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COMPARAÇÃO ENTRE A CAPACIDADE PROGNÓSTICA DO GRAU DE CONGESTÃO PULMONAR AFERIDO PELA ECOGRAFIA PULMONAR E A CORRELAÇÃO DESTA COM A PRESSÃO DIASTÓLICA FINAL DO VENTRÍCULO ESQUERDO EM PACIENTES SUBMETIDOS À ANGIOPLASTIA CORONARIANA PRIMÁRIA

Porto Alegre

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À minha família, sempre.

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RESUMO

O objetivo do presente trabalho foi comparar a capacidade prognóstica do grau de congestão pulmonar aferido pela ecografia pulmonar (EP) na beira do leito, sua relação com avaliação clínica, e a correlação com a pressão diastólica final do ventrículo esquerdo (Pd2VE) em pacientes admitidos com infarto agudo do miocárdio com supradesnivelamento do segmento ST (IAMCSST) submetidos à intervenção coronariana percutânea (ICP) primária. Trata-se de um estudo de coorte prospectivo realizado em um hospital terciário de referência.
A Pd2VE foi aferida imediatamente antes da ICP. Foi feita análise da curva *ROC* (*Receiver operating characteristic curve*) para calcular a área sob a curva (*AUC – area under the curve*) para ocorrência de eventos cardiovasculares adversos maiores (ECAM). A *AUC* da Pd2VE e EP foram 0,63 (*P*=0,002) e 0,71 (*P*<0,001), respectivamente. A correlação de Spearman entre a Pd2VE e EP foi 0.33 (P<0.001). Na análise multivariada, a EP permaneceu como preditor independente de ECAM intra-hospitalares (*odds ratio* [OR] = 1, 14 [IC 95% , 1,06–1,23]; *P*=0,01). A EP quando acrescida à classificação de Killip e Kimball (KK) – classificação LUCK - aumenta a AUC para mortalidade intra-hospitalar de 0,86 para 0,89 (*P*=0.05 para diferença entre as curvas). Em conclusão, encontramos uma fraca correlação entre Pd2VE e EP em pacientes submetidos a ICP primária, demonstrando que manifestação hemodinâmica do aumento da pressão de enchimento do ventrículo esquerdo não se manifesta com alteração radiológica compatível. A classificação LUCK foi mais sensível do que o exame físico isoladamente para identificar pacientes com pior prognóstico. A EP se manteve preditor de ECAM intra-hospitalares.

Palavras-chave: Insuficiência cardíaca, mortalidade, Infarto Agudo do Miocárdio; intervenção coronariana percutânea, ultrassonografia.

ABSTRACT

The objective of the present study was to compare the prognostic ability of pulmonary congestion measured by bedside lung ultrasound (LUS), the association with physical examination and the correlation with left ventricular end-diastolic pressure (LVEDP) and in patients admitted with acute myocardial infarction with ST-segment elevation (STEMI) undergoing to primary percutaneous coronary intervention (PCI). This was a prospective cohort study in a tertiary reference hospital.

LVEPD was measured immediately before (PCI). Receiver operating characteristic curve (ROC) analysis was performed to calculate the area under the curve (AUC) for the occurrence of major adverse cardiovascular events (MACE). The AUC of LVEDP and LUS were 0.63 (P=0.002) and 0.71 (P<0.001). Spearmen's correlation between LVEDP and LUS was 0.33 (P<0.001) In the multivariate analysis, LUS remained an independent predictor of in-hospital MACE (odds ratio [OR] = 1.14 [95% CI, 1.06–1.23]; P=0.01). EP when added to the Killip and Kimball (KK) classification – LUCK classification - increases the AUC for in-hospital mortality from 0.86 to 0.89 (P=0.05 for difference between curves). In conclusion, we found a weak correlation between LVEDP and LUS in patients undergoing primary PCI, demonstrating that hemodynamic manifestation of increased left ventricular filling pressure does not manifest with compatible radiological changes. LUCK classification was more sensitive than physical examination to identify patients at risk of mortality. LUS remained a predictor of in-hospital MACE.

Keywords: heart failure, mortality, myocardial infarction, percutaneous coronary intervention, ultrasonography

LISTA DE ABREVIATURAS E SIGLAS

Língua Portuguesa

AVE: Acidente vascular encefálico

BNP: peptídeo natriurético tipo-B

CRM: Cirurgia de revascularização do miocárdio

EAP: Edema agudo de pulmão

ECAM: Eventos cardiovasculares adversos maiores

ECG: Eletrocardiograma

EP: Ecografia pulmonar

IAM: Infarto agudo do miocárdio

IAMCSST: Infarto agudo do miocárdio com supradesnivelamento do segmento ST

IC: Insuficiência cardíaca

IC95%: Intervalo de confiança de 95%

ICP: Intervenção coronariana percutânea

KK: Classificação de Killip-Kimball

LUCK: ecografia pulmonar associada a classificação Killip

NT-pró BNP: N-terminal do peptídeo natriurético tipo B

Pd2: Pressão diastólica final

Pd2VE: Pressão diastólica final do ventrículo esquerdo

PN: Peptídeo natriurético

VE: Ventrículo Esquerdo

Língua Inglesa

AUC: *Area under the curve*

LVEDP: *Left ventricle end diastolic pressure*

LUS: *Lung ultrasound*

LUCK*: lung ultrasound combined with Killip*

ROC: *Receiver operating characteristic*

STEMI: *ST segment elevation myocardial infarction*

MACE: *Major adverse cardiovascular events*

PCI: *Percutaneous coronary intervention*

OR: *Odds ratio*

95% CI: 95% *confidence interval*

SUMÁRIO

1. INTRODUÇÃO

Apesar dos avanços no diagnóstico e no tratamento da doença arterial coronariana (DAC), ela persiste como uma das principais causas de morbimortalidade no mundo. A Organização Mundial da Saúde estima 18 milhões de óbitos anualmente por doenças cardiovasculares, e que mais de 75% ocorram em países em desenvolvimento como Brasil[1]. No contexto brasileiro, cerca de 25% dos óbitos anuais são atribuídos às doenças cardiovasculares, sendo que metade deles resulta de doenças isquêmicas do coração. Além dos custos associados ao tratamento, essas enfermidades afetam predominantemente indivíduos em idade economicamente ativa, resultando em numerosas internações hospitalares e gerando custos significativos para o Sistema Único de Saúde. Dentre o espectro clínico da doença arterial coronariana, o infarto agudo do miocárdio (IAM) persiste com elevada mortalidade apesar dos avanços terapêuticos nas últimas décadas. No Brasil, conforme dados do DATASUS, foram registradas 90.465 mortes em 2020 por IAM, sendo 4.851 no Rio Grande do Sul [2].

Diversos estudos randomizados que incluíram pacientes submetidos a angioplastia coronariana primária demonstram taxa de reinfarto, revascularização de urgência, trombose de stent e sangramento variando de 1 a 7%, ilustrando a quantidade significativa de ocorrência de complicações mesmo após tratamento adequado e em cenários controlados de pesquisa clínica [3,4]. Em um estudo nacional, refletindo a realidade de muitos pacientes atendidos no Brasil pelo Sistema

Único de Saúde, apenas a taxa de mortalidade intra-hospitalar foi próxima de 10% [5]

A DAC começa a se desenvolver na infância e progride no decorrer de toda a vida [6] Ela ocorre por um processo de obstrução das artérias coronárias devido à formação progressiva da placa ateromatosa dentro das artérias coronárias epicárdicas. A inflamação crônica endotelial é consequência de um desequilíbrio no mecanismo lipídico e uma resposta imune inadequada [7]. Quando a placa atinge um grau de estenose maior que 50% do diâmetro do vaso, levando a uma restrição do fluxo sanguíneo, pode ocorrer um desequilíbrio na oferta e demanda de oxigênio. Nos momentos em que a demanda se encontra elevada, como no exercício físico, esse processo pode levar à hipóxia e causar o sintoma de angina[8]. Além de sintomas anginosos, estas placas eventualmente podem se romper causando o infarto agudo do miocárdio (IAM) e dependendo do grau de acometimento ventricular, insuficiência cardíaca isquêmica, contribuindo para ser uma das principais causas de morbimortalidade mundialmente[9].

O manejo da DAC estável envolve alguns aspectos importantes: (1) identificação e tratamento de comorbidades associadas que podem agravar sintomas de angina, (2) cuidado com fatores de risco para doença coronariana, (3) uso de intervenções farmacológicas e não farmacológicas para prevenção secundária, (4) manejo farmacológico da angina e (5) revascularização por angioplastia com stent ou cirurgia de revascularização do miocárdio (CRM), quando indicado. Das terapias medicamentosas, aspirina, estatinas e inibidores da enzima de conversão da angiotensina (IECA) demonstraram reduzir a mortalidade ou morbidade em pacientes com DAC estável. Em pacientes estáveis com disfunção

ventricular esquerda após infarto do miocárdio, IECA e agentes betabloqueadores reduzem tanto a mortalidade quanto o risco de novo infarto, sendo recomendados em todos esses pacientes, com ou sem angina crônica, juntamente com aspirina, estatinas. O tratamento da DAC estável é multifacetado e visa aliviar os sintomas, prevenir eventos cardiovasculares futuros e melhorar a qualidade de vida do paciente. Além do tratamento farmacológico e procedimentos invasivos, a modificação do estilo de vida desempenha um papel crucial no manejo da DAC estável. Isso inclui a adoção de uma dieta saudável, prática regular de exercícios físicos, controle do peso, abandono do tabagismo e gerenciamento do estresse[9].

A doença arterial coronariana isquêmica pode se manifestar clinicamente como estável (já descrita) ou como síndrome coronariana aguda (SCA). O espectro da SCA inclui o infarto agudo do miocárdio com supradesnivel segmento ST (IAMCSST) e as síndromes coronarianas agudas sem elevação do segmento ST (infarto agudo do miocárdio sem supradesnível do segmento ST – IAMSSST - e angina instável). Estas últimas consistem apresentam apresentações clínicas indistinguíveis na avaliação inicial. Várias características ajudam a diferenciar a SCA da angina crônica estável, incluindo (1) início súbito de sintomas em repouso (ou com esforço mínimo) que duram pelo menos 10 minutos, a menos que sejam tratados prontamente; (2) dor intensa, pressão ou desconforto no peito; e (3) um padrão acelerado de angina que se desenvolve com mais frequência, com maior gravidade, ou que desperta o paciente durante o sono. O eletrocardiograma de 12 derivações (ECG) e marcadores de necrose miocárdica são ferramentas essenciais para distinguir entre os três tipos de SCA mencionados anteriormente[10]. O infarto agudo do miocárdio ocorre quando há injúria e necrose miocárdica. Na prática, ele

pode ser diagnosticado com base na apresentação clínica, eletrocardiograma (ECG), exames laboratoriais e exames de imagens invasivos e não invasivos. Inicialmente, o infarto agudo do miocárdio pode ser classificado de acordo com a presença ou ausência da elevação do segmento ST – que corresponde à presença ou não de necrose transmural da parede [11]. Contudo, ainda pode ser classificado em 6 subtipos de infarto. 1) complicação da doença arterial coronariana, geralmente decorrente da ruptura ou erosão da placa aterosclerótica; 2) desbalanço na oferta-demanda na ausência de complicação aguda aterosclerótica; 3) morte súbita sem confirmação de biomarcador ou por ECG; 4a) relacionado à intervenção percutânea coronariana (ICP); 4b) relacionado à trombose de stent; 5) relacionado à cirurgia de revascularização do miocárdio (CRM) [12].

A ruptura ou erosão da placa aterosclerótica, resultando na exposição do material trombogênico ao sangue circulante, é o mecanismo mais frequente pelo qual o IAM acontece – infarto tipo 1 [13]. Quando a oclusão obstrui toda a luz do vaso, geralmente ocorre o supradesnivelamento do segmento ST no eletrocardiograma, quando isso acontece, temos o IAMCSST.

A terapia de reperfusão através o reestabelecimento do fluxo coronariano é a pedra fundamental do tratamento do IAM. Ela pode ser realizada por meio terapia fibrinolítica ou da intervenção coronariana percutânea. A superioridade de cada terapia depende das condições clínicas e anatômicas de cada paciente. As diretrizes atuais recomendam que a ICP aconteça em um tempo ≤ 90 minutos do primeiro contato médico ou dentro de 12 horas do início dos sintomas [14]. A reperfusão precoce é crucial para o seu desfecho clínico, com redução do tamanho do infarto, preservação da função ventricular e diminuição importante de morbimortalidade.

Atrasos para o diagnóstico, transferência ou início da terapia impactam diretamente na redução do benefício de qualquer tipo de tratamento [15].

De forma geral, a angioplastia reduz a área estenótica e aumenta a área luminal do vaso, visando restabelecer o fluxo. Isso pode ocorrer tanto pela aspiração do trombo, pela insuflação de um balão ou pela introdução de um stent. Quando se compara a terapia fibrinolítica e percutânea, a reperfusão completa acontece em apenas 50 - 60% dos pacientes quando recebem a terapia fibrinolítica, enquanto esse número se eleva para mais de 95% quando são submetidos à ICP. As duas terapias foram avaliadas em uma meta-análise realizada em 2003, com 23 estudos, a qual comparou 3.872 pacientes submetidos à ICP com 3.867 pacientes submetidos à terapia fibrinolítica. Os pacientes submetidos à ICP apresentaram menor taxa de mortalidade, menor taxa de reinfarto, e menos acidente vascular encefálico (AVE)[16].

