences. 2) The idiosyncratic characteristics of stated preferences experiments, as for instance the resort to experimental designs to generate paired comparisons, allows researchers to create “ideal conditions” (e.g., orthogonality) to estimate the relative preference weight placed in different features of a health care intervention or treatment. 3) Furthermore, this type of experiment can be tailored to explore the importance placed in features that are not usually explicitly presented to and considered by health care consumers, patients and caregivers or, as shown in this review, to examine the relative

importance of different classic cardiovascular endpoints that are usually reported together as composite outcomes in clinical studies.

Stated preferences studies are, at times, a target of criticism for using paired comparisons of hypothetical scenarios as an instrument to elicit preference weights. Some may argue that such hypothetical scenarios do not represent the choices that would be made in real life.⁴ The selection of stated rather than revealed preferences in the evaluation of the trade-offs between PCI and CABG is justified since it is very unlikely that previous treatments could represent the choices that patients had made. Previous CABG or PCI does not mean that the patient had the opportunity to choose and had selected according to his or her own values.

The attributes identified in the selected studies represent the different aspects that should be considered when sharing the decision between PCI and CABG. According to utility theory, the best option would be represented by the one with the best combination of risks and benefits (and results in utility maximization).¹² These attributes can be ranked in future trials according to different perspectives such as physicians, patients, caregivers or decision makers, and the selection of the attributes to be considered in composite endpoints should ideally take in consideration their relative weights. We ranked and rated 14 attributes with patients and physicians from a tertiary cardiologic hospital in Rio de Janeiro, Brazil and we identified a significant difference between their perspectives¹³ which is in agreement with the findings of Pandit,⁶ Ahmad⁸ and Kipp⁹ studies.

Interestingly, even though coronary disease is considered a health problem worldwide and there was no language limitation in our literature search, it was only possible to identify studies from the USA and UK. Another notable issue identified in this review was the variety of methods to evaluate the preferences such as rating, ranking, standard gamble and discrete choice experiments which highlights the absence of a gold standard method.

All these findings, associated with the low number of published studies and the total absence of studies funded by manufactures and pharmaceutical companies suggest that the interest in the knowledge of the preferences of patients has not yet reached its apex.

5. CONCLUSIONS

The guidelines recommendations on CAD treatments may be based on endpoints

that do not represent patients' preferences properly. The development of knowledge on patients' preferences, values, and fears could inform policy and enable physicians to be more accountable to the public.

Current evidence on preferences between PCI and CABG is sparse and eliciting patients' preferences are fraught with methodological challenges. The preference studies in this systematic review included heterogeneous populations, different methods to elicit preferences and many distinct outcomes.

Despite these limitations, it was possible to identify many important attributes that may serve as the basis for scenarios design in future stated preference studies and to conclude that different outcomes are valued differently by patients and physicians. Future trials should carefully consider if any relevant outcome was omitted, if the outcomes included are clinically meaningful and to weigh them appropriately according to patients' preferences.

6. FUNDING

There was no funding in this study.

7. DISCLOSURE

The authors report no conflicts of interest in this work.

8. REFERENCES

1. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360(10):961-72.
2. Hornberger J, Bloch DA, Hlatky MA, Baumgartner W. Patient preferences in coronary revascularization. *Am Heart J*. 1999;137(6):1153-62.
3. Purnell TS, Joy S, Little E, Bridges JF, Maruthur N. Patient preferences for noninsulin diabetes medications: a systematic review. *Diabetes care*. 2014;37(7):2055-62.
4. Bridges JFP, Onukwugha E, Johnson R, Hauber AB. Patient Preference Methods - A Patient Centered Evaluation Paradigm. *ISPOR Connections*. 2007. Available from: <https://www.ispor.org/news/articles/Dec07/Bridgesetal2007-Patientpreferencemethods.pdf>.
5. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al.

The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009;62(10):e1-34.

6. Pandit J, Gupta V, Boyer N, Yeghiazarians Y, Ports TA, Boyle AJ. Patient and physician perspectives on outcomes weighting in revascularization. The POWR study. *Int J Cardiol*. 2014;177(2):513-4.

7. Chow RD, Wankhedkar KP, Mete M. Patients' preferences for selection of endpoints in cardiovascular clinical trials. *J Community Hosp Intern Med Perspect*. 2014;4.

8. Ahmad Y, Nijjer S, Cook CM, El-Harasis M, Graby J, Petraco R, et al. A new method of applying randomised control study data to the individual patient: A novel quantitative patient-centred approach to interpreting composite end points. *Int J Cardiol*. 2015;195:216-24.

9. Kipp R, Lehman J, Israel J, Edwards N, Becker T, Raval AN. Patient preferences for coronary artery bypass graft surgery or percutaneous intervention in multivessel coronary artery disease. *Catheter Cardiovasc Interv*. 2013;82(2):212-8.

10. Bowling A, Culliford L, Smith D, Rowe G, Reeves BC. What do patients really want? Patients' preferences for treatment for angina. *Health Expect*. 2008;11(2):137-47.

11. Soekhai V, de Bekker-Grob EW, Ellis AR, Vass CM. Discrete Choice Experiments in Health Economics: Past, Present and Future. *Pharmacoeconomics*. 2018(3):1-26.

12. J. Hellinger, Fred. (1989). Expected Utility Theory and Risky Choices with Health Outcomes. *Medical care*. 1989;(27):273-9.

13. Magliano CADS, Monteiro AL, Tura BR, Oliveira CSR, Rebelo ARO, Pereira CCA. Patient and physician preferences for attributes of coronary revascularization. *Patient Prefer Adherence*. 2018(12):757-764.

Figure 1 PRISMA flow chart of search strategy

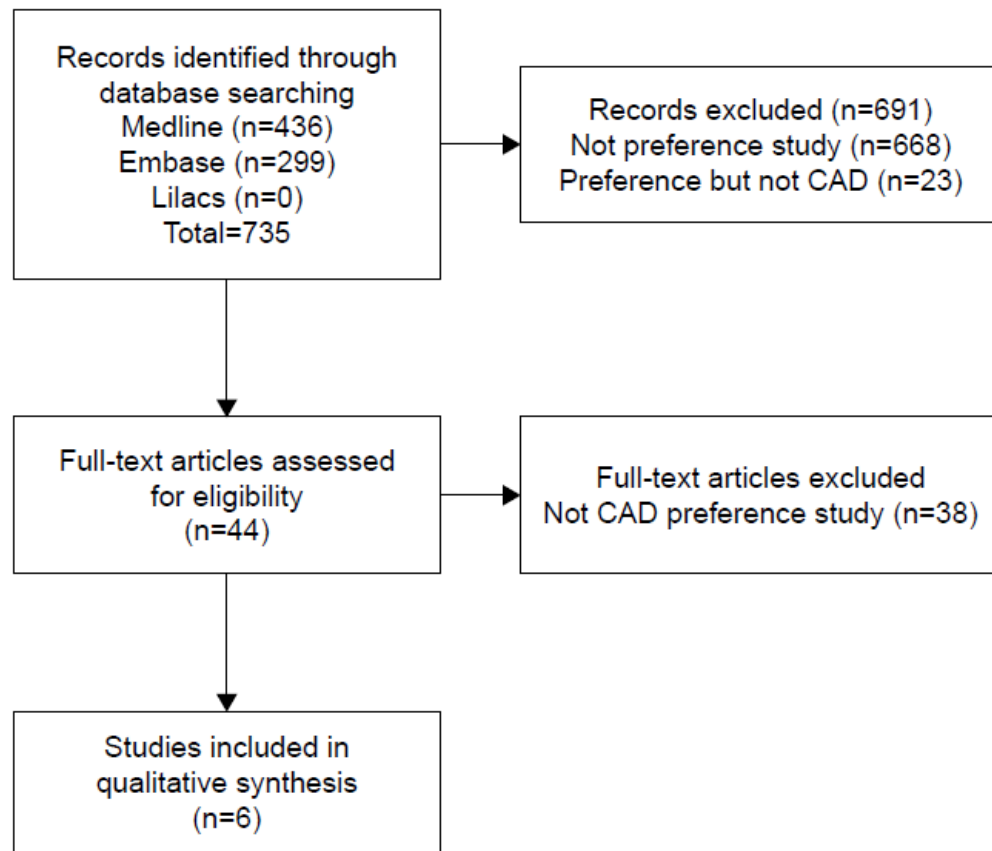


Figure 1 PRISMA flow chart of search strategy.
Abbreviation: CAD, coronary artery disease.

Table 1 Summary of evidence

Study and country	Population	Objectives	Methods	Main results
Pandit et al 2014 ⁶ USA	54 patients, 57 physicians	To assess the relative weight each group (patients and physicians) places on potential adverse outcomes from either PCI or CABG	Rating outcomes on a scale of 0–10	Patients weighted stroke the heaviest and repeat PCI 15 out of 20 outcomes. Physicians weighted death as the heaviest
Chow et al 2014 ⁷ USA	100 patients	To determine the preferences of patients regarding outcomes included on the design of cardiovascular trials	Rating (heart attack, heart death, death, chest pain-hospitalization, repeat revascularization and stroke) on a scale from 1 to 6	Heart attack and death from heart disease were the most important endpoints to be included in a cardiovascular trial.
Ahmad et al 2015 ⁸ UK	113 patients, 50 cardiologists	To determine the preferences of patients regarding outcomes included on the design of cardiovascular trials	Visual analog scale. The relative importance of myocardial infarction, stroke, and repeat revascularization indexed to the death's value	Patients considered stroke worse than death. Patients valued outcomes significantly different than physicians.
Hornerberger et al 1999 ² USA	304 respondents	Determinants of clinical decision-making in patients with stable coronary artery disease	Conjoint analysis, ranking/rating, standard gamble, and WTP. Outcomes: scar, pain, recovery time, days in hospital and repeat revascularization	Repeat revascularization was the most important outcome (28% risk rate threshold to change PCI/CABG.).
Kipp et al 2013 ⁹ USA	585 patients, 31 physicians	Determinants of clinical decision-making in patients with stable coronary artery disease	Mixed effects logistic regression analysis. Outcomes: death, stroke and repeat revascularization	Patients preferred PCI over CABG more than physicians and even when the risk of death was double, and the risk of repeat procedures was more than three times the CABG risks.
Bowling et al 2008 ¹⁰ UK	53 patients	Preferences for angina treatments among patients admitted from emergency with acute coronary syndrome	Rank/rating. Four treatment options: CABG, PCI, drugs to prevent symptoms or to prevent symptoms and partly to reduce the risks of a heart attack	PCI was the preferred treatment (80%), followed by CABG (19%).

