UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS PNEUMOLÓGICAS

TESE DE DOUTORADO

AVALIAÇÃO DOS ASPECTOS ULTRASSONOGRÁFICOS PULMONARES EM PACIENTES SUBMETIDOS A TESTE DE RESPIRAÇÃO ESPONTÂNEA PARA DESMAME DA VENTILAÇÃO MECÂNICA

Ana Carolina Peçanha Antonio

Porto Alegre, 2016

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Orientadora: Prof^{a}. Dr^{a}. Marli M. Knorst

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“*Prediction is very difficult, especially about the future”.*

Niels Bohr, físico dinamarquês (1885-1962)

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LISTA DE ABREVIATURAS EM PORTUGUÊS

BH: balanço hídrico

bpm: batimentos por minuto

cmH_2O: centímetros de água

DPOC: doença pulmonar obstrutiva crônica

FiO_2: fração inspirada de oxigênio

IRpA: insuficiência respiratória aguda

IRRS: índice de respiração rápida superficial

mmHg: milímetros de mercúrio

mpm: movimentos por minuto

PaO_2: pressão parcial de oxigênio no sangue arterial

PEEP: pressão positiva ao final da expiração

POAP: pressão de oclusão da artéria pulmonar

PS: pressão de suporte

TRE: teste de respiração espontânea

UTI: unidade de terapia intensiva

VM: ventilação mecânica invasiva

LISTA DE ABREVIATURAS EM INGLÊS

ANOVA: analysis of variance

APACHE II: Acute Physiology and Chronic Health Evaluation II

ARDS: acute respiratory distress syndrome

ARF: acute respiratory failure

AUC: area under curve

AWS: automated weaning system

BMI: body mass index

BNP: brain natriuretic peptide

CHF: congestive heart failure

COPD: chronic obstructive pulmonary disease

CPAP: continuous positive airway pressure

CXR: chest x-ray

EF: ejection fraction

EVLW: extravascular lung water

FB: fluid balance

ICU: intensive care unit

LUS: lung ultrasound

LV: left ventricle

MHz: megahertz

mL: milliliter

MV: mechanical ventilation

NA: not available

NLR: negative likelihood ratio

NPV: negative predictive value

PEEP: positive end-expiratory pressure

PiCCO: pulse index continuous cardiac output

PLR: positive likelihood ratio

PPV: positive predictive value

PSV: pressure-support ventilation

RCT: randomized controlled trial

ROC: receiver operating characteristic

RRT: renal replacement therapy

RS: radiological score

RSBI: rapid shallow breathing index

RV: right ventricle

SBT: spontaneous breathing trial

SBTF: spontaneous breathing trial failure

SBTS: spontaneous breathing trial success

SD: standard deviation

SOFA: Sequential Organ Failure Assessment

TTE: transthoracic echocardiography

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RESUMO

Introdução: Descontinuação prematura ou tardia da ventilação mecânica invasiva (VM) associa-se a maior morbimortalidade. Redução da pressão intratorácica durante o teste de respiração espontânea (TRE) pode precipitar disfunção cardíaca através da elevação abrupta do retorno venoso e da pós-carga do ventrículo esquerdo. Da mesma maneira, alterações na demanda respiratória e cardíaca que ocorrem ao longo do TRE também podem manifestar-se à ultrassonografia pulmonar. O padrão B é um artefato sonográfico que se correlacionada com edema intersticial. Um ensaio clínico randomizando concluiu que a ultrassonografia pulmonar foi capaz de prever insuficiência ventilatória pós extubação através de variações na aeração pulmonar observadas durante o procedimento de desmame; contudo, a ferramenta não pôde rastrear pacientes antes da submissão ao TRE. O impacto do balanço hídrico (BH) e de sinais radiológicos de congestão pulmonar antes do TRE sobre os desfechos no desmame também precisam ser determinados.

Métodos: Cinquenta e sete indivíduos elegíveis para o desmame ventilatório foram recrutados. Traqueostomizados foram excluídos. Realizou-se avaliação ultrassonográfica de seis zonas pulmonares imediatamente antes e ao final do TRE. Predominância B foi definida como qualquer perfil com padrão B presente bilateralmente em região torácica anterior. Os pacientes foram seguidos por até 48 horas depois da extubação. Após esse estudo piloto, foi conduzido um estudo observacional, prospectivo, multicêntrico em duas unidades de terapia intensiva (UTIs) clínico-cirúrgicas ao longo de dois anos. Os mesmos critérios de inclusão e de exclusão foram aplicados; contudo, a ultrassonografia foi realizada apenas antes do TRE. O desfecho primário foi falha no TRE, definido como incapacidade de tolerar o teste T durante 30 a 120 minutos e, nesse caso, o paciente não era extubado. Dados demográficos e fisiológicos, BH das 48 horas antecedendo o TRE (entrada de fluidos menos débitos durante 48 horas) e desfechos foram coletados. Em uma análise *post hoc* de 170 procedimentos de desmame, um radiologista aplicou um escore radiológico na interpretação de radiografias digitais de tórax realizadas previamente ao TRE – o exame mais recente disponível foi avaliado em termos de congestão pulmonar.