Pacientes com IAMCSST que são inicialmente tratados por fibrinólise em um centro sem ICP devem ser transferidos para um centro com ICP se o paciente desenvolver choque cardiogênico ou tiver falha na reperfusão com fibrinolítico (redução do ST <50% dentro de 60-90 min da administração do fibrinolítico ou presença de instabilidade elétrica ou hemodinâmica, piora da isquemia ou dor persistente. A transferência também deve ser considerada como parte de uma estratégia farmacoinvasiva em pacientes estáveis pacientes com intenção de realizar angiografia dentro de 3 a 24 horas após a fibrinólise [17]

Diversos fatores influenciam a ocorrência de desfechos adversos após um IAMCSST. A identificação de preditores de resultados adversos é crucial para a

estratificação de riscos e o gerenciamento ideal dos pacientes. Algumas diferenças de gênero são evidentes, com homens sofrendo o primeiro IAM em torno de sete anos antes das mulheres. Entretanto, existem estudos sugerindo que as mulheres podem enfrentar taxas de mortalidade mais altas, talvez devido a apresentações tardias ou sintomas atípicos. [18,19] A idade, um preditor bem estabelecido, coloca os indivíduos mais velhos em maior risco de complicações e mortalidade. Estudos também apontam que outras comorbidades como diabetes, hipertensão e doença renal crônica também estão associadas a resultados desfavoráveis.[20–22] A apresentação clínica inicial do infarto com a presença de choque cardiogênico na admissão é um fator prognóstico grave, indicando dano miocárdico avançado com disfunção ventricular significativa e alto risco de mortalidade. Níveis elevados de troponina, uma consequência do dano miocárdico, também se correlacionam com um tamanho maior do infarto, e consequente redução de fração de ejeção do ventrículo esquerdo (FEVE) e maior risco de mortalidade.[22] A FEVE também desempenha um papel prognóstico importante visto que valores reduzidos pós IAMCSST estão associados a uma maior incidência de complicações e eventos adversos, incluindo insuficiência cardíaca, arritmias, internações recorrentes e aumento de mortalidade.[23]

2. REVISÃO DA LITERATURA

2.1 Classificação de Killip e Kimball

Existem diversas formas de estratificar a gravidade dos pacientes com IAMCSST na tentativa de avaliar o risco de mortalidade intra-hospitalar e a necessidade de tratamento especializado em unidades coronárias. A mais utilizada é a classificação de Killip-Kimball (KK), de rápida aplicação e com excelente discriminação prognóstica [24]. Esta classificação foi desenvolvida em 1967 e leva em conta a gravidade de insuficiência cardíaca aguda em pacientes acometidos por IAMCSST, avaliados somente pelo exame clínico da admissão e sem necessidade de exames complementares. De forma simples, avalia a presença de congestão pulmonar e má perfusão periférica. Os pacientes são classificados em: KK I, sem sinais de descompensação cardíaca; KK II, com estertores crepitantes pulmonares, terceira bulha e/ou pressão venosa jugular elevada; KK III, com edema pulmonar agudo (EAP); KK IV, com choque cardiogênico ou hipotensão arterial (medida como PAS < 90 mmHg) e evidência de vasoconstrição periférica (oligúria, cianose ou diaforese). Ao avaliar desfechos em 30 dias, os autores da publicação original encontraram taxas de mortalidade crescente nos pacientes com Killip I, II, III e IV de 6%, 17%, 38% e 81%, respectivamente.

Tabela 1 - Morbidade e mortalidade relacionada à avaliação clínica de 250 pacientes

	KK I	***KK II***	***KK III***	***KK IV***
Distribuição (%)	33	38	10	19
Idade média, anos	58	65	69	67
Arritmias graves (%)	36	46	73	94
Parada cardiorrespiratória (%)	5	15	56	77
Mortalidade (%)	6	17	38	81

Adaptado de Killip T 3rd, Kimball JT. Am J Cardiol. 1967.

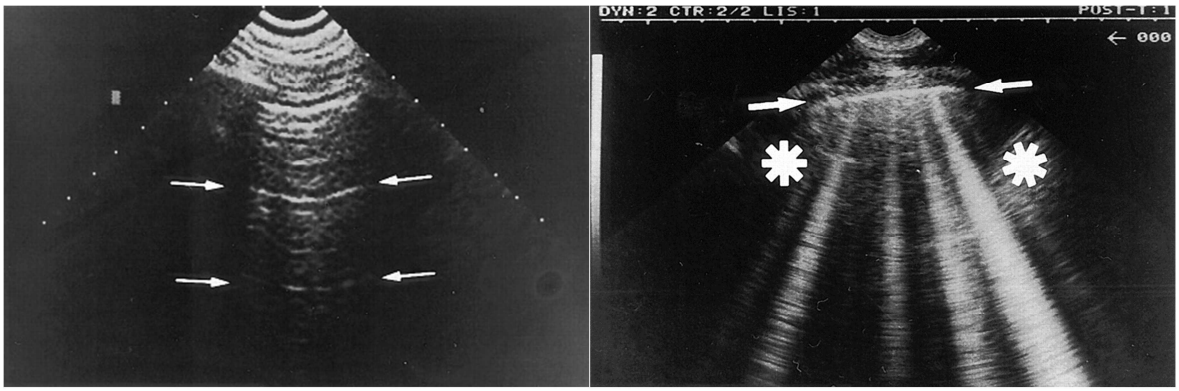
A classificação de Killip-Kimball foi criada antes da era da reperfusão coronariana, porém persiste amplamente utilizada na prática clínica [25]. Estudo realizado por Mello e colaboradores avaliou a classificação de Killip-Kimball na mortalidade tardia e encontraram incidências crescentes: KK I 17,7%; KK II 27,3%; KK III, 30,4%; KK IV 48,8% em um seguimento de até 5 anos[26]. Apesar da redução da mortalidade decorrente dos avanços das técnicas de reperfusão das últimas décadas, a classificação de Killip-Kimball persiste como uma ferramenta rápida e eficaz de avaliação prognóstica tanto a curto quanto a longo prazo. A despeito da sua facilidade de uso e sua capacidade prognóstica ela também apresenta algumas limitações: a distinção entre os grupos Killip II e III é definida pelo nível do tórax em que os estertores são audíveis, e a definição do grupo IV (choque cardiogênico) é igualmente imprecisa.

2.2 Ecografia Pulmonar

A ecografia é um método de diagnóstico pela formação de imagens a partir da absorção e reflexão das ondas sonoras. Por ser um método não invasivo e prontamente disponível, pode complementar o exame físico e avaliação clínica na beira do leito [27,28].

A presença de congestão pulmonar, muitas vezes, é difícil de ser avaliada quando sintomas são discretos. Na década de 90, a ecografia pulmonar foi proposta para detecção de edema agudo de pulmão em pacientes criticamente enfermos [29]. Na avaliação ecográfica de um pulmão sadio, se observa a linha pleural movimentando-se sincronicamente com a respiração: esse movimento horizontal dinâmico é chamado de deslizamento pulmonar (*lung sliding*). Além disso, existem algumas linhas horizontais hiperecogênicas surgindo em intervalos regulares da linha pleural: as linhas A. Quando combinadas com a presença de deslizamento pleural, esses artefatos de reverberação representam um sinal de conteúdo normal de ar no espaço alveolar [30]. Quando o ar é substituído por outras substâncias (sangue, exsudato, transudato, etc) ocorre a criação de artefatos conhecidos como linha B ou “cauda de cometa” [31] Essas linhas surgem da linha pleural, se estendem de forma vertical, e se movem de forma sincrônica com o pulmão. Importante ressaltar que em pacientes sadios uma ou duas linhas B podem ser encontradas por espaço intercostal, sem conotação patológica. Porém, quando em número elevado, representam o preenchimento de um septo interlobular ou intralobular, sugerindo edema pulmonar ou intersticial [32].

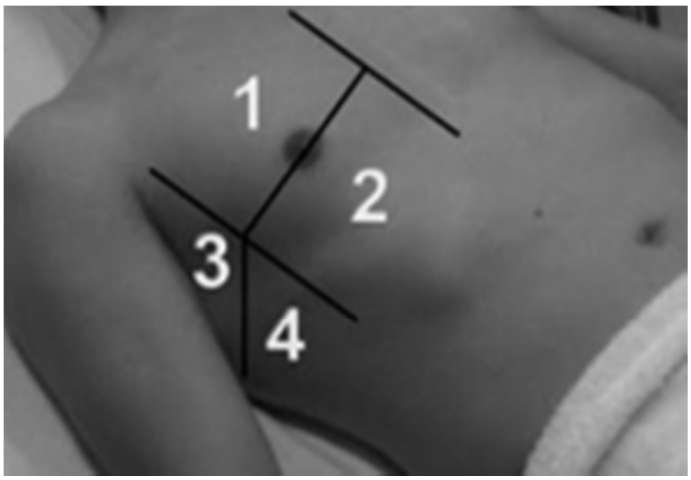
Figura 1 – *Esquerda*: Aparência ultrassonográfica de um pulmão com conteúdo normal de ar no espaço alveolar. As setas indicam as linhas A. *Direita*: Aparência de um pulmão congesto com presenta de Linhas B ou “cauda de cometa”



Adaptado de Lichtenstein *et al*. Am J Respir Crit Care Med. 1997

Existem diversos protocolos para avaliação ecográfica pulmonar. Se preconiza, atualmente, que seja realizada avaliação com 8 campos pulmonares. O transdutor curvilíneo deve ser posicionado em cada um dos campos e mantido de forma estática durante a respiração do paciente. Quando se encontra 3 ou mais linhas B, é considerado um exame alterado [33]

Figura 2 – Protocolo de avaliação ecográfica de 8 campos pulmonares.



Adaptado de Volpicelli *et al*. Am J Emerg Med, 2006.

A ecografia pulmonar pode apresentar uma sensibilidade elevada para detecção de congestão. Em um estudo realizado por Kataoka e Takada, a ecografia pulmonar teve uma sensibilidade de 90% e especificidade de 95% para detecção de congestão, sendo superior aos sinais avaliados do exame físico para o diagnóstico, como crepitantes à ausculta pulmonar, presença de turgência jugular e edema periférico. [34].

Tabela 2 - Valor Diagnóstico Comparativo de Sinais Clínicos Tradicionais e Ecografia Pulmonar para Identificação de Congestão

	Sensibilidade (%)	***Especificidade (%)***	***Acurácia (%)***
Achados no Exame Físico			
Crepitantes	55	91	65
Turgência Jugular	40	86	52
Edema Periférico	37	95	52

Ecografia Pulmonar			
Edema pulmonar	90	95	91

Adaptado de Kataoka e Takada. JACC, 2000.

Desse modo, a ecografia de pulmão tem sido incorporada à prática clínica como uma importante ferramenta na avaliação de congestão e pode complementar o exame físico para insuficiência cardíaca aguda, especialmente quando a ausculta pulmonar é comprometida pela presença de obesidade, doença pulmonar ou ruído externo excessivo.

2.3 Pressão diastólica final do ventrículo esquerdo

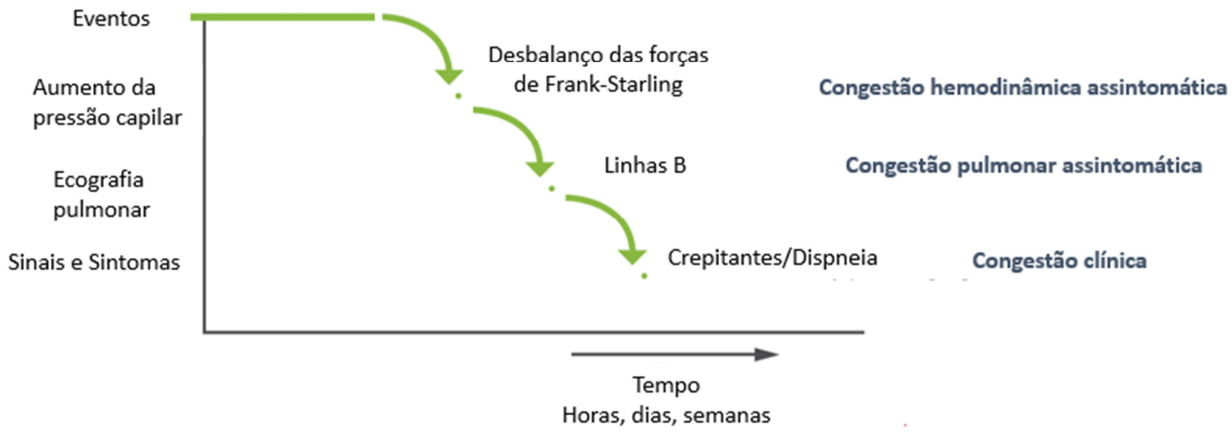
Muitas vezes pacientes podem se apresentar com congestão clínica manifesta, evidenciada através de crepitantes à ausculta pulmonar, turgência venosa jugular e edema periférico. Entretanto, outros podem ter os sinais clínicos de congestão ausentes, porém apresentar pressões de enchimento elevadas no ventrículo esquerdo (Pd2) [35] Assim, os sinais clínicos de congestão podem ser pouco sensíveis e acurados [36].

Essa congestão hemodinâmica ocorre através do aumento na pressão diastólica final (Pd2) do ventrículo esquerdo (VE). A persistência desse processo leva à quebra da barreira alvéolo-capilar, acúmulo de água no interstício e posteriormente sinais clínicos de congestão [37].

A Pd2VE é a pressão aferida dentro do VE imediatamente antes da contração ventricular. Ela pode ser mensurada pela introdução de um cateter através da válvula aórtica no ventrículo esquerdo durante a realização do cateterismo cardíaco esquerdo. Ela é chamada de “pré-carga” do VE, e corresponde

à pressão no interior do átrio esquerdo. Medidas elevadas de Pd2 do VE estão relacionadas à disfunção diastólica, aumento retrógrado da pressão dos capilares pulmonares e consequentemente congestão pulmonar. A esse fenômeno foi denominado a “cascata da congestão”, no qual o aumento da pressão diastólica final do ventrículo esquerdo é o evento inicial para congestão sistêmica (**Figura 4**).

Figura 4 – Cascata da congestão



Adaptado de Picano, et al JACC Vol 1. No 11, 2018

A disfunção diastólica precede o início da disfunção sistólica na isquemia aguda, e a utilidade prognóstica dos índices diastólicos em pacientes com infarto agudo do miocárdio é conhecida[38]. A utilização da Pd2 demonstrou predizer de maneira independente a ocorrência de desfechos cardiovasculares maiores como morte, choque cardiogênico e insuficiência cardíaca em análise de dois grandes ensaios clínicos randomizados no contexto de IAMCSST. No primeiro, realizado por Planer e colegas, com 2797 pacientes, a Pd2VE se mostrou preditor independente de mortalidade e reinfarto em 2 anos, mesmo quando ajustado para fração de ejeção do ventrículo esquerdo. Pacientes que tinham um valor acima de 24 mmHg tinham um risco aumentado para mortalidade a curto e longo prazo[39]. No segundo,

realizado por Bagai e colegas, com 1909 pacientes, a Pd2VE se mostrou preditor independente de mortalidade em 90 dias e desfechos combinados no período hospitalar [40]. Trata-se de medida de fácil e rápida aferição, sem necessidade de materiais específicos e aumento de custos para pacientes submetidos a coronariografia de urgência.