Abbreviations: CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; WTP, willingness to pay.

FEASIBILITY OF VISUAL AIDS FOR RISK EVALUATION BY HOSPITALIZED PATIENTS WITH CORONARY ARTERY DISEASE: RESULTS FROM FACE-TO-FACE INTERVIEWS.

Author name¹ Carlos Magliano

Author name² Andrea Monteiro

Author name³ Bernardo Tura

Author name⁴ Claudia Oliveira

Author name⁵ Amanda Rebelo

Author name⁶ Claudia Pereira

Author affiliations^{1,3,4,5} : NATS, Instituto Nacional de Cardiologia, INC, Rio de Janeiro, Rio de Janeiro, Brazil.

Author affiliations²: Department of Pharmacy Systems, Outcomes and Policy, College of Pharmacy, University of Illinois at Chicago, Illinois, USA.

Author affiliations⁶: Escola Nacional de Saúde Pública, ENSP, FIOCRUZ, Rio de Janeiro, Brazil

Correspondence: Carlos Alberto da Silva Magliano

Rua Mario Pederneiras 55 bloco 2 apto 103 Rio de Janeiro, Brazil, CEP 22261020

Tel +55 21 99680 2076

Fax +55 21 25379739

Email carlosincnats@gmail.com

Abstract:

Purpose: Communicating information about risk and probability to patients is considered a difficult task. In this study, we aim to evaluate the use of visual aids representing perioperative mortality and long-term survival in the communication process for patients diagnosed with coronary artery disease at the National Institute of Cardiology, a Brazilian public hospital specializing in cardiology.

Patients and methods: One-on-one interviews were conducted between August 1st and November 20th, 2017. Patients were asked to imagine that their doctor was seeking their input in the decision regarding which treatment represented the best option for them. Patients were required to choose between alternatives by considering only the different benefits and risks shown in each scenario, described as the proportions of patients who had died during the perioperative period and within five years. Each participant evaluated the same eight scenarios. We evaluated their answers in a qualitative and quantitative analysis.

Results: The main findings were that all patients verbally expressed concern about perioperative mortality and that 25% did not express concern about long-term mortality. Twelve percent considered the probabilities irrelevant on the grounds that their prognosis would depend on “God's will”. Ten percent of the patients disregarded the reported likelihood of perioperative mortality, deciding to focus solely on the “chance of being cured”. In the quantitative analysis, the vast majority of respondents chose the “correct” alternatives, meaning that they made consistent and rational choices.

Conclusion: The use of visual aids to present risk attributes appeared feasible in our sample. The impact of heuristics and religious beliefs on shared health decision making needs to be better explored in future studies.

Keywords: patients' preferences; coronary revascularization; angina; cardiology; coronary artery bypass grafting; percutaneous coronary intervention.

Introduction

Patients are key, albeit often unrepresented, players in health care decision making. Understanding how patients value different aspects of health care interventions may help decision makers optimize resource allocation, foresee treatment uptake and raise treatment adherence.¹ For instance, patients diagnosed with coronary artery disease (CAD) and their clinicians may face difficult decisions regarding treatment options, mainly between coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI). This kind of arrangement may be considered “preference sensitive,” meaning that the “right” treatment choice may depend on the relative weight the patient gives to the risks and benefits of treatments.

Stated preference methods, such as discrete choice experiments (DCEs), may be applied to elicit patients’ preferences regarding the benefits and risks of treatments. However, the inclusion of risk attributes in DCEs should encompass a serious consideration of the best strategy of communicating risk information to patients in an understandable manner. It is well documented that conveying information about risk and probability both to patients and to the general population can be a difficult task.^{2,3}

When patients fail to understand relevant information over the course of a DCE, their response patterns are likely to be affected, which may result in biased estimates.¹ Consequently, their overall engagement with the choice experiment may be affected, and they may resort to simplified decision heuristics to complete the experiment (e.g., they may ignore the risk attributes altogether). These phenomena may be especially relevant among patient groups with low health literacy and low numeracy.^{4,5}

When probability information is not understood as intended, the validity, usefulness, and applicability of the results are limited; therefore, researchers must seek effective means of communication between clinician and patients.^{6,7} In recent years, several efforts have been undertaken to explore effective ways to communicate risk, and best-practices recommendations endorse the use of pictures and graphics to better illustrate the information.^{8,9}

This article discusses the challenges faced by clinicians and patients in using visual aids to represent risk information in an inpatient sample in Brazil.

Material and methods

Data collection was conducted by trained interviewers, comprising one cardiologist and two nurses, at the National Institute of Cardiology (INC – Instituto Nacional de Cardiologia), a public hospital specializing in cardiology. These professionals had not had any previous contact with the participants, and none of them was responsible for the care of any of those patients.

The study used a convenience sample of hospitalized patients with stable CAD, most of them waiting for a coronary revascularization procedure. Respondents were selected randomly based on their ward number using a list of random numbers generated from Microsoft Excel. We chose patients with CAD because we judged that they would be more committed to the interviews than any alternative sample from the general population.

This study was conceived according to the best-practices recommendations. Patients' eligibility to participate in the study was determined by the following inclusion criteria: diagnosis of CAD; willingness to participate in a face-to-face interview and answer questions about preferences regarding possible treatment complications; willingness to have the interview audio recorded; willingness to provide informed consent; and currently being considered for a revascularization treatment. Participants were deemed ineligible if they had already undergone surgery, such as angioplasty, or if they believed themselves unable to understand the experiment. Ethical approval was obtained from the institutional Ethics Board, and written informed consent was obtained from each study participant (CAAE number 63684017.0.0000.5240).

One-on-one interviews were conducted between August 1st and November 20th, 2017. Patients were asked to imagine that their doctor was seeking their input in the decision regarding which treatment represented the best option for them. Visual aids were used as a strategy to support communication by overcoming problems with numerical literacy (figures 1-5).

As no treatment labels were used, the subjects were required to choose between option "A" and option "B," considering only the different benefits and risks shown in each scenario. The risks and benefits were represented by the various proportions of patients who had died during the perioperative period and within five years. The main trade-off was an increase in the risk of dying during the treatment for the benefit of greater long-term (five-year) survival. After each task, we asked the same open-ended question for a think-aloud exercise in which patients were asked to explain in their own words the reasons why they had chosen a particular option. Each participant evaluated the same eight scenarios.

We made the basic assumptions that dying in surgery is worse (less utility) than dying in five years and that dying in five years is worse than being alive. We also assumed that if we presented two options with different percentages of mortality and survival, the individual would choose according to his preferences (the option with the greatest utility) and that his choice would be the same regardless of which options were represented by the letters A and B and independently of the order in which the options had been displayed.

In keeping with economic theory (continuity axiom), we expected that in the first two scenarios patients would choose option “A,” since the first option had lower perioperative and overall risk (figure 1). The third and sixth scenarios had the same probabilities, the only difference being that the options were inverted; consequently, we expected that whoever chose option “A” in the third scenario would choose “B” in the sixth and vice versa (figure 2). The fourth and eighth scenarios contained dominated options and presented the same probabilities in different orders. We expected that the subjects would choose option “A” in the fourth and option “B” in the last scenario (figure 3).

Qualitative approach

We performed a qualitative analysis with the main objective of identifying which arguments would be used by the patients when we asked them why they had made a particular choice. As described earlier, our quantitative analysis was based on "adequate response" assumptions. Notwithstanding, to classify the choices only as right or wrong answers would have been very simplistic. We searched for the words that were most used by the interviewees to justify their choices, expressions that could represent misunderstandings and any other possible reasoning that could have led them to choose in an alternative way (not necessarily meaning they were unable to understand the task). All interviews were audio recorded in a digital format, and the data collected were analyzed qualitatively in a three-stage procedure: (1) transcribing the data in preparation for analysis, (2) reducing the data to themes and (3) representing the data. First, the data were fully transcribed and properly compared with the audio versions to detect errors. Then, we reviewed the data in search of repeated ideas or concepts, which were grouped into categories. A qualitative analysis was conducted on the patients' transcribed responses, preserving the terms they used to justify their choices. Such terms were cataloged in groups with similar meanings. No data analysis software was used to perform this task. Two researchers analyzed the transcripts independently. The criterion used to terminate

data collection was sampling saturation¹⁰.

Quantitative approach

In the first scenario, option “A” presented a risk of perioperative death of 2/50 (4%) and a risk of 18/50 (36%) of dying within five years. Option “B” presented a 30/50 (60%) risk of perioperative death and no deaths later in the five-year period. We assumed that patients would choose the first option because there were fewer perioperative deaths and more long-term survivors (figure 1).

In scenario two, the superiority of option “A” is even greater than in scenario one. The perioperative mortality is 10/50 (20%), as opposed to 30/50 (60%) for the second option. Our assumption was that patients would choose option “A” (figure 1).

Scenario three presented a trade-off between worse/better perioperative mortality and better/worse long-term survival (figure 2). We hypothesized that in scenarios three and six, patients would keep their first choice, regardless of the option, when they repeated the task. We merely inverted the order of the alternatives, maintaining the same proportions of perioperative and long-term deaths.

In scenario four, we assumed that patients would choose option “A”, since there were 30 patients alive within five years in both options, but the option “A” had no perioperative mortality while option “B” had perioperative mortality of 10/50 (20%). We still hypothesized that in scenarios four and eight, patients would keep their first choice, regardless of the option, when they repeated the same task, similar to scenarios three and six. Between scenarios four and eight, we merely inverted the order of the alternatives, maintaining the exact proportions of perioperative and long-term deaths (figure 3).

In scenarios five and seven (figures 4 and 5), there was no assumption of a “right” answer. Scenario seven was designed to estimate the proportion of patients who were choosing between the options using a heuristic based solely on perioperative mortality. With a single perioperative death (2%) and another 39 deaths (78%) within five years, option “A” had a long-term survival of only 10/50 (20%). Option “B” presented high perioperative mortality, 10/50 (20%), and the 5-year survival was 40/50 (80%).