Resultados: No estudo piloto, 38 indivíduos foram extubados com sucesso, 11 falharam no TRE e 8 necessitaram de reintubação em até 48 horas após a extubação. No início do teste T, padrão B ou consolidação já estava presente em porções inferiores e posteriores dos pulmões em mais da metade dos casos, e tais regiões mantiveram-se não aeradas até o final do teste. Perda de aeração pulmonar durante o TRE foi observada apenas no grupo que falhou no mesmo (p= 0,07). Esses pacientes também demonstraram maior predominância B ao final do teste (p= 0,019). Antes do procedimento de desmame, todavia, não foi possível discernir indivíduos que falhariam no TRE, tampouco aqueles que necessitariam de reintubação dentro de 48 horas. Posteriormente, de 2011 a 2013, 250 procedimentos de desmame foram avaliados. Falha no TRE ocorreu em 51 (20,4%). Cento e oitenta e nove pacientes (75,6%) foram extubados na primeira tentativa. Indivíduos que falharam no TRE eram mais jovens (mediana de 66 versus 75 anos, p= 0,03) e apresentaram maior duração de VM e maior prevalência de doença pulmonar obstrutiva crônica (DPOC) (19,6 versus 9,5%, p= 0,04). Predominância B mostrou-se um preditor muito fraco para falha no TRE, exibindo sensibilidade de 47%, especificidade de 64%, valor preditivo positivo de 25% e valor preditivo negativo de 82%. Não houve diferença estatisticamente significativa no BH das 48 horas antecedendo o TRE entre os grupos (falha no TRE: 1201,65 ± 2801,68 ml versus sucesso no TRE: 1324,39 ± 2915,95 ml).

Entretanto, em pacientes portadores de DPOC, ocorreu associação estatisticamente significativa entre BH positivo nas 48 horas antes do TRE e falha no TRE (*odds ratio*= 1,77 [1,24 – 2.53], p= 0,04). O escore radiológico, obtido em 170 testes T, foi similar entre os pacientes com falha e sucesso no TRE (mediana de 3 [2 – 4] versus 3 [2 – 4]), p= 0, 15).

Conclusão: Maior perda de aeração pulmonar observada à ultrassonografia durante o TRE pode sugerir disfunção cardiovascular e aumento na água extravascular, ambos induzidos pelo processo de desmame. BH, sinais radiológicos de congestão pulmonar ou padrão B documentado através de um protocolo ultrassonográfico simplificado não devem contraindicar o TRE em pacientes estáveis hemodinamicamente e adequadamente oxigenados, haja vista o fato de tais variáveis não terem predito maior probabilidade de falha de desmame em pacientes críticos clínico-cirúrgicos. Ainda assim, evitar BH positivo em pacientes com DPOC parece otimizar os desfechos do desmame.

Palavras-chave: desmame do respirador; edema pulmonar; ultrassonografia; tomada de decisões

ABSTRACT

Introduction: Both delayed and premature liberation from mechanical ventilation (MV) are associated with increased morbi-mortality. Inspiratory fall in intra-thoracic pressure during spontaneous breathing trial (SBT) may precipitate cardiac dysfunction through abrupt increase in venous return and in left ventricular afterload. Changes in respiratory and cardiac load occurring throughout SBT might manifest with dynamic changes in lung ultrasound (LUS). B-pattern is an artifact that correlates with interstitial edema. A randomized controlled trial concluded that bedside LUS could predict post extubation distress due to changes in lung aeration throughout weaning procedure; however, it could not screen patients before submission to SBT. The impact of fluid balance (FB) as well as of radiological signs of pulmonary congestion prior to SBT on weaning outcomes must also be determined.

Methods: Fifty-seven subjects eligible for ventilation liberation were enrolled. Patients with tracheostomy were excluded. LUS assessment of six thoracic zones was performed immediately before and at the end of SBT. B-predominance was defined as any profile with anterior bilateral B-pattern. Patients were followed up to 48 hours after extubation. After this pilot report, we conducted a 2-year prospective, multicenter, observational study in two adult medical surgical intensive care units (ICUs). Same inclusion and exclusion criteria were applied; however, LUS was performed only immediately before SBT. The primary outcome was SBT failure, defined as inability to tolerate a T-piece trial during 30 to 120 minutes, in which case patients were not extubated. Demographic, physiologic, FB in the preceding 48 hours of SBT (fluid input minus output over the 48-hour period), and outcomes data were collected. As a *post hoc* analysis in 170 weaning procedures performed in one of the

ICUs, an attending radiologist applied a radiological score on interpretation of digital chest x-rays performed before SBT - the most recent available exam was analyzed regarding degree of lung fluid content.