2.4 Peptídeos Natriuréticos

Os peptídeos natriuréticos (PN) são uma família de hormônios contrarreguladores importantes na insuficiência cardíaca, com efeitos vasodilatadores, antifibróticos e natriuréticos. O pró-hormônio pró-BNP é sintetizado nos miócitos em resposta ao estiramento e em seguida clivado no plasma em peptídeo ativo (peptídeo natriurético tipo-B - BNP) e em um fragmento N-terminal biologicamente inerte (NT-proBNP). O BNP foi inicialmente identificado em cérebros suínos, sendo posteriormente também encontrado em cérebros humanos, embora sua concentração seja mais elevada no tecido miocárdico. O BNP tem uma meia-vida de aproximadamente 20 minutos enquanto o NT-proBNP, apresenta uma meia-vida mais longa, de aproximadamente 1 a 2 horas, levando a níveis circulantes maiores, e com menores flutuações quando comparado com o BNP[41,42].

Estes biomarcadores são encontrados nos cardiomiócitos e liberados na corrente sanguínea em resposta ao estiramento e estresse da parede ventricular e atrial. Diversos fatores podem influenciar nas quantidades séricas de BNP e NT-proBNP, tais como hipertensão pulmonar, idade, insuficiência renal, obesidade,

presença de valvopatias cardíacas e mesmo estados hipercinéticos como sepse ou infarto agudo do miocárdio [43].

BNP desempenha um papel crucial na regulação da pressão arterial, dos eletrólitos e na manutenção da homeostase de volume, sendo predominantemente gerado em resposta ao estresse hemodinâmico. A elevação dos níveis de BNP ocorre principalmente em reação ao estiramento da parede ventricular esquerda e à sobrecarga de volume. O BNP manifesta diversos efeitos sistêmicos, como vasodilatação, aumento do volume urinário e da excreção de sódio, inibição do sistema nervoso simpático e do sistema renina-angiotensina-aldosterona, desempenhando uma função natural de antagonista. Além disso, exerce efeitos antimitogênicos nos tecidos cardiovasculares, influenciando o remodelamento cardiovascular [41,42,44]

A isquemia miocárdica, bem como disfunções diastólicas e sistólicas agudas (sobrecarga de pressão ou volume) levam à elevação de PNs [45]. Em pacientes com IAM com elevação do segmento ST, os PNs aumentam rapidamente e os valores estão correlacionados com tamanho do infarto e disfunção do VE[43]. Além disso, também têm demonstrado boa capacidade para predição de eventos cardiovasculares adversos no contexto de IAMCSST [46,47].

3. JUSTIFICATIVA E OBJETIVOS

3.1 Justificativa

Apesar do escore proposto por Thomas Killip e John Kimball ter sido desenvolvido na era pré-reperfusão, ele segue sendo amplamente realizado pelo fato de nenhuma outra avaliação combinar simplicidade, rapidez e capacidade prognóstica de forma tão eficaz. A ampla disponibilidade da ultrassonografia portátil, sua simples realização e sua excelente acurácia para avaliação de congestão pulmonar, torna esse método com características semelhantes ao escore de Killip-Kimball (simples, rápido e de fácil interpretação). Além disso, existem evidências de que a ecografia pulmonar tem melhor acurácia que o escore de Killip-Kimball especialmente em casos em que a ausculta pulmonar está prejudicada em situações como obesidade, doença pulmonar associada e barulho externo excessivo, além de fornecer um dado mais objetivo de congestão pulmonar. Também o valor prognóstico da EP pode ser tão bom quanto o de biomarcadores e da Pd2, havendo possibilidade de permitir a otimização precoce do tratamento da falha de bomba cardíaca e, talvez, redução de desfechos adversos nestes pacientes.

3.2 Objetivo primário

Comparar a capacidade prognóstica do grau de congestão pulmonar aferido pela ecografia pulmonar, e a correlação desta com a pressão diastólica final do

ventrículo esquerdo em pacientes com IAMCSST submetidos à angioplastia primária.

3.3 Objetivos secundários

- Avaliar a capacidade prognóstica da ecografia pulmonar na beira do leito precoce em pacientes admitidos com IAMCSST
- Determinar se o grau de congestão pulmonar avaliado pela ecografia pulmonar apresenta correlação com desfechos cardiovasculares intra-hospitalares
- Comparar o valor prognóstico da ecografia pulmonar com o escore Killip-Kimball, um marcador clínico de congestão pulmonar que é conhecidamente preditor de desfechos cardiovasculares intra-hospitalares e em 30 dias
- Determinar se o grau de congestão pulmonar avaliado pela ecografia pulmonar se correlaciona positivamente com os valores de pressão diastólica final do ventrículo esquerdo.
- Estabelecer os valores preditivos, curva ROC e determinação da área sob a curva dos métodos avaliados para analisar a precisão e acurácia na predição de eventos adversos.
- Determinar a correlação entre a pressão diastólica final do ventrículo esquerdo e o grau de congestão pulmonar avaliado pela ecografia pulmonar com desfechos cardiovasculares intra-hospitalares.
- Comparar a acurácia prognóstica entre a Pd2 e a ecografia pulmonar para predição de desfechos clínicos cardiovasculares intra-hospitalares e em 30 dias após a alta

- Correlacionar os valores da pressão diastólica final do ventrículo esquerdo, congestão pulmonar avaliado pela ecografia pulmonar e NT-Pró-BNP no contexto do infarto agudo do miocárdio com supradesnível do segmento ST

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Admission bedside lung ultrasound reclassifies mortality prediction in patients with ST-segment elevation myocardial infarction

Running title: Admission bedside lung ultrasound in STEMI patients

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Journal subject terms: percutaneous coronary intervention; ultrasound; heart failure

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ABSTRACT

BACKGROUND: Early risk stratification is essential for in-hospital management of ST-segment elevation myocardial infarction (STEMI). Acute heart failure confers a worse prognosis, and although lung ultrasound (LUS) is recommended as a first-line test to assess pulmonary congestion, it has never been tested in this setting. Our aim was to evaluate the prognostic ability of admission LUS in patients with STEMI.

METHODS: LUS protocol consisted of 8 scanning zones and was performed before primary percutaneous coronary intervention (pPCI) by an operator blinded to Killip classification. A LUS combined with Killip (LUCK) classification was developed. Receiver operating characteristic (ROC) and net reclassification improvement (NRI) analyses were performed to compare LUCK and Killip classifications.

RESULTS: We prospectively investigated 215 patients admitted with STEMI between April 2018 and June 2019. Absence of pulmonary congestion detected by LUS implied a negative predictive value for in-hospital mortality of 98.1% (93.1–99.5%). The area under the ROC curve (AUC) of the LUCK classification for in-hospital mortality was 0.89 ($p = 0.001$), and of the Killip classification was 0.86 ($p < 0.001$) ($p = 0.05$ for the difference between curves). LUCK classification improved Killip ability to predict in-hospital mortality with an NRI of 0.18.

CONCLUSION: In a cohort of STEMI patients undergoing pPCI, admission LUS added to Killip classification was more sensitive than physical examination to identify patients at risk for in-hospital mortality. LUCK classification had a greater AUC and reclassified Killip classification in 18% of cases. Moreover, absence of pulmonary congestion on LUS provided an excellent negative predictive value for in-hospital mortality.

KEYWORDS: Myocardial Infarction, Lung Ultrasound, Prognostic methods

CLINICAL PERSPECTIVE

Recently, there has been a remarkable increase in the use of lung ultrasound (LUS) for the detection of pulmonary congestion in patients with heart failure. Since acute heart failure confers a worse prognosis in STEMI patients, we hypothesized that admission LUS could improve physical examination accuracy to identify higher risk patients and therefore improve in-hospital management. We prospectively investigated 215 patients admitted with STEMI. LUS protocol consisted of 8 scanning zones and was performed before primary percutaneous coronary intervention by an operator blinded to Killip classification. A LUS combined with Killip (LUCK) classification was developed. The primary outcome was in-hospital mortality. Our results demonstrate that admission LUS added to Killip classification was feasible and more sensitive than physical examination to identify patients at risk for in-hospital outcomes. In addition to having the highest AUC to predict in-hospital mortality among classic risk scores, LUCK classification provided a negative predictive value for in-hospital mortality close to 100%. Identifying high risk patients is essential for in-hospital care, in order to select those who may benefit from more intensive monitoring and treatment.

INTRODUCTION

Early risk stratification is essential for in-hospital management of ST-segment elevation myocardial infarction (STEMI). Initially described in 1967[1], Killip classification is based on physical examination performed at the bedside and provides excellent prognostic discrimination in acute coronary syndromes[2,3]. It originated from a series of 250 patients with suspected myocardial infarction (MI) admitted to a coronary care unit and classified as Killip I-IV, ranging from absence of pulmonary congestion to cardiogenic shock. Although Killip classification was developed in the pre-reperfusion era, it is still widely used in STEMI patients because of its simplicity and prognostic ability.

Lung ultrasound (LUS) is a noninvasive imaging method that complements physical examination and clinical evaluation. It has excellent applicability in the differential diagnosis of thoracic disorders[4,5]. LUS technique is simple, standardized, and highly sensitive in evaluating pulmonary congestion and heart failure[6,7]. Indications for LUS are growing in cardiology, and its features of quickness and simplicity are important in the acute setting.

Because of a high sensitivity to detect pulmonary congestion, LUS may complement physical examination for acute heart failure, especially when lung auscultation is compromised by the presence of obesity, lung disease, or excessive external noise. Our aim was to evaluate LUS prognostic ability before primary percutaneous coronary intervention (pPCI) in patients with STEMI, refining Killip classification to increase its accuracy for this purpose.

METHODS

Data, study design and population

The data that support the findings of this study are available from the corresponding author upon reasonable request. This prospective study was conducted in a tertiary university hospital in Southern Brazil between April 2018 and June 2019. Patients eligible for inclusion were consecutive adults (≥ 18 years of age) with suspected STEMI, based on the presence of typical chest pain at rest associated with ST-segment elevation or abnormalities that met the diagnostic criteria for STEMI according to current guidelines[8]. Exclusion criteria were absence of Killip classification or LUS before primary angioplasty and confirmed MI with non-obstructive coronary arteries. All patients provided written informed consent. This study was approved by the Institutional Research Ethics Committee. Manuscript writing was guided according to STARD guideline for diagnostic accuracy studies[9] and Reporting checklist (appendix) for quantification of pulmonary congestion by lung ultrasound[10].

Blood samples were collected by venipuncture on admission for general laboratory testing. All patients were treated with optimal medical therapy according to current guidelines[8]. PCI technical strategies (i.e., pre-dilation, direct stent placement, post-dilation) were performed at the operator's discretion. Echocardiography was performed within 48 hours of admission according to hospital`s routine.

Killip classification

Killip classification was provided by the on-call cardiologist at the emergency department during initial evaluation, according to the original publication[1]: Class I, no evidence of heart failure; Class II, signs indicating mild to moderate degree of heart

failure (S_3 gallop, rales half way up the lung fields, or elevated jugular venous pressure); Class III, acute pulmonary edema (bilateral rales in more than half of both lung fields and dyspnea/respiratory effort at rest); and Class IV, cardiogenic shock (systolic blood pressure < 90 mm Hg and signs of poor perfusion).

Lung ultrasound

A portable ultrasound machine (SonoSite, Bothell, WA) equipped with a 3.5-MHz convex transducer was used. LUS was performed at the Catheterization Laboratory immediately before urgent coronary angiogram. The investigator performing LUS was unaware of the patient's Killip classification provided by the emergency cardiologist. Three specifically trained investigators (interventional cardiology fellows) performed all bedside LUS examinations. Examination consisted of bilateral scanning of the anterior and lateral chest wall, with sagittal (i.e. perpendicular to the intercostal space) probe orientation and the patient in supine position. The chest wall was divided into 8 zones, and 1 scan for each zone was obtained. The zones were 2 anterior and 2 lateral per side[11]. A zone was considered positive if three or more b-lines were present. Pleural effusion was not assessed. Image analysis was performed on site; therefore, it was not recorded for offline evaluation. We named "dry lungs" when all zones were negative for congestion, and "wet lungs" when at least 1 zone was positive. The first 30 examinations were performed twice by 2 independent observers to assess interobserver variability.

Lung Ultrasound combined with Killip Classification

A lung ultrasound combined with Killip (LUCK) classification was developed to reclassify Killip classification according to LUS findings (Figure 1). Since previous

data show that LUS is more specific than auscultation to detect lung congestion, all patients with zero positive zones in our protocol were classified as LUCK I. We also divided patients with 1-8 positive zones into mild (1-3 positive zones) and severe (4-8 positive zones) B Profile. All patients with mild B Profile were classified as LUCK II; patients with Killip I but severe B Profile also upgraded to LUCK II classification. LUCK III classification consisted of either Killip II classification with severe B Profile and Killip III patients. Since mortality is exceptionally high in patients admitted with cardiogenic shock, it seemed reasonable to maintain Killip IV classification as LUCK IV.

Natriuretic peptide analysis

Arterial blood samples were obtained through radial or femoral sheaths used for coronary catheterization before the procedure. N-terminal pro-brain natriuretic peptide (NT-proBNP) analysis was performed using the Elecsys 2010 analyzer (Roche Diagnostics, Mannheim, Germany). The assay became available for this research after the 50th patient had been included.