A z-test for proportions was used to calculate whether choices made by patients were different from random choices. The null hypothesis was that the proportion of “right” answers would be less than or equal to 50%. A p-value less than .05 was considered significant.

The latter part of the questionnaire included questions regarding demographic

information (age, gender, ethnicity, income, and level of education). We summarized the data by means, medians, or percentages, as indicated.

Results

Each interview was approximately 45 minutes in duration. We enrolled 34 respondents; two of them were excluded because they considered themselves unable to understand. Overall, the respondents were likely to be male, retired, married and religious (table 1).

Qualitative analysis results

The transcripts of the 32 interviews were analyzed, and the most frequently used terms were as follows: ‘death’ (85 times), ‘live’ (34 times), ‘cure’ (9 times) and ‘God’ (9 times). The preliminary analysis identified six categories: 1) “concern about perioperative death”, 2) “concern about long-term survival”, 3) “long-term survival depends exclusively on me”, 4) “long-term survival depends exclusively on God’s will”, 5) “the most important attribute is to be cured” and 6) “difficulty in answering the questionnaire”.

Although they were asked to consider exclusively the probabilities presented, 20% of the patients considered the possibility that long-term mortality could be minimized through lifestyle changes. This belief may have impacted their choices. All patients verbally expressed concern about perioperative mortality, and 75% of respondents expressed concern about long-term mortality. Notably, 25% of patients based their decisions only on short-term risk.

Ninety-four percent of the patients were religious, most of them Catholic (53% of all subjects). Considering the small sample size, it is not possible to evaluate differences between religion-based subgroups or the impact of religion on choices. Nonetheless, it is interesting to note that 12% of respondents considered the probabilities irrelevant on the grounds that their prognosis would depend solely on God's will.

In this study, we made assumptions regarding what constitutes a “right answer”. During the interviews, it became evident that some patients were making unexpected choices, but those choices were clearly not related to misunderstanding or low numeracy skills. For example, in scenario one, some subjects reasoned that in option B, if one did not die during the perioperative process, one could be regarded as cured. Ten percent of the patients disregarded the reported probability of perioperative mortality, deciding to focus solely on the chance of being cured.

Finally, although our sample came from a public hospital located in a middle-income country, the subjects' educational levels varied, ranging from patients who studied less than three years to patients with a bachelor's degree. The small sample size limits subgroup analysis by education level. Aside from the two patients who considered themselves incapable of understanding the experiment, only one patient verbally stated that the questionnaire was difficult to interpret.

Quantitative analysis results

For the first two scenarios, 29/32 (90.6%) of respondents chose the "correct" alternative, the one we had considered to have the greater benefit (option "A," figure 1), indicating significant rational economic behavior ($p = .01$). In scenario one, the vast majority of respondents, 30/32 (93.7%), responded according to our assumption ($p < .01$). We had judged option "B" as an irrational economic behavior choice, but some patients considered it reasonable because "if you survived the surgery, you would be cured" since no one died in five years.

In scenario two, the superiority of option "A" was even greater, and there were no patients who died after the perioperative period. We assumed that patients would choose option "A," which occurred in 31/32 cases (97%). The only person who chose option "B" was a patient with a college degree, who did not justify his choice.

In scenario three, fourteen patients chose option "A" and eighteen chose option "B." We wanted to test whether patients would maintain their choice in comparison to scenario six. Most patients, 22/32 (68.7%), kept their choice, although this percentage cannot be considered significantly different from a random choice ($p = .20$).

In scenario four, most respondents 25/32 (78%) chose the "right answer" ($p = .037$). Nonetheless, many patients surprised us with their responses when they consciously opted for option "B." They argued that option "B" presented the lowest risk for those who had survived the surgery. Instead of being a matter of right or wrong answers as we had originally thought, scenarios four and eight could be judged as a preference task. Between scenarios four and eight, the majority of patients 25/32 (78%) maintained their choice, and the consistency of patients' choices was statistically significant ($p = .04$).

In scenarios five and seven (figures 4 and 5), there was no assumption of a "right" answer. Half of the patients chose option "A" in scenario five, mainly because they considered the perioperative mortality in option "B" (20%) too high. The other half of respondents chose option "B", mainly because there was better long-term survival, as they

explained in the recorded conversations. In scenario seven (figure 5), despite the enormous mortality (80% within five years), 25% of respondents preferred option "A", which may be related to a heuristic process as some of these patients declared that they were focusing on perioperative death.

Discussion

Individuals faced with a choice between two treatments need to evaluate the benefits and risks of each option. It is recognized that patients' risk perception and preferences are poorly understood⁶; therefore, it is possible that cardiologists have been making recommendations based on outcomes that may not represent patients' preferences adequately.

There are differences between patients' and physicians' values. For example, compared with physicians, patients seem to be willing to accept considerably heightened risks with PCI to avoid CABG. In a study by Bowling¹¹, angioplasty was the preferred treatment for 80% of respondents, and in this study, when patients were asked which treatment they would prefer between PCI and CABG if the risks and benefits were equal, 94% of patients chose PCI.

We undertook a series of face-to-face semi-structured interviews with stable hospitalized patients with CAD to appraise the feasibility of using visual aids to represent risks. The rationality and consistency of the responses were evaluated quantitatively according to utility assumptions. The pattern of responses was also qualitatively assessed, bringing inferences to inform future studies.

Understanding probabilities may be a challenge for patients, but in this study, we demonstrated that it is possible to present risk trade-offs in scenarios with visual aids and to obtain consistent and rational answers with the potential to reveal patients' preferences. Future studies may test the impact of such visual aids in discussions between stakeholders regarding coronary revascularization treatment options.

Our study does have several limitations. Only a small number of patients were recruited; consequently, the study did not have enough power for subgroup analysis. In addition, the participants came from a single hospital in Brazil; this common factor limits the generalizability of the study. The number of scenarios selected could have led to survey fatigue. Furthermore, the outcome definitions and survey structure were tested in pilot studies but were not validated. Finally, although the use of visual aids was considered feasible, some patients were averse to short-term risks and preferred treatment options with

a lower expected value. The impact of religious beliefs and heuristics on shared healthcare decision making merits future research.

Conclusion

The use of visual aids to present risk attributes was feasible in a sample of hospitalized patients at a public tertiary hospital in Brazil. The patients considered themselves able to understand and participate in decisions, and most of them presented answers consistent with economic theory.

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Disclosure

The author reports no conflicts of interest in this work.

References

1. Ali S, Ronaldson S. Ordinal preference elicitation methods in health economics and health services research: using discrete choice experiments and ranking methods. *British medical bulletin*. 2012 Aug 2;103(1):21-44.
2. Harrison M, Rigby D, Vass C, et al. Risk as an attribute in discrete choice experiments: a critical review. *Patient*. 2014;7:151–70.
3. Vass CM, Payne K. Using Discrete Choice Experiments to Inform the Benefit-Risk Assessment of Medicines: Are We Ready Yet?. *PharmacoEconomics*. 2017 May 23:1-8.
4. Lipkus I, Samsa G, Rimer B. General performance on a numeracy scale among highly educated samples. *Med Decis Mak*. 2001;21:37–44.
5. Gigerenzer G, Gaissmaier W, Kurz-Milcke E, et al. Helping doctors and patients make sense of health statistics. *Psychol Sci Public Interest*. 2007;8:53–96.
6. Ahmed H, Naik G, Willoughby H, Edwards A. Communicating risk. *BMJ*. 2012;344:1–7. 49.
7. Veldwijk J, Essers BA, Lambooi MS, et al. Survival or mortality: does risk attribute framing influence decision-making behavior in a discrete choice experiment? *Value Health*. 2016;19(2):202–9.
8. Price M, Cameron R, Butow P. Communicating risk information: the influence of graphical display format on quantitative information perception—accuracy, comprehension and preferences. *Patient Educ Couns* 2007;69:121–8.
9. Galesic M, Garcia-Retamero R, Gigerenzer G. Using icon arrays to communicate medical risks: overcoming low numeracy. *Health Psychol* 2009;28:210–6.
10. Seale C. Grounding theory. In: Seale C, editor. *The Quality of Qualitative Research*. London: SAGE Publications Ltd; 1999. p. 87-105.
11. Bowling A, Culliford L, Smith D, et al. What do patients really want? Patients' preferences for treatment for angina. *Health expectations: an international journal of public participation in health care and health policy*. 2008;11(2):137-47.

Figure 1 Figure 1 Based upon the benefits and risks, which choice do you prefer?

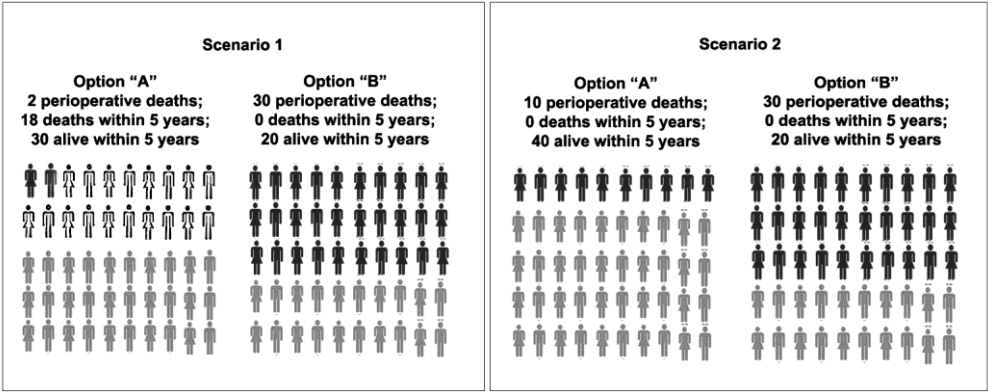


Figure 2 Based upon the benefits and risks, which choice do you prefer?