Results: In the pilot study, 38 subjects were successfully extubated, 11 failed the SBT and 8 needed reintubation within 48 hours of extubation. At the beginning of T-piece trial, B-pattern or consolidation were already found at lower and posterior lung regions in more than half of the individuals and remained nonaerated at the end of the trial. Loss of lung aeration during SBT was observed only in SBT-failure group (p= 0.07). These subjects also exhibited higher B-predominance at the end of trial (p= 0.019). Prior to weaning procedure, however, we were not capable to discriminate individuals who would fail SBT, nor who would need reintubation within 48 hours. Afterwards, from 2011 to 2013, 250 weaning procedures were evaluated. SBT failure occurred in 51 (20.4%). One hundred eighty-nine patients (75.6%) were extubated at first attempt. Individuals who failed SBT were younger (median 66 versus 75 years, p= 0.03), had higher duration of MV (median 7 versus 4 days, p< 0.0001) and higher prevalence of chronic obstructive pulmonary disease (COPD) (19.6 versus 9.5%, p= 0.04). B-predominance was a very weak predictor for SBT failure, showing 47% sensitivity, 64% specificity, 25% positive predictive value, and 82% negative predictive value. There were no statistically significant differences in 48 hour-FB prior to SBT between groups (SBT failure: 1201.65 ± 2801.68 mL versus SBT success: 1324.39 ± 2915.95 mL). However, in COPD subgroup, we found significant association between positive FB in the 48 hours prior to SBT and SBT failure (odds ratio = 1.77 [1.24 – 2.53], p= 0.04). Radiological score, obtained in 170 T-piece trials, was similar between SBT failure and success subjects (median 3 [2 - 4] vs 3 [2 - 4], p= 0.15).

Conclusion: Higher loss of lung aeration observed by LUS during SBT might suggest cardiovascular dysfunction and increases in extravascular lung water, both induced by weaning. Neither FB, nor radiological findings of pulmonary congestion, nor B-pattern detected by a simplified LUS protocol should preclude hemodynamically stable, sufficiently oxygenated patients from performing an SBT, since such variables did not predict greater probability of weaning failure in medical-surgical critically ill population. Notwithstanding, avoiding positive FB in COPD patients might improve weaning outcomes.

Keywords: ventilator weaning; pulmonary edema; ultrasonography; clinical decision-making

1. INTRODUÇÃO

1.1 Desmame da Ventilação Mecânica Invasiva

O processo de desmame da ventilação mecânica invasiva (VM) é gradual e compreende a redução progressiva do suporte até a remoção completa da prótese ventilatória, representando aproximadamente 40% da duração total da VM (1-4). Alguns autores alegam que a terminologia "descontinuação de VM" seria mais apropriada, no intuito de minimizar atrasos equivocados que o conceito original de "desmame" poderia implicar (5). Para esta revisão, ambos os termos serão aplicados de forma intercambiável.

Na maioria dos pacientes, a VM pode ser descontinuada assim que o motivo subjacente à insuficiência respiratória aguda (IRpA) estiver resolvido ou controlado. Contudo, 20 a 30% dos doentes críticos em VM são considerados portadores de desmame difícil ou prolongado (2).

Trinta anos atrás, o processo de desmame da VM despertava pouco ou nenhum interesse dos médicos, não sendo considerado digno de qualquer questionamento científico. Felizmente, esse contexto foi modificado: nenhuma outra área da Medicina Intensiva sofreu tamanha transformação. Entretanto, esta iluminação também gera algumas sombras: o tema é dominado por linguagem imprecisa que prejudica o rigor científico e a correta interpretação de seus resultados. Ainda nos dias de hoje, uma boa parte dos pacientes é removida abruptamente do suporte ventilatório invasivo sem qualquer deliberação a respeito (1).

O desmame da VM costuma ser dividido em sete estágios (figura 1) com o intuito de minimizar a heterogeneidade na determinação de índices e condições capazes de predizer desfechos (1, 2). O estágio 1 corresponde à fase de "pré-desmame”, na qual o paciente encontra-se sob VM e apresenta instabilidade hemodinâmica e respiratória, quando nenhuma tentativa de desmame é desejável, podendo até ser perigosa. Estima-se que entre 13 e 26% dos indivíduos em VM evoluam para óbito ainda no estágio 1. O estágio 2 é o período de “disparo diagnóstico”: o intensivista contempla a possibilidade de desmame. O estágio 3 é o momento de aferir parâmetros fisiológicos que servem como preditores. O estágio 4 compreende o teste de ventilação espontânea ou teste de respiração espontânea (TRE) e o 5, a extubação propriamente dita. O estágio 6 consiste no emprego de ventilação mecânica não invasiva como prevenção de falha de extubação, e se aplica apenas a casos selecionados (6). O estágio 7 ocorre apenas se há reintubação.