Outcomes

The primary clinical outcome was in-hospital mortality. Secondary outcomes included in-hospital new MI, stroke, post-MI ejection fraction, and cardiogenic shock. New MI was defined in accordance with the most recent universal definition of MI[12]. Stroke was defined as a new, sudden-onset focal neurologic deficit, of presumably cerebrovascular cause, irreversible (or resulting in death) and not caused by other readily identifiable causes. Cardiogenic shock was defined as systolic blood pressure

< 90 mm Hg or use of vasopressors with signs of poor peripheral perfusion, any time during hospital stay. In-hospital mortality, new MI or stroke were considered major adverse cardiovascular outcomes (MACE).

Procedural outcomes were also described. Successful procedure was defined as final TIMI 2 or 3 flow and residual stenosis <30%. No reflow was defined as suboptimal myocardial reperfusion through a part of coronary circulation without angiographic evidence of mechanical vessel obstruction. Distal embolization was defined as a distal filling defect with an abrupt 'cutoff' in one of the peripheral coronary artery branches of the infarct-related vessel, distal to the site of angioplasty. Cardiac arrest was defined as cardiac arrest occurring during the procedure and requiring resuscitation procedures (i.e. ventilation, chest compression, defibrillation).

Statistical analysis

For sample size calculation, 50 patients were subjected to LUS examination to determine the expected receiver operating characteristic (ROC) curve for in-hospital mortality. Assuming an incidence of in-hospital mortality of 10%, 165 patients would provide a statistical power of 99% to detect a ROC curve of 0.82, with an alpha value of 0.05.

Continuous variables were expressed as mean (SD) or median (interquartile range). Categorical variables were expressed as relative and absolute frequencies. The correlation between Killip class, LUS, and NT-proBNP was assessed with a nonparametric Spearman correlation coefficient analysis. ROC curves were used to evaluate the discriminatory power of the different classifications, with results expressed as c-statistic. Areas under the ROC curve (AUCs) were compared by DeLong test[13]. Net reclassification improvement (NRI) was used to assess improvement in risk

categories[14]. Statistical tests of sensitivity and specificity were conducted by using the McNemar test for correlated proportions[15]. A generalized linear model with binary logistic regression and a logit link function was performed for each univariate predictor of the main outcome. For multivariate model, clinical and imaging risk factors that were univariate predictors (at $p < 0.10$) were initially considered as factors or covariates. The final model was developed manually in a stepwise fashion, excluding the least significant variable one by one, where clinically important variables as well as the ones that remained statistically significant were included. Data were analyzed using SPSS Statistics (version 23.0.0; IBM Company).

RESULTS

Baseline clinical characteristics

Of 247 patients admitted with suspected STEMI during the study period, 215 were included in the final analysis (Figure 2). Baseline characteristics of patients with (n = 110) and without (n = 105) pulmonary congestion on LUS are summarized in Table 1. Compared to patients with dry lungs, patients with at least 1 positive zone more frequently had diabetes (31% vs 21%, $p = 0.034$), lower body mass index (26 vs 28 kg/m^2, $p = 0.001$), history of heart failure (8% vs 1%, $p = 0.019$), and chronic kidney disease (17% vs 7%, $p = 0.036$). Anterior MI (55% vs 43%, $p = 0.043$) and cardiac arrest (16% vs 2%, $p = 0.001$) before admission were also more frequent in patients with wet lungs. As expected, the distribution of Killip classes was different between the 2 groups, and median NT-proBNP on admission was lower in patients with dry lungs (235 vs 1781, $p < 0.001$).

Baseline clinical examination

The feasibility of LUS examination for the diagnosis of B-lines was 100%, and no patient had uninterpretable images. The examination time never exceeded 3 minutes, not influencing door-to-balloon time. Concordance of the first 30 examinations between the 2 observers was excellent ($k = 0.97$, $P<0.001$).

Of the 215 study patients, 105 (49%) had dry lungs based on LUS examination. Of these, 97 (92%) had no signs of heart failure on physical examination (Killip I). Of 142 Killip I patients, 97 (68%) had dry lungs on LUS. The proportion of LUS zones within Killip classes I–IV is shown in Figure 3.

Spearman correlation between LUS and Killip classification in overall patients was moderate ($n = 215$, $k = 0.55$, $p < 0.001$). A similar correlation was found when only patients with current or previous history of smoking ($n = 117$, $k = 0.56$, $p < 0.001$) and with body mass index > 30 kg/m^2 ($n = 54$, $k = 0.62$, $p < 0.001$) were analyzed.

Primary outcome

Overall in-hospital mortality was 14%. Two patients (1.9%) with dry lungs died during hospitalization, one of them after stroke. The sensitivity of LUS-detected dry lungs for in-hospital survival was 93.3% (77.9–99.1%), with 98.1% (93.1–99.5%) negative predictive value. Four Killip I patients (2.8%) died during hospitalization. The sensitivity of Killip I for in-hospital survival was 86.7% (69.3–96.2%), with 97.1% (92.9–99.2%) negative predictive value.

The unadjusted and adjusted risks of the primary outcome are shown in Table 2. In a multivariate model, where thrombolysis in myocardial infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) risk scores were excluded (due to interaction with other variables of the model), wet lungs (OR 14.4, 95% CI 3.36–105),

shock (Killip/LUCK IV) on admission (OR 15.6, 95% CI 5.36–50.2), and final TIMI flow < 3 (OR 9.29, 95% IC 2.95–32.2) were the remaining significant predictors of in-hospital mortality.

Comparison of LUS and Killip classification to predict in-hospital mortality

AUCs for prediction of in-hospital mortality were 0.80 for LUS ($p < 0.001$), 0.86 for Killip ($p < 0.001$), and 0.89 for LUCK classification ($p < 0.001$). LUCK AUC was borderline higher than that of Killip classification in DeLong test ($p = 0.050$). Adding LUS to Killip classification (i.e. LUCK classification) resulted in a positive NRI of 0.18 to predict in-hospital mortality (NRI 0.18). When Killip IV patients were excluded of the overall analysis, the AUCs were 0.78 for LUS ($p = 0.001$), 0.73 for Killip ($p = 0.008$), and 0.80 for LUCK classification ($p = 0.001$). In Killip I-III patients, LUCK AUC was significantly higher than Killip AUC in DeLong test ($p = 0.041$). The ROC curves of LUS, Killip, and LUCK classification in overall and Killip I-III patients are presented in Figure 4. The AUCs and confidence intervals of Killip, LUCK classification, and TIMI and GRACE risk scores are shown in Table 3.

Secondary outcomes

Procedural outcomes were similar between patients with dry and wet lungs based on LUS examination. Post-MI ejection fraction was lower in patients with wet lungs (43% vs 53%, $p < 0.001$), and cardiogenic shock was more frequent in these patients (33% vs 5%, $p < 0.001$). Moreover, in-hospital mortality was significantly higher in patients with wet lungs (25% vs 2%, $p < 0.001$). Table 4 shows procedural and in-hospital outcomes. The unadjusted and adjusted risks of MACE are provided in the supplementary appendix.

DISCUSSION

In a prospective cohort of STEMI patients undergoing pPCI, we found that admission LUS was significantly correlated with in-hospital mortality. LUS reclassified Killip classification in 18% of patients and had a superior predictive value compared to clinical evaluation alone. Moreover, STEMI patients without LUS B-lines on admission had an excellent negative predictive value for in-hospital mortality.

Although mortality in patients admitted with STEMI is constantly decreasing due to new drugs and devices, it remains high in patients with cardiogenic shock even when early revascularization is performed[16]. Pulmonary congestion is a prominent element in patients with heart failure, and LUS is becoming the standard method for detecting interstitial pulmonary edema[6]. LUS technique is not uniform in cardiology, ranging from complete 28 zones[17] to simplified 8 zones[11] or ultra-simplified 4 zones[18]. We chose the simplified 8-zone method because it is less time-consuming and is currently recommended by point-of-care LUS guidelines in the emergency setting[19].

Although LUS is recommended as a first-line test to assess pulmonary congestion in patients with suspected acute heart failure[20], it has never been tested in newly admitted STEMI patients. Bedetti and colleagues[21] found that lung and cardiac ultrasound added prognostic value to GRACE and TIMI risk scores in 470 patients admitted with acute coronary syndromes. Although STEMI was present in about half of patients, LUS was only performed later during hospitalization along with echocardiographic evaluation. Early risk stratification is essential for in-hospital post-MI care, and we have found a striking 98.1% negative predictive value for mortality in patients with LUS-detected dry lungs. This means that most of these patients will not

benefit from prolonged post-MI intensive monitoring, and early hospital discharge may be considered. Of note, patients with suspected myocardial infarction and nonobstructive coronary arteries were a priori excluded from this analysis, since the prognosis and management of these patients are distinct from the ones with coronary thrombosis submitted to primary PCI[22].

In our analysis, LUCK classification significantly improved Killip prognostic ability, with a greater AUC for in-hospital mortality. This new classification was developed to increase the sensitivity of lung auscultation while maintaining the high-risk features of Killip III and IV. In the best-case scenario, mortality in Killip IV patients is at least about 40%[23], which is vital for the prediction performance of Killip classification. When excluding these patients, pulmonary congestion alone is evaluated as a predictor of mortality.

In emergency care, the absence of B-lines on LUS excludes cardiogenic edema with a negative predictive value close to 100%[24]. However, there is no true gold standard for assessment of pulmonary congestion in this setting. While fluid accumulation and "lung water cascade"[25] are more predictable in chronic heart failure, inflammation and vascular permeability are prominent findings in STEMI. Thus, correlation between filling pressures and lung water may be different in this scenario. Although we found a higher prognostic ability with LUS than with lung auscultation, establishing this method as the gold standard for pulmonary congestion in STEMI may be equivocal.

Potential advantages of LUS in STEMI patients are not limited to prognostic evaluation. Lung and inferior vena cava evaluations are useful to assess volume status and to guide volume or diuretic administration according to pulmonary congestion and inferior vena cava size and variability. Whether LUS is better than physical examination

to guide interventions remains unknown, but large randomized studies are in progress to answer this question (NCT02310061, NCT03262571, NCT02959372, NCT03136198). Another utility of LUS is the possibility to provide a combined cardiac chamber evaluation, searching for abnormalities such as mechanical complications and pericardial effusion. Although the present study used a convex transducer, evaluation of B-lines can be performed with cardiac transducer without loss of accuracy. In the work performed by Bedetti and colleagues[21], described above, LUS and echocardiographic (i.e. ejection fraction and TAPSE) findings were combined and were a good predictor of death or MI after 10 months. But again, our aim was to perform a summarized evaluation and not to delay primary angioplasty, and therefore performing a complete echocardiogram was not feasible. Lastly, right ventricular STEMI is suspected when dry lungs and a full inferior vena cava are noted. Misdiagnosis is not uncommon, since standard 12-lead electrocardiogram is insufficient to assess right ventricular involvement, but recognizing this involvement is essential because of its particular management (fluid infusion, avoiding nitrates).

Limitations

The first limitation of this study is the sample size, which was calculated based on the AUC of a single diagnostic test. However, comparison of two ROC curves would require approximately 2000 patients, which is not feasible in a single center. Thus, the difference found between LUCK and Killip ROC curves may be subject to beta error. Also, this study was not adequately powered to determine predictors of mortality, given the large confidence intervals obtained in both univariate and multivariate analyses. Second, patients with conditions that are known to affect the number of B-lines (e.g. interstitial lung disease, patients on dialysis, etc.) were included in the analysis.

Nevertheless, our objective was to analyze an all-comers population of STEMI patients, and this can be considered a conservative bias considering the results we have found. Third, although LUS was performed by operators blinded to Killip classification, clinical settings such as acute pulmonary edema and cardiogenic shock can be visually distinguished in most of the STEMI patients. This may have biased the overall accuracy of LUS in these patients. Off line image analysis could have reduced bias in LUS image interpretation, but unfortunately was not performed. However, our results are presented based on the LUCK classification that mainly reclassifies Killip I and II patients, in whom blinding is reliable.

CONCLUSIONS

In a cohort of STEMI patients undergoing pPCI, admission LUS added to Killip classification was feasible and more sensitive than physical examination to identify patients at risk for in-hospital outcomes. Identifying these patients is essential for in-hospital care, in order to select those who may benefit from more intensive monitoring and treatment. LUCK classification combines LUS findings and high-risk Killip features, thus reclassifying Killip classification. In addition to having the highest AUC to predict in-hospital mortality among classic risk scores, LUCK classification provides a negative predictive value for in-hospital mortality close to 100%.

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DISCLOSURES

None.