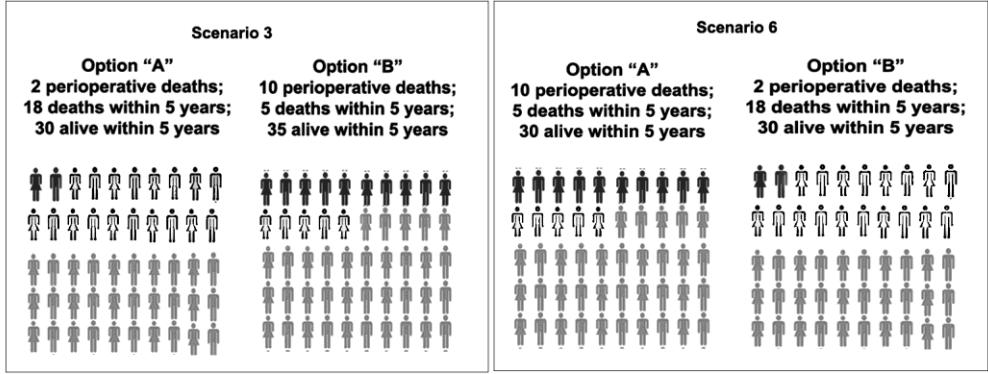


Figure 3 Based upon the benefits and risks, which choice do you prefer?

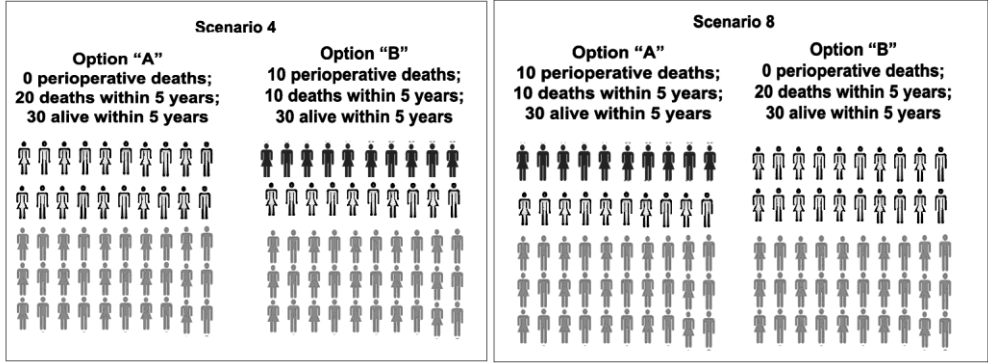


Figure 4 Based upon the benefits and risks, which choice do you prefer?

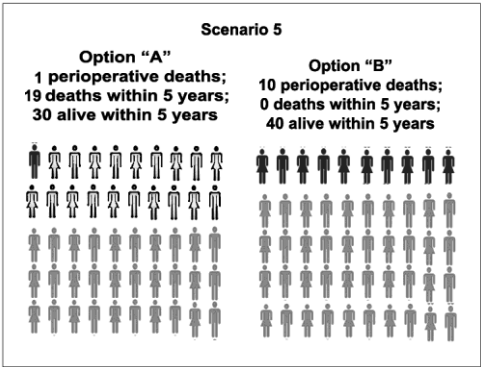


Figure 5 Based upon the benefits and risks, which choice do you prefer?

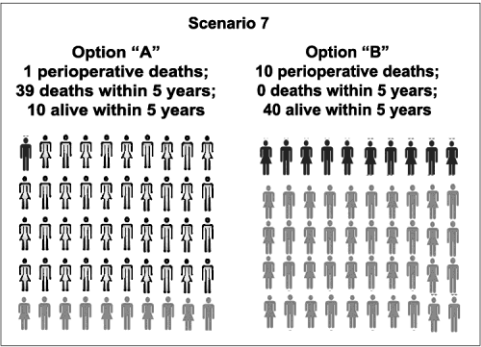


Table 1 Patient sociodemographic characteristics

Number of participants	32
Male	24 (75%)
Female	8 (25%)
Age, mean (SD)	63.3 (8.6)
Religion	
Catholic	17 (53%)
Evangelical	7 (22%)
Spiritist	5 (16%)
Others	3 (9%)
Skin color	
White	14 (44%)
Pardo	14 (44%)
Black	4 (12%)
Years of education	
1-5 years	6 (19%)
6-10 years	8 (25%)
11-13 years	13 (41%)
>13 years	5 (16%)
Income	
Mean (SD)	R\$1,800.00 (R\$2,590.00)

PATIENT AND PHYSICIAN PREFERENCES FOR ATTRIBUTES OF CORONARY REVASCULARIZATION

Carlos Magliano¹

Andrea Monteiro²

Bernardo Tura¹

Claudia Oliveira¹

Amanda Rebelo¹

Claudia Pereira³

¹NATS, Instituto Nacional de Cardiologia, INC, Rio de Janeiro, Rio de Janeiro, Brazil;

²Department of Pharmacy Systems, Outcomes and Policy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA; ³Escola Nacional de Saúde Pública, ENSP, FIOCRUZ, Rio de Janeiro, Brazil

Correspondence: Carlos Alberto da Silva Magliano

Rua Mario Pederneiras 55, bloco 2 apto 103, Rio de Janeiro, Brazil, CEP 22261020

Tel +55 21 99680 2076

Fax +55 21 25379739

Email carlosincnats@gmail.com

Background: Patients with a diagnosis of coronary artery disease (CAD) may face important decisions regarding treatment options, with the “right choice” depending on the relative weights of risks and benefits. Studies performed as discrete-choice experiments are used to estimate these weights, and attribute selection is an essential step in the design of these studies. Attributes not included in the design cannot be analyzed. In this study, we aimed to elicit, rank, and rate attributes that may be considered important to patients and physicians who must choose between angioplasty and surgery for coronary revascularization.

Method: The elicitation process involved performing a systematic review to search for attributes cited in declared preference studies in addition to face-to-face interviews with cardiologists and experts. The interviews were audio-recorded in digital format, and the collected data were transcribed and searched to identify new attributes. The criterion used to finish the data collection process was sampling saturation.

Results: A systematic review resulted in the selection of the following 14 attributes: atrial fibrillation, heart failure, incision scar, length of stay, long-term survival, myocardial infarction, periprocedural death, postoperative infection, postprocedural angina, pseudoaneurysm, renal failure, repeat CABG, repeat PCI, and stroke. The interviews added no new attributes. After rating, we identified significant differences in the values that patients and cardiologists placed on renal insufficiency ($p<0.001$), periprocedural death ($p<0.001$), and long-term survival ($p<0.001$).

Conclusion: Decisions regarding the best treatment option for patients with CAD should be made based on differences in risk and the patient’s preference regarding the most relevant endpoints. We elicited, ranked, and rated 14 attributes related to CAD treatment options. This list of attributes may help researchers who seek to perform future preference studies of CAD treatment options.

Introduction

Coronary artery disease (CAD) is the leading cause of mortality worldwide. For patients with symptomatic CAD refractory to medical therapy, two treatment options are available: percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). Each of these therapies has a different risk and benefit profile. Approximately 12% of affected patients are eligible for either PCI or CABG.¹ Knowing the preferences of the patients who face this scenario may be relevant to decision making because the available treatment options are different, and the stakeholders may value them unequally.

Determining patient preferences may provide insights that lead to more effective management strategies since which treatment is “right” depends on the relative weight the patient gives to the risks and benefits of the different treatment strategies. In this study, we aimed to elicit, rank, and rate attributes that may be considered important to patients and physicians who face choosing between PCI and CABG.

This paper describes a qualitative study that was designed to identify which attributes are important to patients and cardiologists. These attributes may help future studies aimed at exploring the preference for coronary revascularization, such as discrete-choice experiments (DCEs). DCEs are increasingly used as a method to determine patient preferences, and attribute selection is an important step that is rarely reported in detail.²

Method

The first step in this study was to elicit attributes. The second step was to rank and rate the attributes selected by patients and physicians. Finally, we analyzed the attributes to identify differences between these stakeholders’ perspectives.

Attribute elicitation

The elicitation process involved performing a systematic review in addition to conducting face-to-face interviews with patients and experts.

Systematic review

We performed a systematic review of published studies related to declared preferences for PCI or CABG in patients with a diagnosis of CAD. The MEDLINE, Embase, and LILACS databases were searched for studies published on or before 10 August 2017. Our search terms consisted of keywords for coronary revascularization as well as methods used to assess patient preferences (e.g., “patient reported outcome,” “patient satisfaction,” “best–

worst scaling,” “Maxdiff,” “discrete choice experiment,” “preference,” “conjoint studies,” “conjoint choice experiment,” “vignette,” “choice,” “willingness-to-pay,” and “conjoint analysis”).

Patient interviews to elicit attributes

Data collection was conducted by trained interviewers, including one cardiologist and two nurses, at the National Institute of Cardiology, Rio de Janeiro, Brazil. These professionals had no previous contact with the patients, and none of them was responsible for the care of the included patients.

In this study, we used a convenience sample of hospitalized patients with stable CAD, most of whom were waiting for a coronary revascularization procedure. Respondents were selected randomly based on their ward number using a list of random numbers that was generated in Microsoft Excel. We chose patients with CAD since we assumed that they would be more committed to the interviews than any alternative sample population.

Eligibility to participate in the study was defined as follows: a diagnosis of CAD, willingness to participate in a face-to-face interview during which the patient would answer questions about their preferences regarding possible treatment complications, provided written informed consent, and currently being considered for a revascularization treatment. Participants were deemed ineligible if they had already undergone surgery or angioplasty or if they viewed themselves as unable to understand the experiment. Ethical approval was obtained from the National Institute of Cardiology Ethical Department (Comitê de ética e pesquisa do Instituto Nacional de Cardiologia), and written informed consent was obtained from each study participant (CAAE number 63684017.0.0000.5240).

One-to-one interviews were conducted between August 1 and November 20, 2017. Patients were asked to imagine that they were sharing in the decision-making process regarding which treatment option was better for them between PCI and CABG. They were then asked to answer a semi-structured questionnaire. Open-ended questions were presented in the following sequence: 1) Do you know the reason for your hospitalization? 2) What benefits do you expect to achieve from the treatment? 3) Which risks or complications could occur with the treatment? 4) What most concerns you regarding the treatment? 5) Considering that there is no difference in mortality between the two, which procedure would you prefer? 6) What are the differences between surgery and angioplasty?

The latter part of the questionnaire included questions regarding demographic information (age, gender, ethnicity, income, and level of education).

Cardiologist interviews to elicit attributes

All interviews were completed by the first author (CM), who is a cardiologist. The study population was a convenient sample of cardiologists with expertise in CAD.

Physician eligibility was determined according to the following criteria: specialist in cardiology, willing to participate in a face-to-face interview and answer questions about preferences regarding possible treatment complications, and willing to provide informed consent.