Falha de desmame é definida como incapacidade de obter um TRE bem sucedido ou a necessidade de reintubação dentro de 48 horas após a extubação (2). Em um consenso internacional de especialistas sobre desmame da VM (2), propôs-se a classificação do desmame considerando sua dificuldade e duração. Indivíduos então caracterizados como “desmame simples” são aqueles extubados na primeira tentativa. Aqueles denominados “desmame difícil” são extubados em até sete dias da primeira tentativa e o máximo de três TREs são realizados antes da extubação. Pacientes portadores de desmame prolongado são os que falham em pelo menos três TREs e requerem mais de sete dias de tentativas– esse grupo apresenta maior permanência dentro da unidade de terapia intensiva (UTI), bem como maior mortalidade (7).

Além de serem marcadores de pior prognóstico, falha de extubação e subsequente reintubação exacerbam o estado clínico *per se*, associando-se a incremento de 30 a 40% em mortalidade e ao aumento de 6 vezes nas chances de desenvolvimento de pneumonia nosocomial (8, 9). A rapidez com a qual a reintubação é realizada também parece influenciar os desfechos: as taxas de mortalidade se elevam em proporção ao atraso na execução do procedimento (9). Esteban *et al.* (10) demonstraram que o emprego de ventilação mecânica não invasiva em pacientes que apresentavam IRpA após extubação aumentava o risco de óbito em duas vezes, efeito provavelmente mediado pelo atraso em reinstituir a VM. Em contrapartida, a duração da VM tem relação direta com maior morbimortalidade (11); existe acréscimo de 1 a 3% na incidência de pneumonia nosocomial a cada dia em VM (12).

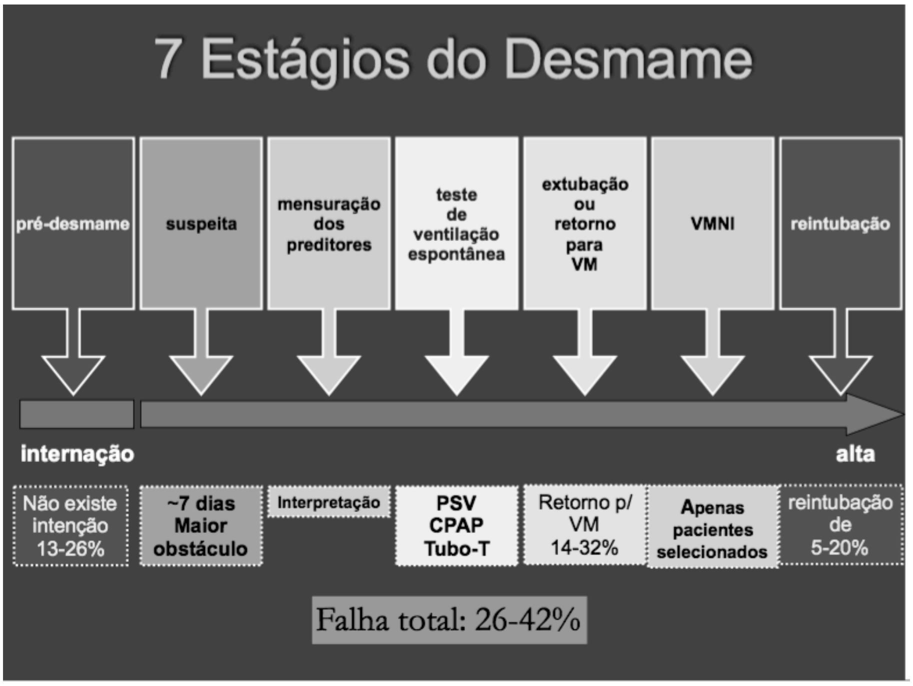

Figura 1. Os sete estágios do desmame e os percentuais aproximados de indivíduos alocados em cada um. Ver texto para maiores detalhes (1, 2).

Portanto, o desafio clínico é equilibrar segurança e agressividade. Um indicador de qualidade comum abordando esta questão é a taxa de reintubação. Um percentual muito baixo sugere atrasos desnecessários na descontinuação da VM; um valor elevado indica seleção equivocada de indivíduos ainda não prontos para o desmame ou mau uso de ferramentas de rastreamento. Embora jamais tendo sido objeto de rigorosa análise de custo-efetividade, é geralmente considerada aceitável a incidência de reintubação entre 5 e 20% (9, 13-15).