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Table 1: Baseline demographic characteristics

	Overall (n= 215)	**Dry lungs (n = 105)**	**Wet lungs (n = 110)**	***p***
Demographics				
Age (SD)	61 (±12)	58 (±11)	63 (±12)	0.193
Male sex	150 (70%)	78 (74%)	72 (66%)	0.198
Hypertension	149 (70%)	68 (65%)	81 (74%)	0.128
Diabetes	58 (27%)	22 (21%)	36 (33%)	0.034
Body mass index (kg/m^2)	27 (±4)	28 (±4)	26 (±4)	0.001
Smoking (previous or current)	117 (54%)	54 (51%)	63 (58%)	0.349
Previous ASA use	45 (21%)	18 (17%)	27 (24%)	0.181
Previous MI	29 (14%)	12 (11%)	17 (16%)	0.372
Previous stroke	19 (9%)	8 (8%)	11 (10%)	0.524
Heart failure	10 (4.7%)	1 (1%)	9 (8%)	0.019
COPD	35 (16%)	12 (11.4%)	23 (21%)	0.064
Chronic kidney disease	24 (11%)	7 (7%)	17 (16%)	0.036
Admission characteristics				
Pain-to-door, hours (IQR)	5.5 [3.5, 8]	6 [3.5, 8.5]	6 [3, 10]	0.895
Door-to-balloon, minutes (IQR)	72 [57, 86]	74 [55, 83]	72 [60, 86]	0.557
Systolic blood pressure	130 (±33)	139 (±29)	122 (±35)	<0.001
Diastolic blood pressure	76 (±17)	80 (±14)	71 (±23)	<0.001
Heart rate (bpm)	82 (±20)	78 (±16)	85 (±23)	0.009
Creatinine	1.06 [0.87, 1.40]	0.96 [0.84, 1.14]	1.15 [0.89, 1.78]	<0.001
Anterior MI	106 (49%)	45 (43%)	61 (55%)	0.043
Cardiac arrest	19 (9%)	2 (2%)	17 (16%)	0.001
Complete AV block	13 (6%)	4 (4%)	9 (8%)	0.173
Killip classification				
I	142 (66%)	97 (92%)	45 (41%)	<0.001
II	35 (16%)	7 (7%)	27 (25%)	<0.001
III	11 (5%)	0 (0%)	11 (10%)	--
IV	27 (13%)	1 (1%)	26 (24%)	<0.001
TIMI risk score	4 [2, 7]	2 [2, 4]	6 [4, 8]	<0.001
GRACE risk score	120 [100, 145]	108 [90, 122]	133 [118, 175]	<0.001
NT-proBNP	416 [116, 3033]	235 [55, 433]	1781 [208, 6279]	<0.001
Inferior vena cava > 2 cm	108 (50%)	43 (41%)	65 (59%)	<0.001

Values are expressed as mean (SD), median [IQR], or n (%). ASA, acetylsalicylic acid; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; bpm, beats per minute; AV, atrioventricular; TIMI, thrombolysis in myocardial infarction; GRACE, Global Registry of Acute Coronary Events; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Table 2: Unadjusted and adjusted odds of the primary outcome

Univariate predictors of in-hospital mortality

Characteristic	**OR**	**95% CI**	***p***
Pain-to-door (hours)	1.04	1.01 – 1.07	0.015
Complete AV block	5.50	1.52 – 18.6	0.006
Cardiac arrest	15.36	5.40 – 46.6	<0.001
Age (years)	1.04	1.01 – 1.07	0.034
Male sex	1.40	0.61 – 3.10	0.410
Diabetes	1.34	0.55 – 3.09	0.502
Creatinine (mg/dL)	1.54	1.19 – 2.13	0.003
Hemoglobin (g/dL)	0.78	0.65 – 0.94	0.009
Wet lungs (≥ 1 positive LUS zones)	17.9	5.19 - 113	<0.001
Killip II or III	**1.41**	**0.55 – 3.30**	**0.449**
Shock (Killip/LUCK IV)	26.2	10.2 – 72.2	<0.001
TIMI risk score > 6	16.32	6.74 – 44.38	<0.001
GRACE risk score > 140	9.66	4.20 – 23.90	<0.001
TIMI flow < 3 after pPCI	5.12	2.23 – 11.7	<0.001

Multivariate predictors of in-hospital mortality

Characteristic	**OR**	**95% CI**	**P**
Age (years)	1.01	0.97 – 1.05	0.712
Creatinine (mg/dL)	1.36	0.94 – 1.89	0.078
Wet lungs (≥ 1 positive LUS zones)	11.9	2.71 – 86.8	0.004
Shock (Killip/LUCK IV)	12.5	4.09 – 31.4	<0.001
TIMI flow < 3 after pPCI	8.69	2.65 – 31.4	0.001

AV, atrioventricular; LUS, lung ultrasound; LUCK, LUS combined with Killip classification; TIMI, thrombolysis in myocardial infarction; GRACE, Global Registry of Acute Coronary Events; pPCI, primary percutaneous coronary intervention.

Table 3: Areas under the ROC curve of different scores to predict in-hospital

mortality

	AUC	95% CI
Killip classification	0.86	0.78 – 0.94
LUCK classification	0.89	0.82 – 0.96
TIMI risk score	0.84	0.76 – 0.92
GRACE risk score	0.88	0.82 – 0.94

ROC, receiver operating characteristic; AUC, area under the curve; LUCK, lung ultrasound combined with Killip; TIMI, thrombolysis in myocardial infarction; GRACE, Global Registry of Acute Coronary Events.

Table 4: Procedural and in-hospital outcomes

	Overall (n= 215)	Dry lungs (n = 105)	Wet lungs (n = 110)	*p*
Procedural details and outcomes				
Single-vessel disease	86 (40%)	43 (43%)	43 (43%)	0.466
Success rates	186 (89%)	93 (91%)	93 (87%)	0.214
No reflow / distal embolization	42 (19%)	21 (20%)	21 (20%)	1.000
Cardiac arrest	14 (7%)	6 (6%)	8 (7%)	0.420
Periprocedural mortality	5 (2%)	1 (1%)	4 (4%)	0.186
In-hospital outcomes				
Post-MI ejection fraction (SD)	48% (±12%)	53% (±12%)	43% (±10%)	<0.001
New MI	6 (3%)	2 (2%)	4 (4%)	0.451
Stroke	4 (2%)	2 (2%)	2 (2%)	0.947
Cardiogenic shock	41 (19%)	5 (5%)	36 (33%)	<0.001
In-hospital mortality	30 (14%)	2 (2%)	28 (25%)	<0.001

Values are expressed as mean (SD) or n (%). MI, myocardial infarction.

FIGURE LEGENDS

Figure 1: Study flowchart.

Figure 2: Proportion of positive lung ultrasound (LUS) zones in patients with Killip I–IV.

Figure 3: Lung ultrasound combined with Killip (LUCK) development and prognostic characteristics across the classification. “A” and “B” profiles were defined by lung ultrasound; acute pulmonary edema and cardiogenic shock were defined after clinical evaluation.

Figure 4: Receiver operating characteristic (ROC) curves for lung ultrasound (LUS), Killip, and LUCK classification in overall and Killip I-III patients.

6. SEGUNDO ARTIGO ORIGINAL

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Comparison of admission lung ultrasound and left ventricle end-diastolic pressure in patients undergoing primary PCI

Short-title: Lung ultrasound vs LVEDP in STEMI

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ABSTRACT

Background: Left ventricle end-diastolic pressure (LVEDP) is related to ventricular dysfunction and increased retrograde pulmonary capillary pressure. Lung ultrasound (LUS) is a sensitive and easy to use method for assessment of pulmonary congestion. Both methods have shown prognostic value in patients with ST-segment elevation myocardial infarction (STEMI). Our aim was to evaluate the correlation between LVEDP and bedside LUS and to compare their prognostic value in patients undergoing primary percutaneous coronary intervention (pPCI).

Methods: Prospective cohort study of STEMI patients treated in a tertiary care hospital in Brazil. LUS was performed immediately before coronary angiography. LVEDP was recorded before pPCI, blinded to LUS results. Primary outcome was any in-hospital major adverse cardiovascular event (MACE), defined as in-hospital mortality, new myocardial infarction, stroke, and new cardiogenic shock.

Results: In total, 218 patients were included; their mean age was 60 (±12) years and 64% were male. Cardiogenic shock was present in 16.5% patients on admission. Overall in-hospital mortality was 15%. Median LVEDP was 19 mmHg [interquartile range (IQR) 13-28]; median LUS zones positive for pulmonary congestion were 1/patient [IQR: 0-5]; Spearman correlation between them was 0.33 ($p<0.001$). LVEDP and LUS C-statistic for in-hospital MACE was 0.63(95% confidence interval [CI]0.55-0.70, $p=0.002$) and 0.71(95%CI =0.64 - 0.77, $p<0.001$), respectively. In multivariable analysis, LUS remained associated with in-hospital MACE (OR 1.14, 95%CI=1.06-1.23, $p=0.01$, for every positive LUS zone); LVEDP, however, did not (OR 1.01, 95%CI=0.99-1.03, $p=0.23$).

Conclusions: We found a weak correlation between LVEDP and LUS in our cohort of STEMI patients undergoing pPCI. Pulmonary congestion in acute heart failure is a complex pathophysiological process and goes beyond fluid overload and hemodynamics. Unlike LVEDP, LUS was significantly associated with in-hospital MACE, new cardiogenic shock, and in-hospital mortality in multivariable analysis.

Keywords: Mortality; percutaneous coronary intervention; myocardial infarction; ultrasound; heart failure; left ventricular end-diastolic pressure

CLINICAL PERSPECTIVES

Compared to diastolic dysfunction and increased LVEDP, pulmonary congestion may be considered a late consequence of the ischemic cascade initiated by an acute insult. Pulmonary congestion in acute heart failure is a complex pathophysiological process and goes beyond fluid overload and hemodynamics. We found a low correlation between LVEDP and LUS in our cohort of STEMI patients undergoing pPCI. Additionally, multivariable analysis demonstrated that only LUS was found to be an independent predictor of in-hospital MACE in our cohort.

Recent studies have shown that LUS might be a useful tool to improve care and guide therapeutic decisions in STEMI patients. Additional studies focusing specifically in the cardiogenic shock clinical scenario can ratify the usefulness of LUS as a non-invasive alternative to identify patients who can benefit more from mechanical support before pPCI.

INTRODUCTION

Intracardiac pressure measurement provides an accurate real-time evaluation of cardiac filling and mechanical performance. Increased left ventricular end-diastolic pressure (LVEDP) is related to ventricular dysfunction, increased retrograde pulmonary capillary pressure, and pulmonary congestion[1]. Diastolic dysfunction precedes the onset of systolic dysfunction in acute ischemia[2], and the prognostic value of LVEDP in ST-segment elevation myocardial infarction (STEMI) is well described. Although LVEDP had low predictive value for major cardiovascular outcomes such as death and cardiogenic shock in a sub-analysis of two randomized clinical trials[3,4], it has been widely used for diagnostic and therapeutic purposes in this particular clinical context.

Bedside lung ultrasound (LUS) is a noninvasive method that complements physical examination and clinical evaluation, with immediate application in the assessment of chest disorders[5]. It is recommended as a first-line test to assess pulmonary congestion in patients with suspected acute heart failure[6], and recent evidence has shown its applicability in patients admitted with STEMI[7].

Compared to diastolic dysfunction and increased LVEDP, pulmonary congestion may be considered a late consequence of the ischemic cascade initiated by an acute insult. Although it is associated with increased filling pressures, other mechanisms may be responsible for lung fluid extravasation, including inflammation and patient comorbidities, such as previous heart failure and chronic kidney disease. Our aim was to evaluate the correlation between admission LVEDP and LUS and to assess their prognostic value in STEMI patients undergoing pPCI.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study design, data, and population

This was a prospective cohort study conducted in a tertiary care hospital in southern Brazil. Patients eligible for inclusion were consecutive adults (≥ 18 years of age) admitted with STEMI, based on the presence of typical chest pain at rest associated with ST-segment elevation or abnormalities that met the diagnostic criteria for STEMI according to current guidelines[8]. Our group have recently published a study with STEMI patients and admission LUS evaluation included between April 2018 and June 2019[7]. Thus, a total of 112 patients included between August 2018 and June 2019 were involved in both analyses. Exclusion criterion was absence of LUS evaluation or LVEDP measurement before primary percutaneous coronary intervention (pPCI). Patients with suspected STEMI but a different final diagnosis (e.g., myocarditis) were also excluded. This study was approved by the local institutional review board (Grupo de pesquisa e pós graduação do Hospital de Clinicas de Porto Alegre – GPPG HCPA – project number 2018-0205) and all the patients gave informed consent. Manuscript writing was guided by a reporting checklist for the quantification of pulmonary congestion by lung ultrasound[9].

Blood samples were collected by venipuncture on admission for general laboratory testing. Neutrophil-to-lymphocyte ratio (NLR), a known marker of inflammation related to adverse outcomes in STEMI patients[10], was calculated by dividing neutrophil count by lymphocyte count, both obtained from the same blood sample drawn on admission. Technical pPCI strategies were performed at the operator's

discretion. Inpatient management was guided according to current guidelines[8]. All patients discharged alive had a 30-day follow-up in an outpatient clinic.

Lung ultrasound

A portable ultrasound machine (SonoSite, Bothell, USA) equipped with a 3.5-MHz convex transducer was used. LUS was performed at the catheterization laboratory immediately before pPCI and could not delay an urgent procedure by more than 3 minutes. The investigator performing LUS was unaware of the patient's Killip classification provided by the emergency cardiologist. Three specifically trained investigators (interventional cardiology fellows) performed all bedside LUS examinations. The examination consisted of bilateral scanning of the anterior and lateral chest wall, with sagittal (i.e., perpendicular to the intercostal space) probe orientation and the patient in the supine position. The chest wall was divided into eight zones, and one scan for each zone was obtained. The zones were two anterior and two lateral per side[11]. A zone was considered positive if it had at least three B-lines and "lung congestion" was diagnosed by the presence of at least one positive zone on LUS. Pleural effusion was not assessed. Image analysis was performed on-site; therefore, it was not recorded for offline evaluation. Interobserver variability was assessed in another study conducted by our group[7].

Left ventricle end-diastolic pressure

The fluid-filled pressure transducer was aligned with the midchest, and zero levels were achieved around 5 cm below the left sternal border at the fourth left intercostal space. Before coronary angiography, either a single-hole 5-French diagnostic catheter or a 6-French guiding catheter was positioned in the left ventricle (LV) to

measure LVEDP. If the LV was not accessed after 1 minute, LVEDP was not measured in order not to delay reperfusion. Also, its measurement was not attempted in patients with aortic valve surgical prothesis or those with known or suspected LV thrombus. LVEDP was measured at the Z point, which is identified on the LV pressure trace as the point at which the slope of the ventricular pressure upstroke changes, which coincides with the R wave on electrocardiographic tracking[12]. Pressure tracing was analyzed offline by an operator blinded to LUS findings.

Laboratory analysis

Arterial blood samples were obtained through radial or femoral sheaths used for coronary catheterization before pPCI was performed. N-terminal pro-brain natriuretic peptide (NT-proBNP) analysis was performed in 183 patients using the Elecsys 2010 analyzer (Roche Diagnostics, Mannheim, Germany). Unfortunately, our hospital's laboratory changed the NT-proBNP assay during the study, and brain natriuretic peptide (BNP) (Abbott Diagnostics, Illinois, USA) was then measured in 35 patients. Blood counts were also analyzed and neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing neutrophil count by lymphocyte count. Both NT-proBNP (or BNP) and NLR were divided into low and high using the median value of each of the variables as a cutoff point. The same method was used to divide patients into short and long pain-to-door time.