The experts were asked to enumerate the risks and benefits they usually consider when exploring the trade-offs between PCI and CABG.

Qualitative analysis of interviews

The interviews were audio-recorded in digital format, and the data collected were qualitatively analyzed. First, the data were transcribed integrally and properly contrasted with the audio versions to detect errors. Then, we reviewed the data to identify any attribute that had not been previously identified in the systematic review. We then sought to identify the terms that were most commonly used by patients to describe clinical outcomes. The criterion used to finish data collection was sampling saturation.³

Ranking

The attributes selected in the previous step were randomly and individually presented to patients and physicians. We used cards that were similar in color and size, with each card containing the name of an attribute in layperson's terms. The amount of explanatory/background information was equivalent for all attributes, and this information was presented according to a pre-established script to avoid overstating the importance of any single attribute.

The following pre-established question was presented to all patients: "Consider you have angina, a chest pain that indicates a heart problem. Your treatment options are medicine, angioplasty (catheterization with stent placement) or bypass surgery. These different treatments are related to different benefits and risks. I have a list of possible complications resulting from these treatments, and I would like to know how concerned you are in relation to each one. Please, put in order of relevance from one to fourteen your concerns, i.e., one being the most concerned to fourteen the least concerned."

The following similar pre-established question was presented to all physicians: "Imagine

that you are responsible for defining the treatment of a patient who is complaining about angina. The available treatment options include adjusting medications, angioplasty with stents or coronary bypass surgery. These different treatments are related to different benefits and risks. I have a list of possible complications from these treatments and I would like to know how concerned you are about each one. Please, put in order of relevance from one to fourteen your concerns, i.e., one being the most concerned to fourteen the least concerned.”

Rating

After ranking, each participant received 10 identical black dots. They were instructed to distribute the dots in such a manner that the most relevant attributes received proportionally more points. The participant was asked to define the proportion by considering the relative importance of each attribute. There was no limit to how many points each attribute could receive. It was possible to reorder the attributes during this phase. This method is known as dotmocracy (Figure 1).

Statistics

Descriptive statistics were used to summarize the sociodemographic and clinical characteristics of the sample. We summarized the data as means, medians, or percentages, as indicated. An unpaired *t*-test was used for comparisons between group data. All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients prior to their inclusion in the study.

Results

The interviews were approximately 15 min in duration. We enrolled 76 respondents, comprising 22 cardiologists and 54 patients (32 for elicitation and 22 for ranking and rating). Overall, the majority of respondents were male, Caucasian, retired, married, and religious (Table 1). All physicians were cardiologists and had a mean \pm SD 15.6 \pm 1.2 years of clinical experience.

Attribute selection in the systematic review

We used a systematic review to search for stated preference studies that evaluated CAD

treatments. Both patient and physician preferences were surveyed. Of a total of 735 citations (436 from MEDLINE and 299 from Embase), 44 articles were eligible for full-text review. Six studies^{1,4-8} that met our inclusion criteria were included in the final report. The attributes most often cited in these studies coincided with those already used in clinical trials: death,^{4,6-8} stroke,^{4,6-8} myocardial infarction,^{4,7} and repeat revascularization.^{1,6-8} Other attributes examined within these studies included heart attack,⁶ hospitalization,⁶ repeat PCI,⁴ repeat CABG,⁴ atrial fibrillation,⁴ mediastinitis,⁴ postoperative chronic pain,^{1,4} postprocedural angina,^{4,6} length of stay,^{1,4} duration of recovery,^{1,4} depression,⁴ procedural cost,⁴ incision scar,^{1,4,5} pseudoaneurysm,⁴ pneumonia,⁴ long-term use of clopidogrel,⁴ renal failure,⁴ acute respiratory distress syndrome,⁴ bleeding,⁴ symptom control, medication side effects, comfort in taking medication, well-being, the ability to do things, the prolonging of life, and cure.⁵

Procedural and other costs, such as medications, were avoided as possible attributes in this study because the included patients were being treated in the Brazilian public health system and therefore had no co-payments. Prolonged use of medications or their side effects were also not included as attributes because our goal was to study preferences between angioplasty and surgery.

We selected the following 14 attributes based on the attributes identified in the systematic review: 1) atrial fibrillation; 2) heart failure; 3) incision scar; 4) length of stay; 5) long-term survival, 6) myocardial infarction, 7) periprocedural death, 8) postoperative infection, 9) postprocedural angina, 10) pseudoaneurysm, 11) renal failure, 12) repeat CABG, 13) repeat PCI, and 14) stroke (Table 2).

Attributes selected from patient and physician interviews

Interviews with cardiologists and patients did not add new attributes. Notably, the patients exhibited discomfort when encouraged to cite possible complications and claimed that they had not spoken to their physicians about these. The complications most prevalent from a patient perspective were death and stroke, which were cited by 68.75% and 50% of the patients, respectively.

Attribute importance

After ranking and rating the identified attributes, our survey revealed that in some attributes, there was a major discordance between patients and cardiologists. Periprocedural death was ranked as the most important outcome by cardiologists, while

renal failure was the most important to patients. Incision scars were considered the least important for both groups. There was a significant difference between patients and cardiologists in the value they placed on renal insufficiency ($p<0.001$), periprocedural death ($p<0.001$), and long-term survival ($p<0.001$). The results are shown in Table 3.

Discussion

We would like to highlight some of the important findings of this study. First, neither the patients nor the physicians considered all clinical endpoints equal, and future trials should therefore be careful when considering composite endpoints. Second, patients and physicians do not weigh many relevant cardiovascular outcomes similarly (e.g., renal failure, periprocedural death, long-term survival, and atrial fibrillation), and this should be considered during decision making. Third, repeat revascularization is not highly valued by either doctors or patients and should therefore not substantially impact the decision-making process.

In this study, we identified some important aspects that should be explored in future trials. The attributes that were more frequently cited in the systematic review of preference studies coincided with the attributes already used in clinical trials. The patient and physician interviews did not add any new attributes. This finding may indicate that these attributes are indeed the most relevant, or it may reflect the impact of previously published trial outcomes on current medical reasoning. One relevant question is that of whether physicians make their decisions based exclusively on the outcomes used in previous trials rather than considering all possible patient-relevant outcomes.

Another important issue related to outcomes is the use of composite endpoints. Death, stroke, myocardial infarction, and repeat revascularization are frequently grouped into a category called major adverse cardiovascular events (MACE). The use of MACE has been justified as an attempt to capture the overall treatment effect. The main advantage of using composite outcomes is that it reduces the duration, sample size, and costs of clinical trials.^{1,6} In this study, we found that these outcomes are weighted differently, and this represents one limitation of the use of MACE as a composite endpoint. This finding is in accordance with those presented in the literature.^{4,6,7}

It is important to note that even though the difference was not statistically significant ($p=0.054$), the patients rated “repeat surgery” as the fourth most important attribute, and they gave it more than twice the points given by physicians, who considered it the eighth most important. In addition, one endpoint that is very commonly used in composite

analysis, “repeat PCI,” was viewed as one of the least important by both patients (13th out of 14) and physicians (10th out of 14). This finding is similar to that of Pandit et al.⁴ Based on these findings, future studies should avoid grouping “repeat surgery” and “repeat PCI” in addition to avoiding the use of the combined outcomes of death, stroke, myocardial infarction, and “repeat revascularization” because these outcomes are valued differently by patients and physicians.

We considered it essential to clarify the clinical meaning of the endpoints provided during the interviews. For example, stroke was presented as permanent stroke. This is not likely to be the reality in many clinical trials in which there are several different types of stroke, which can range from a mild transient ischemic event to a large disabling neurological insult. Similarly, myocardial infarction may range from a trivial troponin rise to severe ventricular dysfunction. Future studies should report results stratified by attributes and clinical relevance.

Stroke was identified as an important attribute and was the third most important to both patients and physicians. However, it was not more important than death. This finding is different from that reported in the Pandit and Ahmad studies.^{4,7} Future trials should explore cultural aspects that are potentially related to differences in preferences between populations.

Patients and physicians weighted some attributes differently. Patients appear to place considerably less value on “long-term survival.” The Kipp study⁸ reached a similar conclusion, wherein patients chose PCI over CABG across nearly all hypothetical PCI risk scenarios, while physicians were significantly less likely to choose PCI over CABG. During the decision-making process, physicians must recognize that there are possible divergences in the weighted preferences for some relevant attributes, and they should therefore seek the patient’s opinion during this process.

Our study does have several limitations. The number of attributes selected could have resulted in respondent fatigue. Furthermore, the outcome definitions and survey structure were tested in pilot studies but were not validated. Our study was not powered for a subgroups analysis. The patients selected were from a convenience sample from a public health hospital in Brazil, and most of the participants were at the lower end of educational completion, which limits the ability to generalize the study’s conclusions to the overall population. On the other hand, these findings highlight the necessity of elicitation preferences in each scenario before making recommendations.

Another important limitation of our attribute ranking analysis was the absence of attribute

levels. This was because we believed that presenting several attributes with different levels would result in excessive cognitive demand. Thus, the attributes were provided with no information regarding risk rates, and we must acknowledge that this could have impacted the results.

As cited by Ciccone et al, building on treatment recommendations should take a broad perspective and consider the medical, social, behavioral, and emotional impact on the patient's quality of life.⁹ The current guidelines and recommendations regarding CAD treatment seem to be based on endpoints that do not properly represent patient preferences. Further developing what is known about patients' preferences, values, and fears may better inform policy and enable physicians to be more accountable to the public.

Conclusion

It is vital that decision makers understand how patients value the aspects associated with a health-care intervention. Incorporating their values may ultimately result in clinical and policy decisions that better reflect patient preferences.