O intensivista é diariamente confrontado com a seguinte questão: os esforços para a descontinuação da VM podem ser iniciados? Este é o estágio 2 do processo de desmame e, curiosamente, é onde se encontra o maior empecilho para tal, pois frequentemente o médico apresenta autoconfiança excessiva em seu julgamento e negligencia aspectos objetivos nos quais a sua decisão deveria estar realmente baseada (16). O "comportamento clínico" é considerado razão fundamental pela qual os pacientes seriam incapazes de prosseguir o desmame - mesmo intensivistas muito experientes não percebem em tempo hábil que a retirada do suporte ventilatório é possível e assumem posturas excessivamente conservadoras (5, 17, 18). Os intensivistas também podem afetar adversamente a capacidade de o paciente lidar com o desmame ao adotarem, por exemplo, estratégias ventilatórias não protetoras ou que gerem dissincronias, através da prescrição inadvertida de sedativos e bloqueadores neuromusculares ou pela omissão de aporte nutricional apropriado (19). Da mesma maneira, não existe duração "mínima" de VM, ou seja, um período mínimo pré-estabelecido no qual o paciente deva permanecer intubado para a resolução da condição que o levou à VM. Neste sentido, a primeira recomendação de uma força-tarefa internacional de especialistas visando à elaboração de diretrizes para a descontinuação da VM (3) enfatiza a implementação de busca ativa de causas que expliquem a não viabilização de desmame já nas primeiras 24 horas de VM.

Nota-se que os critérios empregados pelo intensivista para determinar a reversão da condição subjacente à disfunção ventilatória, que motivou a indicação de intubação traqueal e conexão ao aparelho de VM, são complexos, variáveis e subjetivos, além de nunca terem sido analisados prospectivamente em um estudo controlado. Assim, corre-se o risco de incorrer-se em práticas potencialmente equivocadas que atrasam o desmame. Altamente discutíveis são, por exemplo, a verificação rotineira de imagens radiológicas (20) e implementação de balanço hídrico (BH) negativo (21) como itens básicos no processo de seleção de pacientes para o próximo passo, que é a submissão ao TRE. A tabela 1 mostra os critérios de eligibilidade preconizados para o TRE (2, 3). Reconhece-se, todavia, que alguns indivíduos podem apresentar êxito na extubação sem necessariamente preencherem todos esses critérios (22). Modernamente, tem-se vinculado estratégias de otimização de sedoanalgesia aos protocolos de desmame (23).

Tabela 1. Critérios de elegibilidade para o teste de respiração espontânea (TRE) (2, 3)

Causa da falência respiratória resolvida ou controlada;
Pressão parcial de oxigênio no sangue arterial (PaO_2) ≥ 60 mmHg com fração inspirada de oxigênio (FiO_2) ≤ 0,4 e pressão positiva ao final da expiração (PEEP - *positive end-expiratory pressure*) ≤ 8 cmH_2O;
Hemodinâmica estável, com boa perfusão tecidual, sem ou com doses baixas de vasopressores, ausência de insuficiência coronariana descompensada ou arritmias com repercussão hemodinâmica;
Paciente capaz de iniciar esforços inspiratórios;
Equilíbrio ácido-base e eletrolítico normais.

Questão de grande divergência entre os especialistas é a aplicação de índices fisiológicos cujos resultados teriam o potencial de cancelar ou ratificar a indicação do TRE (6). Centrada na análise do índice de respiração rápida superficial (IRRS) – o qual é composto pela razão entre frequência respiratória e volume corrente em litros obtida nos primeiros 3 minutos de desconexão do ventilador - resultados de uma metanálise de estudos observacionais (24) evidenciaram acurácia modesta do mesmo para predição de desfechos relacionados ao desmame. Em seguida, uma diretriz internacional (3) posicionou-se contra o emprego de preditores de desmame para guiar a tomada de decisão. Em resposta (25), alguns autores argumentaram que a acurácia modesta constatada pela metanálise devia-se a 1) vieses de seleção, pois valores dos índices já haviam sido levados em consideração nos critérios de elegibilidade; 2) viés de má classificação, porque falha no TRE e reintubação foram agregados como sendo o mesmo desfecho; e 3) viés de confusão, em virtude de pressão de suporte (PS) ter sido utilizada como TRE. Alguns estudos posteriores (26, 27) não observaram otimização das taxas gerais de sucesso com a aplicação sistemática de índices preditores de desmame, sobretudo em casos de desmame simples.