Outcomes

The primary outcome of our study was any in-hospital major adverse cardiovascular event (MACE), defined as in-hospital mortality, new myocardial infarction (MI), stroke, and new cardiogenic shock (excluding patients classified as

Killip IV at admission). Secondary outcomes were MACE at 30-day follow-up and separate components of MACE (in-hospital mortality, new MI, stroke, new cardiogenic shock). New MI was based on its most recent universal definition[13]. Stroke was defined as a new, sudden-onset focal neurologic deficit of a presumably cerebrovascular cause, irreversible (or resulting in death), and not caused by other readily identifiable causes. Cardiogenic shock was defined as systolic blood pressure < 90 mm Hg or use of vasopressors in patients with signs of poor peripheral perfusion at any time during hospital stay.

Periprocedural outcomes were also described. Successful pPCI was defined as final Thrombolysis In Myocardial Infarction (TIMI) 2 or 3 grade flow and residual stenosis < 30% in infarct-related coronary artery. No-reflow was defined as suboptimal myocardial reperfusion in a section of the coronary circulation without angiographic evidence of mechanical vessel obstruction. Distal embolization was defined as a filling defect with an abrupt "cutoff" in the distal branches of the infarct-related vessel. Cardiac arrest was considered when occurring during pPCI and requiring resuscitation procedures (i.e., ventilation, chest compression, defibrillation).

Statistical analysis

Continuous variables were expressed as mean (standard deviation, SD) or median (interquartile range, IQR) based on the presence of symmetrical or asymmetrical distribution, respectively. Normality was assessed by the Shapiro-Wilk test. Categorical variables were expressed as relative and absolute frequencies. The correlation between LVEDP and LUS was assessed with Spearman correlation coefficient analysis. Correlation between 0 and 0.39 was considered weak; between 0.40 and 0.69 was considered moderate; and over 0.70 was considered high. Receiver

operating characteristic (ROC) curves were used to evaluate the discriminatory power of the different classifications, with results expressed as C-statistic. Areas under the ROC curve (AUCs) were compared by the DeLong test[14]. Statistical tests for sensitivity and specificity were conducted using the McNemar test for correlated proportions[15]. A generalized linear model with binary logistic regression and a logit link function was performed for each univariate predictor of the main outcome.

For multivariable model, clinical and imaging risk factors that were univariate predictors (at $p < 0.10$) were considered as factors or covariates, as well as other relevant variables that could be incremental based on clinical experience. The final model was developed manually in a stepwise fashion. Multicollinearity among variables included in the regression model was computed by the variance inflation factor. Data were analyzed using IBM SPSS Statistics for Windows, Version 21.0., IBM Corp., Armonk, New York, USA.

Based on a recent study[16], we estimated that a sample of 292 patients would provide 80% power, at a two-sided significance level of 0.05, to detect a statistically significant difference between ROC curves with respect to the primary outcome, assuming that AUC would be 0.75 for LUS and 0.60 for LVEDP[17].

RESULTS

Baseline clinical characteristics

Of 323 patients with suspected STEMI admitted between August 2018 and January 2020, 218 were included in the final analysis (**Figure 1).** Sixty-five patients were excluded because LVEDP could not be performed for different reasons. In other 16 patients, LUS could not be performed timely. The feasibility of LUS examination for the diagnosis of B-lines was 100%, and no patient had uninterpretable images.

Examination time never exceeded 3 minutes in the patients included, with no influence on door-to-balloon time. Concordance between observers has been described elsewhere[7] and was excellent ($k = 0.97$, $p < 0.001$). The clinical characteristics and laboratory finding between included and not included patients did not differ between groups (supplemental table I[27]).

The mean age of our sample was 60 (± 11) years, and 64% were male. Sixteen percent of patients were classified as Killip IV at admission. Median LVEDP was 19 mm Hg [IQR 13 - 28] and median number of positive LUS zones was 1 [IQR 0 - 5]. Baseline characteristics for overall sample as well as for patients with and patients without MACE are summarized in **Table 1**.

Comparison between LVEDP and LUS

There was a weak correlation between positive LUS zones and LVEDP (Rho = 0.33, $p < 0.001$). (**Figure 2**). When we removed patients with admission Killip IV, correlation between positive LUS zones and LVEDP was similar (Rho = 0.27, $p \leq 0.001$) (n = 182 patients).

Patients were divided into short and long pain-to-door time, low and high NLR and low and high NT-proBNP (or BNP) according to the median value of these variables. In patients with short and long pain-to-door time (median = 5 hours), correlation between LVEDP and LUS was 0.372 ($p < 0.001$) and 0.462 ($p < 0.001$), respectively. Correlation between LVEDP and LUS was 0.504 ($p < 0.001$) and 0.349 ($p < 0.001$) in patients with low and high NLR (median = 6.45), respectively. Correlation between LVEDP and LUS was 0.265 ($p = 0.009$) and 0.504 ($p < 0.001$) in patients with low and high NT-proBNP or BNP (median NT-proBNP = 423 pg/dL; median BNP = 55.5 pg/dL), respectively. Correlation between admission LUS zones and post-MI

pulmonary artery systolic pressure (measured within 48 hours of admission) was higher compared to LVEDP (Rho = 0.40, $p < 0.001$).

We also evaluated the ability of LUS to predict increased LVEDP (> 19 mm Hg). A greater number of patients with at least one positive LUS zone presented with LVEDP > 19 mm Hg (75 [59%] vs 52 [41%], $p < 0.001$). LUS C-statistic for predicting LVEDP > 19 mm Hg was 0.67 (0.60-0.73, $p < 0.001$).

Outcomes

MACE occurred in 50 (22.9%). patients during hospitalization. At 30-day follow-up, mortality and MACE occurred in 36 (16%) and 63 (29%) patients, respectively. There were no rehospitalizations with cardiogenic shock. Procedural outcomes are described in **Table 2**.

LVEDP and LUS unadjusted AUCs were, respectively, 0.63 (95% CI = 0.56 - 0.70, $p = 0.002$) and 0.71 (95% CI = 0.64 - 0.77, $p < 0.001$) for MACE, with $p = 0.08$ for DeLong comparison between curves. We have also determined LVEDP and LUS unadjusted AUC for in-hospital mortality (0.60 [95% CI = 0.53 - 0.66, $p = 0.050$] and 0.69 [95% CI = 0.62 - 0.75, $p = 0.0002$], respectively, with $p = 0.11$ for DeLong comparison between curves] and new cardiogenic shock (0.64 [95% CI = 0.57 - 0.70, $p = 0.02$] and 0.68 [95% CI = 0.61 - 0.74, $p = 0.004$], respectively, with $p = 0.62$ for DeLong comparison between curves).

In univariate analysis, LVEDP was significantly associated with MACE (OR = 1.03, 95% CI = 1.01-1.06, $p = 0.01$) and cardiogenic shock (OR = 1.04, 95% CI = 1.01-1.08, $p = 0.01$). There was no statistically significant association between continuous LVEDP (mm Hg) and in-hospital mortality (OR = 1.03, 95% CI = 1.00-1.06, $p = 0.06$). We found no association in univariate analysis when we categorized LVEDP > 19 mm

Hg regarding MACE (OR = 1.60, 95% CI = 1.02-2.78, p = 0.042), in-hospital mortality (OR = 1.26, 95% CI = 0.68-2.36, p = 0.45) and cardiogenic shock (OR = 2.33, 95% CI = 0.93-5.84, p = 0.07).

Adjusted models

A multivariable analysis was performed including LVEDP, number of positive LUS zones, diabetes, admission creatinine, age, sex and cardiac arrest. Admission LUS, creatinine and cardiac arrest were the only variables independently associated with in-hospital MACE in both unadjusted and adjusted analysis (**Table 3**).

Patients with higher baseline creatinine may have higher levels of fluid retention and, therefore, a higher number of positive LUS zones. This possible interaction was evaluated with a collinearity analysis between the number of positive LUS zones and admission creatinine. The results showed no collinearity.

When we analyzed 30-day outcomes with the same model, admission LUS, creatinine and cardiac arrest remained independent predictors of MACE (OR 1.15, 95% CI = 1.06-1.24, p < 0.001; OR 1.25, 95% CI = 1.16-1.34, p < 0.001; OR 2.58, 95% CI = 1.62-4.11, p < 0.001, respectively). Unlike LUS, LVEDP did not independently predict in-hospital mortality (OR 1.00, 95% CI 0.97 – 1.03) or cardiogenic shock (OR 1.01, 95% CI 0.97 – 0.05) in our analysis. Multivariable analysis of secondary outcomes can be found in supplemental table II[28].

DISCUSSION

In patients with STEMI admitted to a tertiary care hospital, the correlation between increased LVEDP and pulmonary congestion evaluated by LUS (both assessed before emergency coronary angiography) was low. Unlike previous studies, LVEDP did

not independently predict adverse in-hospital outcomes in these patients. Moreover, LUS had a numerically greater AUC than LVEDP to predict in-hospital outcomes, being also an independent predictor of in-hospital cardiogenic shock, mortality, and MACE.

MI is an acute form of coronary artery disease and may range from a relatively benign presentation with limited involvement of the myocardium to a proximal coronary occlusion with extensive myocardial damage associated with cardiogenic shock and death[18]. Since a pioneer study conducted by Killip and Kimball[19], mortality in STEMI patients is known to be strictly associated with the presence and severity of heart failure based on clinical evaluation at hospital admission. In the present study, around 20% of patients were admitted with Killip III/IV, contributing to the increased mortality observed in this cohort. Prolonged pain-to-door time and 11% cardiac arrest at admission also contributed to the poor prognosis of these patients, even though it empowered statistical analysis due to an increased number of outcomes.

The main theoretical mechanism associated with acute pulmonary congestion in STEMI is impairment of ventricular compliance leading to diastolic dysfunction, which is a direct consequence of myocardial ischemia[2]. Increased LVEDP transmits pressure retrogradely to lung capillaries, leading to disturbances in Starling forces[20] and fluid extravasation. However, previous study has failed to find a strong association between lung congestion evaluated by LUS and filling pressures evaluated by echocardiography (E/e`) in patients with acute heart failure[21]. The authors argue that while pulmonary congestion potentially resolve rapidly, hemodynamic decongestion may be delayed despite aggressive diuretic therapy. Different from our study, only 46% of the patients had an ischemic etiology, and E/e` is only an indirect measurement of filling pressures.

Other mechanisms, such as increased vascular permeability due to a proinflammatory state, also play an important role in the development of lung congestion. Inflammation mediates the whole spectrum of coronary artery disease and contributes decisively to the development and evolution of acute coronary syndromes[22]. Previous studies showed that lung fluid in acute heart failure has increased concentrations of proinflammatory cytokines and oxidative stress biomarkers[23]. In the present study, the correlation between LVEDP and lung congestion was lower in patients with increased inflammatory state, measured by higher NLR values. Since an increased inflammatory state affects permeability independently of LVEDP, when inflammation is at higher level, the origin of B-lines is likely to be a change of permeability rather than an increase in pressure. Early coronary reperfusion and stent implantation are known to reduce the inflammatory cascade[24], and delays in performing primary angioplasty may increase the role of inflammation in acute heart failure. Interestingly, the correlation between LVEDP and lung congestion seemed to be higher in patients with delayed reperfusion and higher levels of NT-proBNP (or BNP).

Unlike two previous studies of patients admitted with STEMI[3,4], we did not find LVEDP to be an independent predictor of in-hospital mortality. Those studies were both subanalyses of large randomized clinical trials and included thousands of patients. However, data collection was not standardized (before or after primary angioplasty) and the proportion of patients in whom LVEDP was not measured was unclear (in one of the studies[4], pressure measurement was performed at the discretion of the operating physician). Moreover, they found a low magnitude hazard ratio (HR 1.22, 95% CI 1.02-1.46, per 5-mmHg increase, $p = 0.044$ in one study[4], while multivariable analysis of mortality alone was omitted in the other), and that should be interpreted with caution.

Although some authors consider increased LVEDP to be a diagnostic criterion for cardiogenic shock (together with other clinical and hemodynamic variables)[25], LVEDP was not found to have a strong predictive value or AUC for cardiogenic shock in our study. One of the current practical uses of LVEDP is to guide whether mechanical assist–device is indicated in patients with cardiogenic shock[26], which, despite having physiological rationale, is based on expert opinion and needs further confirmation in a randomized fashion. Based on our results, LVEDP is a too sensitive marker of diastolic dysfunction, meaning that it may increase too early, even before any clinical or ultrasound manifestation, and may potentially decrease almost instantly when early reperfusion is achieved. We believe this is why LVEDP also did not correlate with mortality in our study, and may not correlate at all when larger dedicated studies are performed. Furthermore, we also found that LUS is a stronger predictor of cardiogenic shock than LVEDP, meaning that it might have a role as a noninvasive method to guide mechanical assist device indication.

Our study has some limitations. First, patients with conditions that are known to affect the number of B-lines (e.g., interstitial lung disease, patients on dialysis etc.) were included in the analysis, which may have decreased the correlation between LUS and LVEDP. Second, fluid-filled catheter is not the gold standard to evaluate LVEDP. Tip sensor catheters (micromanometer) are more accurate to evaluate intracardiac pressures and are commonly used for research purposes[27]. However, we evaluated LVEDP in a STEMI context as previous studies have done.

In conclusion, we found a low correlation between LVEDP and LUS in our cohort of STEMI patients undergoing pPCI. Pulmonary congestion in acute heart failure is a complex pathophysiological process and goes beyond fluid overload and

hemodynamics. Unlike LVEDP, LUS was significantly associated with in-hospital MACE, new cardiogenic shock, and in-hospital mortality in multivariable analysis.

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DISCLOSURES

None.

SUPPLEMENTAL MATERIAL

Supplemental tables I-II.

References 27-28.

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Figure 1 – Study Flowchart.

STEMI indicates ST-segment elevation myocardial infarction, LUS indicates bedside lung ultrasound; LVEDP indicates left ventricular end-diastolic pressure and MACE indicates major adverse cardiovascular event.

Figure 2 - Correlation between positive LUS zones and LVEDP (left) and Distribution of left ventricular pressure and congestion in lung ultrasound (right).