In this study, we elicited, ranked, and rated 14 attributes related to CAD treatment options. Patients and cardiologists valued many of these attributes differently. This list of attributes may help researchers seeking to use discrete choice experiments to develop future preference studies related to CAD treatment options.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Hornberger J, Bloch DA, Hlatky MA, Baumgartner W. Patient preferences in coronary revascularization. *Am Heart J*. 1999;137(6):1153–1162.
2. Bridges JF, Hauber AB, Marshall D, et al. Conjoint analysis applications in health--a checklist: a report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value Health*. 2011;14(4):403–413.
3. Prakke H, Wurster J. [Quality criteria for qualitative research]. *Pflege*. 1999;12(3):183–186.
4. Pandit J, Gupta V, Boyer N, Yeghiazarians Y, Ports TA, Boyle AJ. Patient and physician perspectives on outcomes weighting in revascularization. The POWR study. *Int J Cardiol*. 2014;177(2):513–514.
5. Bowling A, Culliford L, Smith D, Rowe G, Reeves BC. What do patients really want? Patients' preferences for treatment for angina. *Health Expect*. 2008;11(2):137–147.
6. Chow RD, Wankhedkar KP, Mete M. Patients' preferences for selection of end-points in cardiovascular clinical trials. *J Community Hosp Intern Med Perspect*. 2014;4.
7. Ahmad Y, Nijjer S, Cook CM, et al. A new method of applying randomised control study data to the individual patient: A novel quantitative patient-centred approach to interpreting composite end points. *Int J Cardiol*. 2015;195:216–224.
8. Kipp R, Lehman J, Israel J, Edwards N, Becker T, Raval AN. Patient preferences for coronary artery bypass graft surgery or percutaneous intervention in multivessel coronary artery disease. *Catheter Cardiovasc Interv*. 2013;82(2):212–218.
9. Ciccone MM, Aquilino A, Cortese F, et al. Feasibility and effectiveness of a disease and care management model in the primary health care system for patients with heart failure and diabetes (Project Leonardo). *Vasc Health Risk Manag*. 2010;6:297–305.

Table 1 Patients' sociodemographic characteristics

Number of participants	54
Gender	
Male	40 (74)
Female	14 (26)
Age (years), mean±SD	62.5±8.6
Religion	
Catholic	25 (46)
Evangelical	16 (30)
Spiritism	6 (11)
Other	7 (13)
Ethnicity	
White	27 (50)
Pardo	22 (41)
Black	5 (9)
Years of education	
1–5	13 (24)
6–10	12 (22)
11–13	18 (33)
>13	11 (21)
Retired	37 (69)
Married	37 (69)
Monthly income (R\$), median±SD	2205.37±2890.26

Note: Data are shown as n (%) unless otherwise indicated.

Table 2 Definitions of attributes

Attribute	Definition
Atrial fibrillation	Permanent atrial fibrillation, patient received anticoagulation
Heart failure	Symptomatic heart failure, NYHA class III or IV. Class III: marked limitation of physical activity in which less than ordinary activity results in fatigue, palpitation, dyspnea, or angina pain, but the person is comfortable at rest. Class IV: inability to carry on any physical activity without discomfort, symptoms of heart failure or angina syndrome even when at rest, and increased discomfort if any physical activity is undertaken
Incision scar	Median sternotomy incision scar
Length of stay	Hospitalization length of stay
Long-term survival	5 year survival after treatment
Myocardial infarction	Myocardial infarction not related to death. “Commonly known as a heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. The most common symptoms are chest pain or discomfort that may travel into the shoulder, arm, back, neck, or jaw. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat, or feeling tired”
Periprocedural death	Death within 30 days after treatment
Postoperative infection	Infection after surgery, including skin infections, pneumonia, or mediastinitis
Postprocedural angina	Return of angina symptoms despite treatment, including chest pain or pressure, which is usually related to exercise or emotional stress
Pseudoaneurysm	Femoral pseudoaneurysm. A pseudoaneurysm, also known as a false aneurysm, is a collection of blood that forms between the two outer layers of an artery. It is caused by an injury to the

	femoral vessel that occurs during angioplasty. Correction may require surgery
Renal failure	Chronic kidney failure, also known as renal failure or renal insufficiency, is a medical condition in which the kidneys do not work properly, and dialysis is needed to perform their function
Repeat CABG	The necessity to redo surgery
Repeat PCI	The necessity to redo angioplasty
Stroke	Permanent stroke. Signs and symptoms of a stroke may include an inability to move, the loss of feeling on one side of the body, problems understanding or speaking, feeling like the world is spinning, or loss of vision to one side

Note: <https://emedicine.medscape.com/article/2500037-overview>.

Abbreviations: NYHA, New York Heart Association; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

Table 3 Ranking and rating of attributes according to patients and cardiologists

Attribute	Patients		Cardiologists		<i>p</i>
	Ranking	Rating	Ranking	Rating	
Renal failure	1st	50	6th	10	<0.001
Periprocedural death	2nd	43	1st	72	<0.001
Stroke	3rd	25	3rd	26	NS
Repeat surgery	4th	19	8th	8	NS
Myocardial infarction	5th	16	4th	18	NS
Heart failure	6th	15	5th	15	NS
Angina	7th	12	9th	4	NS
Atrial fibrillation	8th	10	12th	1	0.01
Postoperative infection	9th	9	7th	4	NS
Long-term survival	10th	9	2nd	53	<0.001
Length of stay	11th	4	11th	2	NS
Pseudoaneurysm	12th	2	13th	1	NS
Repeat angioplasty	13th	2	10th	2	NS
Incision scar	14th	0	14th	0	NS

Abbreviation: NS, not significant.

Figure 1 The dotmocracy rating method.



PATIENTS' PREFERENCES FOR CORONARY REVASCULARIZATION: DISCRETE CHOICE EXPERIMENTS.

Carlos Alberto da Silva Magliano, Andrea L. Monteiro, Amanda Rebelo, Giovanna F. Santos, Braulio S. Junior, Nicolas Krucien, Bernardo Rangel Tura, Claudia C. A. Pereira.

Abstract

Objective

The aim of this study was to evaluate the trade-offs that patients are willing to make between percutaneous coronary intervention and coronary artery bypass graft.

Methods

A discrete choice experiment (DCE) was undertaken with hospitalized patients in a tertiary cardiology hospital in Brazil (n = 159). The DCE consisted in a paper-based questionnaire including 12 choice tasks comparing percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) options. Each choice option was described with four risk attributes: perioperative death; long-term death; myocardial infarction; the need to repeat the revascularization. The analysis of 1.908 patients' choices was undertaken using conditional logit regression models.

Results

The majority of patients (73%) preferred open surgery when facing realistic levels of risks and benefits. The coefficients had significant different weights and they were statistically significant at a 5% level for all attributes, except for percutaneous perioperative death, surgery myocardial infarction and the need to repeat surgery.

Conclusions

Despite the important trade-offs between coronary revascularization treatments, patients' preferences are poorly explored. This study provides important insights such as the evidence of a significant variation in the perceived utility of treatments and the noteworthy overall preference for the most invasive option.

The results of the logit model showed that changes in the efficacy such as the reduction of the risk of repeat revascularization might influence patients' choices and the consideration of composite endpoints that accurately reflect the severity of each individual endpoint component may change current guidelines recommendations and improve patient utility.

Introduction

Coronary heart disease is the leading cause of mortality and disability worldwide, being responsible for about one-third of all deaths in people over 35 years of age [1, 2]. Nowadays, the possible revascularization treatments include percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). The least invasive option is PCI, as it does not require open-heart surgery. On the other hand, CABG is the gold standard approach for some patients, mainly for those with multivessel disease, diabetes, left main coronary disease or left ventricular dysfunction [3].

The selection of a therapeutic approach for illnesses with more than one viable option involves trade-offs between beneficial and deleterious outcomes that may be valued differently by patients and physicians [4]. Determining patients' preferences may provide insights that would lead to more appropriate management strategies since the choice of the "best" treatment is likely to depend on the importance given to the risks and benefits of PCI and CABG.

While researchers investigate which treatment represents the best alternative, little is known about the viewpoint of patients. Evidence about patients' values on coronary disease treatments is scarce and the methods used to estimate preferences are heterogeneous, varying from rating potential outcomes such as heart attack, death and stroke [4-6] to more complex techniques of preference assessment such as conjoint analysis and standard gamble [7].

Discrete choice experiments (DCEs) are frequently used in health to measure health professionals', patients and public preferences in a wide range of situations [8]. In this study, a DCE was undertaken to measure patients' preferences between PCI and CABG in a sample of hospitalized patients who were, in fact, dealing with the expectation of being submitted to one of these treatments.

Methods

Development of the DCE survey – Selection of attributes and values

To identify treatment attributes for the DCE survey, we followed a mixed-methods approach combining a systematic review of the existing literature on patients' preferences for coronary revascularization (n = 6), and semi-structured individual interviews with patients (n = 54) and physicians (n = 22) from the National Institute of Cardiology. A detailed presentation of this method can be found in [9]. This approach led to the identification of 14 attributes: renal failure, perioperative death, stroke, repeat CABG,

myocardial infarction, heart failure, angina, atrial fibrillation, postoperative infection, long-term survival, hospitalization period, pseudoaneurysm, repeat PCI and incision scar. Whilst cost was identified as a relevant attribute in most studies, we have decided not to include this attribute in our DCE because the treatments of heart conditions are provided for free at the point of delivery in Brazil (i.e., out-of-pocket cost for the patients is null).

As it might be too difficult for patients to compare treatment options based on 14 attributes, we decided to build the DCE scenarios using only four attributes, which were selected considering two points: 1) being the most relevant attributes accordingly to patients ranking [6], and 2) having a significant difference in incidence between PCI and CABG (as a risk attribute with the same probability of occurring in both treatment options would not help to choose one of them). The four attributes selected were: perioperative death, risk of death within five years, risk of having a myocardial infarction within five years and risk of the necessity to redo the treatment within five years.

When describing the treatment options, the four risk attributes were operationalised by giving them specific values. Regarding risk of death, myocardial infarction and to redo procedure within five years, the values came from recent studies that have compared PCI versus CABG [3, 10-14]. The perioperative mortality risk was presented in three levels: 1%, 2% or 3% for PCI and 4%, 6% and 8% for CABG. These levels were selected based on the respectively 2.21% and 6.23% mean PCI and CABG perioperative mortality according to the Brazilian National Database years 2016 and 2017 (DATASUS) [15]. The list of attributes and values included in the DCE can be found in Table 1.

Development of the DCE survey – Designing of the choice tasks

Experimental designing techniques were used to generate the list of choice tasks [16]. The experimental design was D-Efficient design with null prior information about patients' preferences and included 12 choice tasks. In each task, two hypothetical descriptions of the PCI and CABG treatments were compared and the patients were asked to choose their preferred treatment option (Figure 1). The order of the choice tasks was randomised across the participants.