A execução do TRE também é motivo de intenso debate. Opções incluem suplementação apenas de oxigênio através do conector T de Ayres, ajuste do ventilador com um nível de CPAP (*continuous positive airway pressure*) equivalente à pressão positiva ao final da expiração (PEEP – *positive end-expiratory pressure*) ou proporcionar um nível de assistência baixo (PS de 5 a 8 cmH_2O ou emprego de compensação automática de tubo). Alguns autores defendem que o uso de PS baixas (de 3 a 14 cmH_2O, média de 7 cmH_2O) seja necessário para suplantar o trabalho adicional imposto pelo tubo traqueal e, portanto, PS seria equivalente ao teste com tubo T – ou, simplesmente, teste T - em termos de taxas de reintubação (13, 28-30). Uma metanálise recente (29) demonstrou maiores taxas de falha durante o TRE com o teste T quando comparado à PS, mas percentuais equivalentes no que concerne à reintubação. No entanto, Straus *et al.* (31) documentaram experimentalmente que o esforço respiratório dissipado através da via aérea supraglótica após a remoção do tubo traqueal é praticamente idêntico ao trabalho respiratório despendido através desta interface durante o TRE. Assim sendo, a aplicação de qualquer nível de PS pode subestimar a resistência respiratória que o paciente seja capaz de tolerar após a extubação. Além do componente resistivo de vias aéreas, a adição de PS e de PEEP produzem incrementos substanciais no débito cardíaco particularmente em pacientes portadores de insuficiência cardíaca, novamente sendo capaz de subestimar a tolerância de alguns indivíduos à ventilação espontânea (32, 33). Atualmente, não existe recomendação formal de um método de TRE em detrimento de outro, porém, de maneira geral, sugere-se o emprego de teste T em indivíduos sob maior risco de falha de desmame (20).

A duração do TRE deve ser de 30 a 120 minutos (2, 3, 34), período o suficiente para a avaliação do potencial de descontinuação do suporte ventilatório. Uma série de parâmetros fisiológicos bem como o próprio julgamento clínico – alguns de difícil quantificação, tais como ansiedade e desconforto - conceituam o desfecho de falha no TRE (tabela 2) (2, 3). Estima-se que cerca de 20% dos indivíduos apresentem disfunção ventilatória durante o TRE (3, 13, 18, 34) e requeiram reconexão ao ventilador. Deve-se, nesse caso, proceder a nova tentativa em 24 horas (3). Não há evidência que um TRE adequadamente monitorado, porém não exitoso, desencadeie desfechos piores, contanto que a VM seja prontamente reinstituída tão logo a falha for reconhecida (26, 35). Além disso, o TRE *per se* promove recondicionamento muscular (1).

Tabela 2. Sinais de intolerância ao teste de respiração espontânea (TRE) (2, 3)

Frequência respiratória > 35 mpm
Saturação arterial de oxigênio ($SatO_2$) < 90%
Frequência cardíaca > 140 bpm
Pressão arterial sistólica > 180 mmHg ou < 90 mmHg
Sinais e sintomas de agitação, sudorese, alteração do nível de consciência.

As causas para falha no TRE são numerosas e incluem fraqueza muscular, trabalho ventilatório excessivo devido a infecção, secreções, sepse não resolvida e acúmulo de sedoanalgesia. Mais recentemente, sobrecarga volêmica e insuficiência cardíaca têm sido reconhecidas como condições relevantes nesse contexto (36). Por outro lado, ao ser bem sucedido no TRE, não necessariamente está garantida a capacidade de o indivíduo respirar apropriadamente sem a interface ventilatória (37). Reintubação pode estar relacionada ou não à circunstância que desencadeou a primeira IRpA: comumente é identificada nova sepse, aspiração, tosse ineficaz com excesso de secreções, obstrução de vias aéreas, novo evento neurovascular, complicações cirúrgicas etc. Considerando a heterogeneidade de razões subjacentes às falhas de extubação, uma avaliação centrada em fisiologia respiratória pode não fornecer dados apropriados para a decisão de extubação (37).

1.2 Desmame e Interação Coração-Pulmão

A instituição de VM exerce efeitos hemodinâmicos negativos em indivíduos com função cardíaca normal, principalmente devido à redução no retorno venoso induzido pela pressão intratorácica positiva a cada insuflação. Em contraste, pacientes com edema pulmonar cardiogênico classicamente se beneficiam da terapêutica, contando com o auxílio adicional na diminuição da pós-carga do ventrículo esquerdo. Desta forma, quando da instituição do teste T, a inversão súbita de gradientes de pressão com a consequente elevação do retorno venoso e da pós-carga, o aumento do trabalho respiratório global e a descarga catecolaminérgica resultante contribuem para o desenvolvimento de disfunção miocárdica. Além disso, em pacientes com insuficiência de ventrículo direito pré-existente, o surgimento eventual de hipoxemia e de PEEP intrínseca durante o teste T corroboram para o incremento abrupto da pós-carga do ventrículo direito e alargamento desta câmara, o que, por mecanismo de interdependência ventricular, prejudica o enchimento do ventrículo esquerdo e exacerba a insuficiência cardíaca (1, 38, 39). O processo de desmame é, por isso, um teste de esforço (1).