Graph abstract - STEMI, ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; CHF, congestive heart failure; CKD, chronic kidney disease; PCP, pulmonary capillary pressure; LVEDP, left ventricular end-diastolic pressure; LUS, bedside lung ultrasound; MACE, major adverse cardiovascular event; OR, odds ratio

Table 1: Baseline patient characteristics

	Overall (n = 218)	**No MACE (n = 168)**	**MACE (n = 50)**	**p**
Demographics				
Age (yers)	60 (12)	59 (± 12)	61 (± 12)	0.532
Male sex	140 (64)	113 (67)	27 (54)	0.086
Hypertension	127 (58)	94 (56)	33 (66)	0.206
Diabetes	76 (35)	52 (31)	24 (48)	0.028
Body mass index (kg/m^2)	26.8 (± 4.7)	27.0 (± 4.8)	26.1 (± 4.2)	0.256
Smoking (previous or current)	128 (41)	102 (60)	26 (52)	0.272
Previous ASA use	48 (22)	29 (17)	19 (38)	0.002
Previous MI	30 (13)	20 (11)	10 (20)	0.145
Previous stroke	19 (9)	12 (7)	7 (14)	0.131
Heart failure	7 (3)	5 (3)	2 (4)	0.718
COPD	35 (16)	28 (16)	7 (14)	0.652
Chronic kidney disease	18 (8)	7 (4)	11 (22)	< 0.0001
Admission characteristics				
Pain-to-door (hours)	5 (3.0-8.2)	5 (3.3-8.0)	6.2 (2.0-10.0)	0.978
Door-to-balloon (minutes)	75 (58-86)	76 (58.2-86.0)	70.0 (53.5-85.0)	0.241
Systolic blood pressure (mm Hg)	131 (± 34)	136 (± 31)	114 (± 38)	< 0.0001
Diastolic blood pressure (mm Hg)	76 (± 17)	77 (± 16)	69 (± 18)	0.004
Heart rate (bpm)	84 (± 21)	82 (± 18)	91 (± 29)	0.042
Creatinine (mg/dL)	1.03 (0.84-1.38)	0.97 (0.79-1.18)	1.54 (0.99-2.42)	0.01
Anterior MI	111 (50)	80 (47)	31 (62)	0.074
LAD artery	102 (47%)	19 (47%)	83 (47%)	0.541
Right coronary artery	75 (35%)	10 (25%)	65 (37%)	0.109
Cardiac arrest	25 (11)	8 (4)	17 (34)	< 0.0001
Complete AV block	14 (6)	7 (4)	7 (14)	0.013
Killip classification				
I	136 (62)	120 (71)	16 (32)	<0.0001
II	36 (16)	26 (15)	10 (20)	0.449
III	10 (4)	6 (3)	4 (8)	0.189
IV	36 (16)	16 (9)	20 (40)	<0.0001
NT-proBNP (pg/mL)*	423 (127)	365 (123-2034)	1334 (187-13177)	0.019
Peak Troponin (pg/ml)	4035 [1360 – 9945]	2204 [539 – 9794]	6115 [1299 – 16805]	0.209
NLR	6.4 [3.6 – 10.3]	6.4 [3.57 – 9.9]	6.8 [4.1 -12.1]	0.469
Neutrophil ($10^3\mu l$)	10.2 [7.3 – 13.3]	9.8 [7.2 – 13.0]	11.5 [7.8-18.1]	0.044
Lymphocyte ($10^3\mu l$)	1.6 [1.0 – 2.2]	1.6 [1.1 – 2.2]	1.8 [1.2 – 2.2]	0.151

Lung ultrasound (# of zones)	1 [1 - 5]	1 [0 - 4]	4 [1 - 7]	<0.001
Inferior vena cava > 2 cm	150 (69.8)	124 (75.2)	26 (52.0)	0.002
LVEDP (mm Hg)	19 [13 - 28]	17 [12 - 26]	23 [16 - 31]	0.002

Values are expressed as mean (standard deviation), median [interquartile range], or n (%). ASA, acetylsalicylic acid; AV, atrioventricular; BNP, brain natriuretic peptide; bpm, beats per minute; COPD, chronic obstructive pulmonary disease; LVEDP, left ventricle end-diastolic pressure; MI, myocardial infarction; LAD, Left anterior descendent; NT-proBNP, N-terminal pro-brain natriuretic peptide. *n = 183 patients.

Table 2: Procedural outcomes

	Overall (n = 218)	**No MACE (n = 168)**	**MACE (n = 50)**	**p**
Procedural details and outcomes				
Single-vessel disease	85 (39.0)	73 (43.7)	12 (24.0)	0.001
Success rate	192 (88.5)	156 (93.4)	36 (72.0)	< 0.0001
Multivessel PCI	9 (4.1%)	6 (3.5%)	3 (6%)	0.804
Impella	2 (0.9%)	1 (0.6%)	3 (3%)	0.001
IABP	11 (5%)	4 (2.4%)	7 (14%)	0.012
No-reflow/distal embolization	34 (15.4)	24 (14.3)	10 (20.0)	0.328
Cardiac arrest	28 (12.8)	7 (4.2)	21 (42.9)	< 0.0001
Post-MI ejection fraction	48.65 (13.2)	50.4 (11.9)	40.8 (15.8)	< 0.0001

Values are expressed as mean (standard deviation) or n (%). PCI, percutaneous coronary intervention; IABP, intra-aortic balloon pump; MACE, major cardiovascular adverse outcome; MI, myocardial infarction.

Table 3: Unadjusted and adjusted ORs for in-hospital outcomes

	Unadjusted			**Adjusted**		
	OR	CI	p	OR	CI	p
MACE						
LVEDP (mm Hg)	1.03	1.01-1.06	0.001	1.01	0.99-1.03	0.23
LUS (# of zones)	1.19	1.11-1.27	< 0.0001	1.14	1.06-1.23	0.01
DM	1.64	1.02-2.64	0.03	1.38	0.87-2.18	0.16
Creatinine (mg/dL)	1.25	1.16-1.34	< 0.0001	1.25	1.17-1.34	< 0.0001
Age (years)	1.02	1.00-1.03	0.03	0.99	0.98-1.01	0.80
Male sex	0.78	0.51-1.21	0.78	0.72	0.45-1.64	0.18
Cardiac Arrest	3.95	2.62-5.966	<0.0001	2.68	1.67-4.28	<0.0001

CI, confidence interval; DM, diabetes mellitus; LUS, lung ultrasound; LVEDP, left ventricular end-diastolic pressure; OR, odds ratio.

Table S.1 – Comparison of patients included and not included inf final analysis

	Included (n = 218)	**Not Included (n = 105)**	**p**
Demographics			
Age (years)	60 (12)	63 (± 12)	0.043
Male sex	140 (64)	72 (68.6)	0.441
Hypertension	127 (58)	67 (63.8)	0.324
Diabetes	76 (35)	26 (24.8)	0.028
Body mass index (kg/m^2)	26.8 (± 4.7)	27.8 (± 5.3)	0.494
Smoking (previous or current)	128 (41)	58 (55.2)	0.576
Previous ASA use	48 (22)	27 (25.7)	0.461
Previous MI	30 (13)	20 (19)	0.225
Previous stroke	19 (9)	10 (9.5)	0.714
Heart failure	7 (3)	8 (7.6)	0.718
COPD	35 (16)	23 (12.9)	0.652
Chronic kidney disease	18 (8)	14 (13.3)	0.117
Admission characteristics			
Pain-to-door (hours)	5 (3.0-8.2)	6.5 (4-18.0)	0.236
Door-to-balloon (minutes)	75 (58-86)	74 (62-92.2)	0.537
Systolic blood pressure (mm Hg)	131 (± 34)	127 (± 34)	0.350
Diastolic blood pressure (mm Hg)	76 (± 17)	74 (± 16)	0.277
Heart rate (bpm)	84 (± 21)	84 (± 20)	0.903
Creatinine (mg/dL)	1.03 (0.84-1.38)	1.08 (0.85-1.45)	0.230
Anterior MI	111 (50)	47 (45.6)	0.376
Cardiac arrest	25 (11)	18 (17.3)	0.154
Complete AV block	14 (6)	3 (2.9)	0.176
Killip classification			
I	136 (62)	64 (61)	0.804
II	36 (16)	19 (18.1)	0.723
III	10 (4)	3 (3)	0.459
IV	36 (16)	19 (18.1)	0.723

Table S2: Unadjusted and adjusted ORs for in-hospital outcomes

	Unadjusted			**Adjusted**		
	OR	CI	p	OR	CI	p
All-cause mortality						
LVEDP (mm Hg)	1.02	0.99-1.06	0.06	1.00	0.97-1.03	0.81
LUS (# of zones)	1.20	1.10-1.32	< 0.001	1.15	1.04-1.28	0.007
DM	2.08	1.13-3.85	0.01	2.00	1.11-3.60	0.02
Creatinine (mg/dL)	1.22	1.07-1.39	0.002	1.19	1.03-1.38	0.01
Age (years)	1.01	0.98-1.04	0.26	1.00	0.97-1.02	0.98
Male sex	0.80	0.42-1.49	0.48	0.87	0.54-2.04	0.87
Cardiac Arrest	5.65	3.26-9.81	<0.001	4.00	2.18-7.34	<0.0001
New cardiogenic shock						
LVEDP (mm Hg)	1.04	1.00-1.08	0.02	1.01	0.97-1.05	0.37
LUS (# of zones)	1.20	1.06-1.36	0.004	1.22	1.03-1.43	0.01
DM	1.24	0.49-3.09	0.64	0.56	0.21-1.43	0.22
Creatinine (mg/dL)	1.29	1.22-1.36	< 0.001	1.32	1.20-1.46	< 0.0001
Age (years)	0.98	0.96-1.01	0.43	0.98	0.96-1.00	0.13
Male sex	0.84	0.36-1.97	0.69	0.75	0.34-1.67	0.48
Cardiac Arrest	2.6	1.06-6.68	0.03	1.51	0.56-4.08	0.41

CI, confidence interval; DM, diabetes mellitus; LUS, lung ultrasound; LVEDP, left ventricular end-diastolic pressure; OR, odds ratio.

7. CONCLUSÕES E CONSIDERAÇÕES FINAIS

Os resultados do presente estudo demonstraram uma baixa correlação entre a pressão diastólica final do ventrículo esquerdo pressão e a quantidade de zonas positivas na ecografia pulmonar em nossa coorte de IAMCSST submetidos à percutânea primária intervenção coronária, provavelmente devido, entre outras causas, a:

1) Aumento da permeabilidade vascular por estado pró-inflamatório mais do que por congestão hemodinâmica.

2) Achados hemodinâmicos são muito sensíveis e sujeitos a mudanças rápidas em seu padrão (tempo de apresentação do IAM, terapia de reperfusão), podendo ser rapidamente revertidos caso haja reperfusão coronariana precoce, não conseguindo assim uma alteração inicial observada da PD2 discriminar o prognóstico adequadamente nesses casos.

Os resultados encontrados também demonstram que a EP, realizada na admissão hospitalar, adicionada à classificação Killip-Kimball (classificação LUCK) é viável e mais sensível do que o exame físico para identificar pacientes em risco para desfechos intra-hospitalares. A classificação LUCK foi capaz de reclassificar a gravidade de 18% dos pacientes, quando comparado à classificação de Killip-Kimball. Além de ter a maior área sob a curva para prever mortalidade intra-hospitalar entre os escores clássicos de risco, um escore LUCK baixo forneceu um valor preditivo negativo para mortalidade intra-hospitalar próximo de 100%.

Análise multivariada demonstrou que apenas a EP se manteve como preditora independente de eventos cardiovasculares adversos maiores intra-hospitalares em nossa coorte. A presença de congestão pulmonar à EP provavelmente reflete o espectro final e a consequência clínica inicial da cascata hemodinâmica desencadeada com o insulto isquêmico no IAM, o que talvez explique sua melhor habilidade de predizer desfechos. Identificar pacientes de alto risco é essencial para atendimento hospitalar para selecionar aqueles que podem se beneficiar de monitoramento e tratamento mais intensivos.

8. ANEXO I

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Título do Projeto: Comparação entre a pressão diastólica final do ventrículo esquerdo e a ecografia pulmonar na beira do leito na admissão em pacientes submetidos à angioplastia coronariana primária.

Você está sendo convidado (a) a participar de uma pesquisa cujo objetivo é verificar se o exame de ecografia pulmonar pode contribuir para uma melhor avaliação prognóstica de pacientes que sofreram infarto agudo do miocárdio. Esta pesquisa está sendo realizada pelo Serviço de Hemodinâmica do Hospital de Clínicas de Porto Alegre (HCPA). Dessa forma, estamos realizando este convite porque você teve o diagnóstico de infarto agudo do miocárdio e foi indicado como tratamento a realização de angioplastia coronariana no HCPA.

Se você aceitar participar da pesquisa, os procedimentos envolvidos em sua participação são os seguintes:

A - Durante sua avaliação inicial para o cateterismo cardíaca (que inclui avaliação de pulsos arteriais e eletrocardiográfica, tricotomia, entre outros) realizada no Serviço de Hemodinâmica, a equipe realizará, para fins desta pesquisa, um exame de ecografia. Este exame servirá para avaliar o grau de congestão pulmonar, ou seja, se há presença de líquido em seu pulmão. O exame será realizado em até 3 minutos e não atrasará o seu atendimento.

B - Será medida a pressão dentro do ventrículo esquerdo através do posicionamento dentro do coração do mesmo cateter diagnóstico que será realizado para o cateterismo cardíaco, antes da realização da angioplastia, prática usual e de rápida realização.

C - Durante a coleta de sangue que você realizará assistencialmente, conforme indicação médica, será reservada uma pequena parte deste sangue (cerca de 5ml, ou uma colher de sopa) para avaliar a presença de um marcador (BNP) que indica também se há congestão pulmonar. O resultado deste exame no sangue será relacionado com o resultado da ecografia.

D – Durante sua internação hospitalar, será realizada uma nova ecografia transtorácica para avaliar se existe correlação do grau de congestão pulmonar com o desenvolvimento de perda de função ventricular pós-infarto.

Em geral, os pacientes com o seu diagnóstico retornam para uma consulta ambulatorial de acompanhamento em torno de um mês após a alta. Gostaríamos de solicitar sua autorização para consultar os registros desta consulta em seu prontuário. Caso você não tenha consulta agendada ou não compareça a esta consulta, pedimos permissão para realizar contato telefônico, através do número que você indicar, para saber sobre seu estado de saúde.