To test respondents' understanding of the choice tasks, we also included two quality checks after the 12 experimental tasks. In the first check (as task #13), the PCI option dominated the CABG option on every attribute (i.e., the less invasive option associated with the lower risks of dying, having a myocardial infarction or to redo treatment) and then respondents were expected to choose PCI. The second check (as task #14) was a repetition

of the first task (randomly selected) and was used to verify consistency in respondents' choices. Respondents were defined as carefully completing the DCE when three conditions are met: (i) they chose PCI in task #13; (ii) They made the same choices in tasks #1 and #14; (iii) They did not choose the same treatment option (i.e., either PCI or CABG) in every task (At the opposite, a respondent systematically selecting PCI/CABG would indicate a non-trading choice behaviour and thus would not allow for estimation of preferences for the risk attributes). In addition to the choice tasks, the questionnaire also collected standard socio-demographic information (i.e., age, sex, income, marital status, study level and the number of previous PCI or CABG).

The survey was pilot tested among 12 patients when a systematic description of the experiment, attributes and treatments options was presented using both figures and numbers (figure 1), since low numeracy was expected. All patients considered themselves able to fully understand the tasks and 14 scenarios a manageable number, so no additional issues were included in the final version.

Study Sample

Following Orme's rule [17] for DCE sample size computation and anticipating that 40% of the patients would be considered as traders and consistent, it was necessary to recruit a minimum of 158 participants. The patients were recruited at the National Institute of Cardiology (a tertiary hospital specialized in cardiology) located in Rio de Janeiro, Brazil. The patients were deemed eligible if they were hospitalized due to a cardiac disease requiring surgery or PCI and if they were 18 years or over. The DCE questionnaire was administered to the patients in face-to-face by trained interviewers and took around 30 minutes to complete. Ethical approval was obtained from the National Institute of Cardiology Ethics Board, and written informed consent was obtained from each study participant (CAAE number 63684017.0.0000.5240).

Statistical analysis

A conditional logit model was used to analyse the patients' choices. The four risk attributes entered the model as continuous and linear variables. Only choices from the 12 experimental tasks were included in the analysis. Analyses were conducted including the answers in two subgroups, one considering all respondents and the other group including only patients who carefully completed the DCE. We accounted for the panel nature of the data (i.e., each respondent providing 12 observations) by fitting an error component logit

model [18].

Once patients' preferences for the risk attributes are estimated, it is possible to compute marginal rates of substitution (MRS) telling us how much of one attribute patients are willing to sacrifice to obtain more of another attribute. Due to the linear specification of the model, the MRS simply consists in the ratio of two estimated coefficients. We follow this approach to compute Maximum Acceptable Risks (MAR) [19] with a 1% increase in the CABG perioperative mortality risk as reference. The MAR would for example indicates which benefits such as long-term risk reduction of infarction, death or to redo procedure would compensate the higher CABG perioperative mortality risk in relation to the PCI perioperative mortality risk.

Results

Out of 160 patients approached, 159 agreed to take part to the study. The mean age in our sample was 56.8 (SD = 12.3) years of age; 70.4% were men and most patients were married (57.23%), white (50.3%), with a low level of education and low income. The demographics of responders are shown in table 2.

Each respondent answered 12 choice tasks, providing thus a total of 1,908 (i.e., 159 x 12) observations for the analysis. Less than half of the patients (44%) successfully passed the three DCE quality checks: 62.3% chose the PCI option in task #13; 88.1% made the same choices in tasks #1 and #14; and 59,8% did not systematically selected PCI or CABG as preferred treatment option. Most patients (79.5%) preferred CABG over PCI ($P < 0.001$). Overall, patients had strong negative preferences on PCI (-0.65). In other words, regardless of the actual probability of risks, patients were 48% less likely to choose PCI (odds ratio 0.52; 95% CI, 0.38–0.72).

Figure 2 provides a visual presentation of estimated relative preference weights and the results for the estimation of preferences are reported in Table 3. The regression coefficients were statistically significant at 5% level for all attributes, except for the PCI perioperative mortality risk ($P = 0.06$). The negative coefficients indicate that patients considered the attributes as something undesirable (more is worse than less).

Discussion

In this study, using a Discrete Choice Experiment (DCE), we elicited relative preferences for attributes of coronary revascularization treatments. To reduce the

hypothetical bias, caused by patients' disinterest or inattention related to hypothetical scenarios, a sample of hospitalized patients with cardiovascular disease who were waiting for PCI or cardiac surgery was chosen. Theoretically, patients facing the health problem would be more involved with the experiment.

The application of DCEs as a tool to elicit preferences for coronary revascularization is rare. Considering our systematic review, most studies (83%) used ranking or rating as the method to identify patients' preferences and only two studies (33%) [7, 20] used hypothetical scenarios. Hornberger et al. [7] studied a nationwide sample of respondents in a conjoint analysis study considering appearance, pain, recovery time, days in hospital and redo rate. It is noteworthy that the participants considered that PCI would be a better option than CABG only if the 3-year risk of redoing revascularization declined to less than 28%. Kipp et al. [20], using a mixed logistic regression analysis, identified that patients preferred PCI over CABG, even when the risk of death was double the risk with CABG or the risk of repeat procedures was more than three times that for CABG. Both studies identified similar results

In contrast with the Kipp study [20], the majority of the patients (73%) in this study chose the most invasive option: CABG. This difference highlights the necessity to analyse patients' preferences locally but besides that, we must consider some differences in the studies designs. Kipp et al [20] made their conclusions based on a threefold risk to repeat PCI in relation to the risk to redo CABG and repeat procedures were described as either repeat PCI or repeat CABG, with levels between 2 and 5%. We considered the risks to repeat procedures separately for PCI and CABG and with higher absolute and relative risks (CABG risk between 1% and 7%; PCI risk between 13% and 35%). This high necessity to redo PCI was observed in diabetic patients in the Syntax trial [21], where 35.3% of patients followed for 5 years had to undergo a new revascularization procedure. The higher levels of risk to redo the procedure in our study may have influenced patients' choices. Based on the mean preference weights of CABG perioperative mortality and the necessity to redo PCI, we can estimate that patients would be willing to accept an increase of 4.4% in the risk of redoing the procedure to each 1% increase in risk of CABG perioperative death.

In practical terms, analysing the Brazilian Government Database (2016 and 2017) [15], the mean CABG perioperative mortality is 6.23% and the PCI perioperative mortality is 2.21%. Based on the 4.02% difference in perioperative mortality and the 4.46% marginal acceptable benefit (table 3), we could expect that our patients sample would value PCI positively in relation to CABG if the risk of redoing the procedure was inferior or equal to

17.9%. Notably, this level of acceptance is superior to the number of repeated PCI in recent studies using second-generation stents, 12% in Best trial [14] with 4.6 years of follow-up and 11% in Excel [22] trial with median three years of follow-up. Based on the mean weights, it suggests that the incorporation of the second-generation stents in the Brazilian public health system could lead to a greater number of patients choosing PCI.

Current guidelines may have to be revised to include patients' preferences into the recommendations which should not be based only on direct comparison between outcomes. In our study, for each 1% risk of death within five years after CABG, the patients considered a 1.34% increase in the risk of death within five years after PCI as the Maximum Acceptable Risk. In other words, as an example, taking into account the results for patients with three-vessel disease of the Syntax trial [23], the 11.4% five years mortality in the CABG group would be equivalent to a 15.3% mortality rate in the PCI group. So based exclusively on long-term mortality, even with higher mortality rate (13.9%), PCI could be considered as the choice of preference in our population.

Despite this conclusion regarding long-term mortality, recommendations should also consider other relevant endpoints. Endpoints such as death, stroke, myocardial infarction and repeat revascularization are frequently grouped into a category called major adverse cardiovascular events (MACE) in clinical trials. The use of MACE has been justified as an attempt to capture the overall treatment effect and their main advantage is the reduction of the duration, sample size and costs of a clinical trial [5].

The use of MACE assumes that all its components are of equal clinical severity and patients and physicians have similar perception of each component, assumptions that were false both in our study and in the studies selected in the systematic review [4-6]. In Pandit, Ahmad and Chow studies [4-6], a statistically significant difference in the weighing attributed to most outcomes and a significant difference between patients and physicians' values were identified. For instance, in Pandit trial [4], while the patients weighed stroke the heaviest (8.83 out of 10), physicians weighed death the heaviest (8.63 out of 10) and Ahmad et al. [6] observed that stroke was considered worse than death for patients and equal for physicians. Neither patients nor physicians considered all clinical end points equally.

The appropriate weight of each component of composite endpoint would provide a more refined interpretation of the trial data. Besides that, our data suggests that patients and physicians weigh attributes differently reinforcing the necessity of sharing decisions and the development of tools to help communication between patients and physicians. Cur-

rently, there is some evidence that few cardiologists discuss the evidence-based results of PCI and some implicitly or explicitly overstated the benefits, leading to misunderstanding and choices not evidence-based [24].

The crucial finding in this study is the patients' preference for the most invasive option: CABG. We presume that this preference is attributable to the sample's features, mainly that our sample was made up in their majority (84%) of patients who had already undergone at least one intervention and had to redo the procedure. Many of these patients considered that CABG could have avoided the necessity of reintervention. The influence of previous treatment experience on patients' preferences between PCI and CABG must be searched in future trials.

This study has some limitations. The high ratio of patients who failed the test for carefully completing responses (56%) raises concerns about patient understanding and the validity of our findings. However, a high percentage of irrational answers in health experiments is not unusual. For instance, in a Discrete Choice Experiment regarding patients' preferences in anticoagulant therapy, Najafzadeh M et al. [25] identified 36% patients who failed the test for rational responses.

Irrational choices are considered a methodological problem of choice experiments, when respondents avoid the intellectual effort of thoroughly considering the trade-offs between different alternatives that are the essence of every choice experiment. Irrational choices may represent simplifying decision heuristics (that are inconsistent with utility maximization assumption); respondent fatigue (resulting from evaluating many choice questions); misunderstanding (heterogeneous interpretation by respondents); or inattention, resulting from the hypothetical context of the study [26]. We opted not to exclude irrational respondents and to analyse the results in both groups. The parameters difference between these two groups was not significantly different in practise, meaning that both groups ranked the attributes in the same order and with similar relative weights. Even with the high number of considered irrational responses, when asked about their understanding, most patients (69.2%) considered that they had understood, and they were secure about their choices.