O padrão áureo para a comprovação de falha de desmame induzida por insuficiência cardíaca requer a monitoração hemodinâmica através de cateter de artéria pulmonar, sendo evidenciada elevação pronunciada da pressão de oclusão da artéria pulmonar (POAP) durante o teste T, associado ou não ao aumento no diâmetro diastólico final do ventrículo esquerdo à cintilografia miocárdica (39, 40). Contraintuitivamente, crescimento nos valores de POAP não é acompanhado de decréscimo no débito cardíaco (39-41). Na realidade, o teste de esforço imposto pelo TRE deve gerar aumento no débito cardíaco necessário para compensar a maior necessidade de entrega de oxigênio aos tecidos. Por esse motivo, pacientes com falha no TRE induzida por disfunção miocárdica podem apresentar redução nos valores de saturação venosa mista identificados ao final do teste (42). Através da mensuração de velocidade de fluxo transmitral (ondas E e A) e do ânulo da mitral (onda Ea), a ecocardiografia também é capaz de documentar aumentos de POAP ao final do teste T com acurácia moderada (41). Valores de peptídeo natriurético cerebral (BNP – *brain natriuretic peptide*) antes ou durante o TRE são pouco úteis para determinar a causa de falha, bem como valores basais de fração de ejeção (38). Mais recentemente, um grupo francês constatou que o aumento de água pulmonar extravascular - obtida através de termodiluição usando cateter de PiCCO (*Pulse index Continuous Cardiac Output*) - durante o TRE apresenta bom desempenho para diagnóstico de falha de TRE induzida por disfunção miocárdica: sensibilidade de 67% e especificidade de

100% (43). Contudo, o incremento na concentração de proteínas plasmáticas totais e de hemoglobina ao longo do TRE parece ser o teste alternativo com maior acurácia para predizer tal desfecho até o presente momento (38, 43, 44).

Em virtude desse mecanismo estressor durante o teste T, a atitude de administrar empiricamente diuréticos em todos os pacientes classificados como desmame difícil tem sido habitual. Não obstante, alguns autores hesitam em endossar tal recomendação haja vista que condições não cardíacas são responsáveis por falha no desmame em pelo menos 50% desse grupo (32, 38, 39, 44). Também muito atraente tem sido a associação entre sobrecarga hídrica e falha no desmame sugerida por alguns estudos (45, 46), embora outros trabalhos observacionais questionem sua relação causa-efeito (47, 48). Um ensaio clínico randomizado documentou redução de 16 horas no tempo de VM através da administração de diuréticos guiada por BNP (49). O benefício parece ter ocorrido preponderantemente em pacientes que apresentavam insuficiência cardíaca sistólica e, se contabilizado o tempo de uso de ventilação mecânica não invasiva após a extubação, não mais foram observadas diferenças no tempo de desmame.

1.3 Conceitos de Ultrassonografia Pulmonar

Ultrassonografia pulmonar é a aplicação básica da ultrassonografia na UTI e na Sala de Emergência, que é a estratégia que alia diagnósticos de urgência à necessidade de decisões terapêuticas imediatas. Disponibilidade à beira do leito, acurácia comparável a da tomografia computadorizada mas sem emissão de radiação e fácil processo de aprendizado tornaram o método essencial nos mais diversos cenários da doença aguda (50). Sua primeira utilização dentro da UTI foi registrada em 1983 na França (51); desde então, o conceito de ultrassonografia de “corpo inteiro” tem sido difundido (52, 53).

Os princípios básicos da ultrassonografia pulmonar são (50, 54): emprego de um equipamento simples, não sofisticado; gás e fluidos apresentam dinâmicas gravitacionais opostas e, por isso, serão observadas condições diferentes em regiões pulmonares dependentes e não dependentes; todos os achados derivam da linha pleural; praticamente todas as afecções pulmonares se estendem à pleura visceral e, portanto, podem ser verificadas com o ultrassom; a visualização se baseia na análise de artefatos; como o pulmão é o órgão mais volumoso do corpo, zonas ou regiões de exame são passíveis de determinação – ao se questionar onde colocar o transdutor, a resposta é simples: nos mesmos locais em que se coloca o estetoscópio. Justamente por se tratar de análise de artefatos, é fundamental desligar filtros dinâmicos que equipamentos mais modernos possuem (55).

A linha pleural origina o “sinal da asa do morcego” – *bat sign* -, um ponto de referência permanente visível em todas as circunstâncias: paciente agitado, obeso, portador de enfisema subcutâneo etc. (figura 2).

A superfície pulmonar normal associa o deslizamento pleural com repetições horizontais da linha pleural, denominadas linhas A (figura 2). Elas indicam gás. O deslizamento pulmonar é um movimento que acompanha a expansão pulmonar, com uma apresentação “para frente e para trás”. Sua presença indica que a linha pleural contém a pleura parietal e visceral justapostas; sua ausência, por outro lado, é absolutamente inespecífica, podendo ser encontrada em uma série de condições críticas tais como pneumotórax, fibrose pulmonar, atelectasia e síndrome da angústia respiratória do adulto. O achado correspondente às linhas A no modo M é o “sinal do litoral” – *seashore sign -,* e confirma a presença de deslizamento pleural (figura 2).