A equipe de pesquisa também consultará seus dados de prontuário contendo informações sobre seu estado de saúde atual, resultados de exames e descrição de procedimentos. Por isso, solicitamos a sua autorização para este acesso.

A participação ou não deste estudo não terá nenhuma interferência no tratamento clínico ou cirúrgico indicado pela equipe assistencial, que será o mesmo independentemente de você aceitar ou não a participação na pesquisa.

Não são conhecidos riscos adicionais pela participação na pesquisa. A realização da ecografia necessita da utilização de um gel em contato com a sua pele, que pode causar uma sensação térmica gelada, a qual pode ser motivo de desconforto para algumas pessoas. Também poderá haver algum, desconforto ao responder perguntas ao telefone. Tendo em vista que a amostra de sangue para o exame da pesquisa será coletada no mesmo momento da coleta assistencial, não haverá a necessidade de nova punção (picada).

Não é esperado nenhum benefício direto ao participante, pois não será realizado nenhum tratamento adicional, mas as informações obtidas podem servir para aprimorar o atendimento futuro de pacientes nesta mesma situação.

Sua participação na pesquisa é totalmente voluntária, ou seja, não é obrigatória. Caso você decida não participar, ou ainda, desistir de participar e retirar seu consentimento, não haverá nenhum prejuízo ao atendimento que você recebe ou possa vir a receber na instituição.

Não está previsto nenhum tipo de pagamento pela sua participação na pesquisa e você não terá nenhum custo com respeito aos procedimentos envolvidos.

Os dados coletados durante a pesquisa serão sempre tratados confidencialmente. Os resultados serão apresentados de forma conjunta, sem a identificação dos participantes, ou seja, o seu nome não aparecerá na publicação dos resultados.

Caso você tenha dúvidas, poderá entrar em contato com o pesquisador responsável Rodrigo Vugman Wainstein, com o pesquisador Rafael Coimbra Ferreira Beltrame, pelo telefone (51) 33598342 ou com o Comitê de Ética em Pesquisa do Hospital de Clínicas de Porto Alegre (HCPA), pelo telefone (51) 33597640, ou no 2º andar do HCPA, sala 2229, de segunda à sexta, das 8h às 17h.

Esse Termo é assinado em duas vias, sendo uma para o participante e outra para os pesquisadores.

_____
Nome do participante da pesquisa

_____
Assinatura

_____
Nome do responsável (se aplicável)

_____
Assinatura

_____
Nome do pesquisador que aplicou o Termo

_____
Assinatura

Local e Data: _____

9. ANEXO II

REGRISTRO IAM ACTP PRIMARIA

1. **Paciente:_____**
2. **Data do Procedimento: ____/____/_____**
3. **Data Alta ____/____/____**
4. **Sexo: (M) (F)**
5. **Idade: _____**
6. **Cor:_____**
7. **Telefones: ( )_____**
8. **Prontuário:_____**
9. **Número do Exame:_____**
10. **Procedência:_____**
11. **Entrada via: (1) E-HCPA (2)SAMU (3)Intra-Hosp (4) Transferência**

Quadro Clínico

Primária Território (1) Anterior (2) Inferior (3) Lateral (4) Antero-lateral (5) Inferior + VD (6) Posterior
Tempo dor-porta: _____H_____min Tempo porta-balão:_____min
Tempo lido-balão: _____min Tempo cronômetro-balao: _____min
Tempo de Transferência:_____H_____min
Horário: (1) 08-20 horas (2) 20-24h (3)24-08h
Dia Semana: (1) Segunda a Sexta (2)Sábado ou domingo

Exame Físico na Chegda

Killip I (1) Killip II (2) Killip III (3) Kilip IV (4)
BAVT (0) Não (1) Sim **PCR** pré hospitalar (0) Não (1) Sim Assistida (0) Não (1) Sim
Necessidade de MP (0) Não (1) Sim **Extra-hospitalar** (0) Não (1) Sim **ROSC** _____min
PA admissão:_____/_____mmHg **Ritmo:** (1) FV (2) TV (3) AESP (4) Assistolia (99) Não identificado
FC admissão:____ bpm **ECG:** (1) Supra-ST (2) BRE (3) BRD (4) ASRV (5) Não isquêmico

Características Clínicas

HAS (0) Não (1) Sim **HF** (0) Não (1) Sim
DM (0) Não (1) Sim **Insulina** (0) Não (1) Sim
Tabaco (0) Não (1) Sim (2) Ex-Tabagista **Fibrilação Atrial** (0) Não (1) Sim
AAS: (0) Não (1) Sim **Clopidogrel:** (0) Não (1) Sim **Varfarin:** (0) Não (1) Sim **NOAC:** (0) Não (1) Sim
IAM Prévio (0) Não (1) Sim
AVC Prévio (0) Não (1) Sim **DPOC:** (0) Não (1) Sim
ICC conhecido (0) Não (1) Sim
IRC conhecida (DCE< 60) (0) Não (1) Sim **Dialítica** (0) Não (1) Sim
DVP (0)Não (1) Sim

TIMI SCORE

- Idade > 75 (3)
- Idade 65-74 (2)
- DM/HAS OU Angina (1)
- PAS < 100mmHg (3)
- FC>100 bpm (2)
- Killip II, III ou IV (2)
- Peso < 67kg (1)
- Delta T até reperfusão >4horas (1)
- Supra de ST na parede Anterior ou BRE de 3º Grau (1)

TOTAL(0-14):_____

Avaliação Laboratorial Basal Pré Procedimento

Creatinina _____mg/dL **MDRD (caso <60): _____CKD-EPI_____**
Creatinina **Pós Procedimento**: _____mg/dL
Troponinas admissão: _____ng/mL Troponinas Pico_____ng/mL Potássio _____mEq/L
Plaquetas_____ x10³/µL VPM: _____fl

Hemoglobina _____g/dL Hematócrito: _____% RDW:_____% Leucócitos Totais_____ x10³/µL Neut. Segmentados: _____x10³/µL Bastões _____ x10³/µL Linfócitos:_____ x10³/µL

Ecocardiograma:

AE:___ Diâmetro VE (Diastólico/ Sistólico):___/___ Fração Ejeção:_____ % Disfunção diastólica (0) Não (1) Leve (2) Moderada (3) Severa Disfunção VD: (0) Não (1) Sim PSAP:____ Peso:____kg Altura:____cm

Padrão Coronariano

-Extensão da doença coronária (>70% e > 50% TCE)

(1)Uniarterial (2) Biarterial (3)Triarterial (4)TCE + 1 vaso (5) TCE + 2 vasos (6) TCE+3vasos

Intervenção prévia: (0) Não (1)Sim (2) CRM

Informações Gerais sobre a Intervenção Terapêutica

Via de Acesso: (1) Radial (2)Femoral (3) Conversão **Lado do Acesso:** (1)Direito (2)Esquerdo

Introdutor (1) 05f (2)06 f (3)07f

Características angiográficas/tratamento:

Coronária/enxertos: (1) Coronária nativa (2) MAM-E (3) PVS

Vaso Culpado

(1) ACD (2) ADA (3)ACX (4) TCE (5) Diag ou intermédio (6) MArg (7)DP (8) Ponte Safena (9) Mamaria (10) Posteriolateral

TIMI Pré (0) (1) (2) (3)

Fibrinólise (0) Não (1) Resgate (3)Facilitada (4) Fármaco-Invasiva

Tratou a lesão (0) Não (1) Sim / Se **Não**: (1) CRM (2) Reperfusão Espontânea (3)Fibrinólise (4) vaso fino / oclusão distal (5) outro diagnóstico (6) óbito pré procedimento

Fluxo após passagem guia 0.014 TIMI (0) (1) (2) (3) (99) NSA

Fluxo pós Aspiração TIMI (0) (1) (2) (3) *(99) Não se aplica*

Tipo de Lesão Tratada: (1) Artéria Nativa (2)Trombose Intrastent (99) NSA

Stent Direto (0) Não (1) Sim (99) NSA

Pós Dilatação (0) Não (1) Sim (99) NSA

Overlapping (se >1 stent) (0) Não (1) Sim *(9) Não se aplica*

Aspiração Trombo (0) Não (1) Sim (2) Aspiração de Resgate (99) NSA

Materiais

Só Balão (0) Não (1) Sim (99) NSA

Stent Farmacológico (0) Não (1) Sim (99) NSA

Stent 1 _____ ___	**Stent 2** _____	**Stent 3** _____	**Stent 4** _____
Diâmetro _____mm	Diâmetro _____mm	Diâmetro _____mm	Diâmetro _____mm
Comprimento _____mm	Comprimento _____mm	Comprimento _____mm	Comprimento _____mm

Quantidade de Stents utilizados no procedimento _____

Grau de Estenose após Procedimento: _____%

Timi Pós (0) (1) (2) (3) | **Sucesso Angiográfico Final** (1)Sucesso (0)Insucesso (99) NSA

Medicações Administradas durante Procedimento

( ) AAS
( ) Clopidogrel
( ) Heparina não Fracionada
( ) Heparina de baixo peso molecular
( ) Abciximab
( ) Ticagrelor

Contraste volume: _____ml

Complicações alérgicas (0) Não (1) Sim

Dose de Radiação_____Gy

Tempo de Escopia:_____min

Complicações Durante o Procedimento

(0) Não (1) no reflow (2) embolização distal (3) re-oclusão (4) perfuração (5)óbito (6) Oclusão de Ramo (7) Estenose Residual (8) Arritmia com Instabilidade - TV, FV (9) AVC

Lesão Grave Não culpada

(0)Não (1) ADA (2) CD (3) ACX (4) DG (5) MG (6) TCE (7) DP (8) Ponte Safena (9) Mamaria (10) Posteriolateral

TTO ad hoc (0) Não (1) Sim (99) NSA
(1)ACTP Vaso (1) ADA (2) CD (3) ACX (4) DG (5) MG (6) TCE (7) DP (8) Ponte Safena (9) Mamaria (10) Posteriolateral
Mesma internação? (0) Não (1) Sim [se *Adhoc* = (1), *mesma internação* = (1)]
(2)CRM
(3)Tratamento clínico otimizado

Número Total de Vasos Tratados: _____

SEGUIMENTO HOSPITALAR

Complicações vasculares antes da alta hospitalar
(0) Não (1) Hematoma >5cm (2) Fístula AV (3) Pseudo Aneurimas (4) Hematoma retroperitoneal
(5) perfuração radial
Classificação de Sangramento GUSTO
(0) Não (1)Menor (Sangramento sem repercussão hemodinâmica ou necessidade de diálise)
(2)Moderado (Necessidade de transfusão sem instabilidade hemodinâmica)
(3) Severo (instabilidade hemodinâmica)
Transfusão durante a internação: (0) Não (1) Sim
Arritmia pós IAM (0) Não (1) Fibrilação Atrial – FA (2) Taquicardia ventricular não sustentada – TVNS (3) Bloqueio de ramo novo (4) Ritmo idioventricular acelerado – RIVA (5) PCR pós procedimento
Tempo entre Procedimento e Arritmia (0) Sem Arritmia (1) < 48h (2) >48h
Complicações antes alta:
Óbito (0) Não (1) Sim Ó**bito durante ACTP** (0) Não (1) Sim **Óbito CV?** (0) Não (1) Sim **AVC** (0) Não (1) Sim
Novo IAM (0) Não (1) Sim **Trombose Stent** (0) Não (1) Sim
Choque (0) Não (1) Cardiogênico (2) Outros **Inotrópico** (0) Não (1) Sim **Vasopressor**: (0) Não (1) Sim
BIA (0) Não (1) Sim **Impella** (0) Não (1) Sim **ECMO** (0) Não (1) Sim **Dispositivo:** (0) Não (1) Pré (2) Pós
Tempo de dispositivo: ____ min **Complicação mecânica** (0) Não (1) Sim _____
Nova Diálise (0) Não (1) Sim **Complicação infecciosa** (0) Não (1) Sim Qual?_____

Seguimento Por contato telefônico 30 dias

Realizado ( ) Sim ( ) Não
Complicações
1.Depois da alta do HCPA, o Sr teve alguma nova internação hospitalar? Baixou hospital de novo?
( ) Sim ( ) Não
Qual Hospital?
Foi feito novo cateterismo cardíaco?
Foi colocado stent?
2.Teve alguma visita à a emergência? **( ) Sim ( ) Não ( ) NSA**
Quando? Qual Hospital?
3. Foi feito diagnóstico de novo infarto ? ( ) Sim ( ) Não ( ) NSA
4. Depois da alta do HCPA, teve algum problema sério de saúde como derrame, AVC, isquemia cerebral? ( ) Sim ( ) Não ( ) NSA
Quando? Qual Hospital?
5. Depois da alta do HCPA, vem sentido dor no peito, angina?
( ) Sim ( ) Não ( ) NSA Classe (I) (II) (III) (IV)
6. Depois da alta do HCPA, vem sentindo falta de ar ou cansaço?
( ) Sim ( ) Não ( ) NSA NYHA Casse (I) (II) (III) (IV)

IMPRESSÃO (BANCO)

Óbito (0) Não (1) Sim

Novo IAM (0) Não (1) Sim
Reestenose de Stent (0) Não (1) Sim
AVC (0) Não (1) Sim
Trombose Stent (0) Não (1) Sim
Angina Classe 3 ou classe 4 (0) Não (1) Sim
Nova revascularização (0) Não (1) Sim
Reinternação por ICC (0) Não (1) Sim

Medicação Alta

- AAS (0) Não (1) Sim
- Clopidogrel (0) Não (1) Sim
- IECA –Enalapril - (0) Não (1) Sim
- Estatina (0) Não (1) Sim
- BetaBloq – Metoprolol - (0) Não (1) Sim
- Outro AntiPlaq – Ticagrelor (0) Não (1) Sim
- BRA – losartana - (0) Não (1) Sim
- Antagonista Aldosterona - Espironolactona - (0) Não (1) Sim
- Digitálico (0) Não (1) Sim
- AntiCoagulante – warfarina (0) Não (1) Sim
- Antagonista Canal de Ca (0) Não (1) Sim