Other limitations are related to how we modelled the attributes. They were modelled as continuous variables to make it easier to understand and we considered the effect of levels preferences as linear, which may not be realistic. Finally, our sample was selected from a tertiary hospital in Rio de Janeiro and may not fully represent all patients with cardiovascular disease in Brazil.

In conclusion, choosing the “best” treatment option is a demanding challenge. This study evaluated attributes and levels that could be used in future trials to explore stated preferences between PCI and CABG; reaffirmed that attributes are valued differently and they should be analysed properly in composite endpoints and; estimated the relative weights of preference in a convenience sample of hospitalized patients. Incorporating patients’ perspective into recommendations may help enhance the value of decisions both individually and for the health system.

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References

1. Benjamin EJ, Virani SS, Callaway CW, et al. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation* 2018;137(12):e67-e492.
2. Roger VL. Epidemiology of myocardial infarction. *Med Clin North Am* 2007;91(4):537-52; ix.
3. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *NEJM* 2009;360(10):961-72.
4. Pandit J, Gupta V, Boyer N, Yeghiazarians Y, Ports TA, Boyle AJ. Patient and physician perspectives on outcomes weighting in revascularization. The POWR study. *Int J Cardiol* 2014;177(2):513-4.
5. Chow RD, Wankhedkar KP, Mete M. Patients' preferences for selection of endpoints in cardiovascular clinical trials. *J Community Hosp Intern Med Perspect* 2014;4.
6. Ahmad Y, Nijjer S, Cook CM, et al. A new method of applying randomised control study data to the individual patient: A novel quantitative patient-centred approach to interpreting composite end points. *Int J Cardiol* 2015;195:216-24.
7. Hornberger J, Bloch DA, Hlatky MA, Baumgartner W. Patient preferences in coronary revascularization. *Am Heart J*. 1999;137(6):1153-62.
8. de Bekker-Grob EW, Ryan M, Gerard K. Discrete choice experiments in health economics: a review of the literature. *Health Econ* 2012;21(2):145-72.
9. Magliano CAS, Tura BR, Oliveira CSR, Rebelo ARO, Pereira CCA. Patient and physician preferences for attributes of coronary revascularization. *Patient Prefer Adherence* 2018;12:757—64.
10. Kapur A, Hall RJ, Malik IS, et al. Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients. 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial. *J Am Coll Cardiol* 2010;55(5):432-40.
11. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *NEJM*. 2012;367(25):2375-84.
12. Kamalesh M, Sharp TG, Tang XC, et al. Percutaneous coronary intervention versus coronary bypass surgery in United States veterans with diabetes. *J Am Coll Cardiol* 2013;61(8):808-16.

13. Morice MC, Serruys PW, Kappetein AP, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. *Circulation* 2014;129(23):2388-94.
14. Park SJ, Ahn JM, Kim YH, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. *NEJM* 2015;372(13):1204-12.
15. DATASUS. Tabnet. Available at: <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/qiuf.def>. [Accessed March 1, 2018].
16. ChoiceMetrics (2012) Ngene 1.1.1 User Manual & Reference Guide, Australia.
17. de Bekker-Grob EW, Donkers B, Jonker MF, Stolk EA. Sample Size Requirements for Discrete-Choice Experiments in Healthcare: a Practical Guide. *The patient*. 2015;8(5):373-84.
18. McFadden D, Train K. Mixed MNL models for discrete response. *J Appl Econ* 2000;15(5):447-70.
19. Van Houtven G, Johnson FR, Kilambi V, Hauber AB. Eliciting benefit-risk preferences and probability-weighted utility using choice-format conjoint analysis. *Med Decis Making* 2011;31(3):469-80.
20. Kipp R, Lehman J, Israel J, Edwards N, Becker T, Raval AN. Patient preferences for coronary artery bypass graft surgery or percutaneous intervention in multivessel coronary artery disease. *Catheter Cardiovasc Interv* 2013;82(2):212-8.
21. Kappetein AP, Head SJ, Morice MC, et al. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. *Eur J Cardiothorac Surg* 2013;43(5):1006-13.
22. Stone GW, Sabik JF, Serruys PW et al. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. *NEJM* 2016;375(23):2223-35.
23. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet*. 2013;381(9867):629-38.
24. Goff SL, Mazor KM, Ting HH, Kleppel R, Rothberg MB. How cardiologists present the benefits of percutaneous coronary interventions to patients with stable angina: a qualitative analysis. *JAMA Intern Med* 2014;174(10):1614-21.

25. Najafzadeh M, Gagne JJ, Choudhry NK, Polinski JM, Avorn J, Schneeweiss SS. Patients' preferences in anticoagulant therapy: discrete choice experiment. *Circ Cardiovasc Qual Outcomes* 2014;7(6):912-9.
26. Reed Johnson F, Lancsar E, Marshall D, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. *Value Health* 2013;16(1):3-13.

Table 1. Attributes and values used to describe treatment options in the DCE

Attribute	PCIs	CABG
Perioperative death	1% - 2% - 3%	4% - 6% - 8%
Death within 5 years	8% - 15% - 22%	7% - 11% - 15%
MI within 5 years	6% - 10% - 14%	3% - 5% - 7%
Redo procedure	13% - 24% - 35%	1% - 4% - 7%

CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Table 2. Baseline socioeconomic and characteristics of respondents

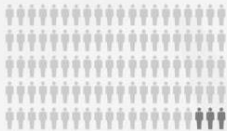






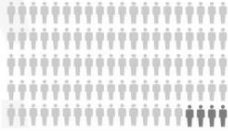
Characteristic	Data (all patients) N = 159	Data (rational) N = 70
Age in years, mean (SD)	56.8 (12.3)	56 (13)
Sex, number (%)	Male 112 (70.4%)	Male 51 (73%)
Annual income (U\$), mean (SD)	6.888,31 (851.79)*	8909.3 (742.4)*
Marital status	Married 91 (57.2%) Single 38 (23.9%) Other 30 (18.9%)	Married 45 (64%) Single 16 (23%) Other 30 (13%)
Level of education, number (%)	≤ 1 year: 6 (3.8%) 2 – 5 years: 41 (25.8%) 6 – 9 years: 33 (20.7%) 10 – 12 years: 47 (29.6%) College degree: 32 (20.1%)	≤ 1 year: 1 (1.4%) 2 – 5 years: 17 (24.3%) 6 – 9 years: 15 (21.3%) 10 – 12 years: 21 (30%) College degree: 16 (23%)

CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention; SD, standard deviation. *conversion based on <http://www4.bcb.gov.br/pec/conversao/conversao.asp> (1 U\$ = 3.49 R\$).

Table 3. Estimated Relative Preference Weights (All respondents, N = 159).

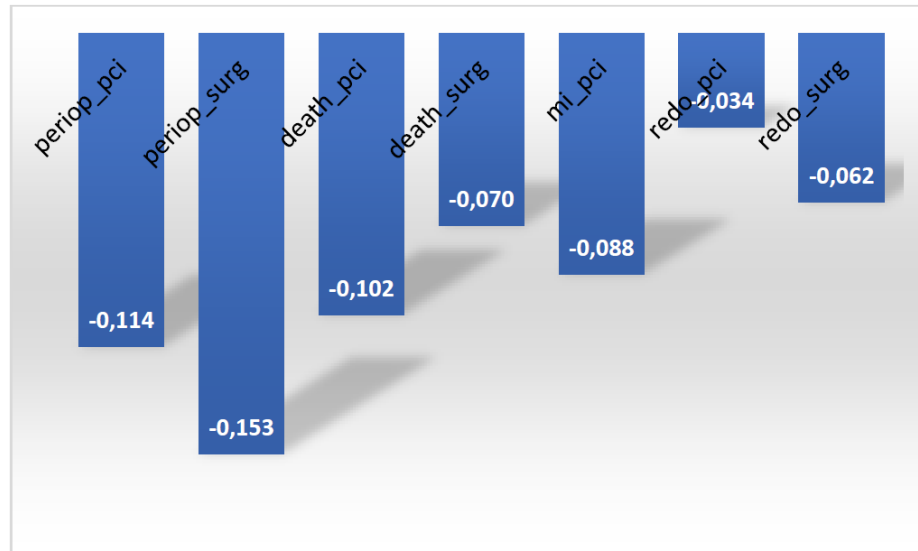
Attribute	CABG MAR	CABG OR (95% CI)	PCI MAR	PCI OR (95% CI)
Perioperative death	1	0.86 (0.81 to 0.91)	1.34	0.89 (0.79 to 1.01)
Death in 5 years	2.18	0.98	1.49	0.90 (0.89 to 0.92)
MI in 5 years	-1.61	0.93 (0.90 to 0.96)	1.74	0.973 (0.956 to 0.990)
Redo in 5 years	2.48	0.94 (0.90 to 0.98)	4.46	0.97 (0.96 to 0.98)

Figure 1. A sample Discrete Choice Experiment Choice

ATTRIBUTES	ANGIOPLASTY	SURGERY
Perioperative death	 3%	 8%
Death in 5 years	 22%	 15%
Myocardial infarction in 5 years	 14%	 7%
Redo Procedure	 13%	 4%
I PREFER	()	()

*Suppose that you have chest pain. Your doctor tells you that you are at increased risk of heart attack and that there are 2 treatment options: 1) PCI, a less invasive option, in where a catheter is feed up through arteries and a stent is inserted into the narrowed coronary improving blood flow and 2) surgery, a chest opening is required and the narrowed coronary will be bypassed by a new artery. Both treatments can reduce the risk of heart attack and death. However, your doctor warns you that they have different levels of risk as shown in the picture. **If PCI or surgery were your only options, which one would you choose?***

Figure 2. Relative preferences weights of patients for percutaneous coronary intervention versus open surgery in coronary disease (All respondents, N = 159).



CI: confidence interval; MAR: Maximum Acceptable Risk with CABG perioperative death as reference; MI: myocardial infarction; OR: odds ratio. $n = 3840$, number of events = 1920 Intercept: 2.54420. Likelihood ratio test = 995.9 on 8 df, $p < 2e-16$. Wald test = 780.1 on 8 df, $p < 2e-16$. Score (logrank) test = 924.9 on 8 df, $p < 2e-16$.