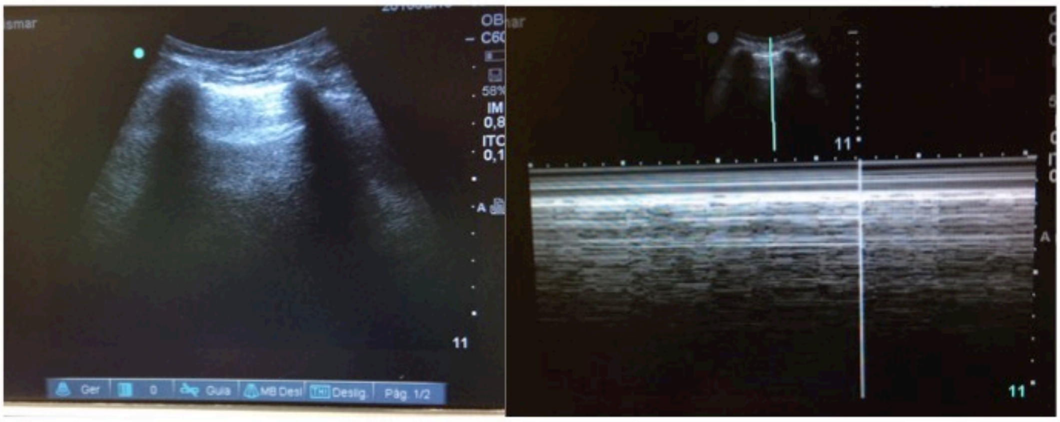

Figura 2. À esquerda, observam-se linhas horizontais repetitivas – reverberações da linha pleural – que constituem as linhas A e indicam presença de gás no interior do alvéolo. A linha pleural e as sombras acústicas das costelas, vertical e bilateralmente, compõem o "sinal da asa do morcego". À direita, no modo M, encontra-se o "sinal do litoral" que confirma o deslizamento pleural.

As linhas B são definidas como linhas verticais em formato de *laser* que se originam da linha pleural, estendem-se até o final do campo de imagem sem evanescer, determinam o apagamento das linhas A e movem-se sincronicamente com o deslizamento pleural (figura 3). Antigamente também denominadas "caudas de cometa", são artefatos de reverberação hiperecoicos (50, 54, 56). A presença de três ou mais linhas B no plano longitudinal entre duas costelas determina "região positiva". Idealmente, devem ser escaneadas 8 regiões pulmonares - zonas 1, 2, 3 e 4 bilateralmente, conforme figura 4 (57).

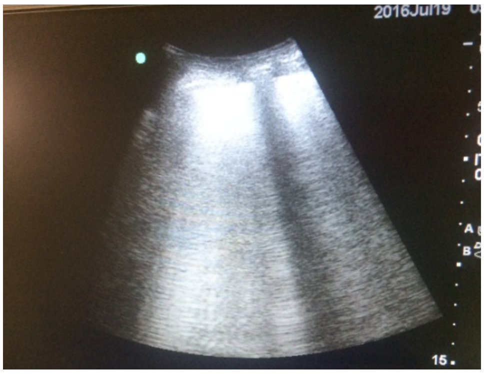

Figura 3. Linhas B são linhas verticais oriundas da linha pleural, movimentam-se com o deslizamento pleural, não evanescem e causam o apagamento das linhas A. Múltiplas linhas B configuram a síndrome intersticial.

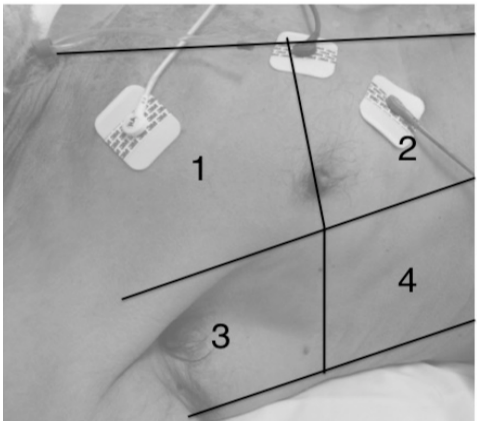

Figura 4. Protocolo de quatro regiões ou zonas pulmonares que devem ser escaneadas em cada lado do tórax. Duas ou mais regiões com presença de linhas B bilateralmente correspondem ao padrão B.

A síndrome intersticial observada em pacientes críticos é geralmente decorrente do espessamento de septos interlobulares, que representam as linhas de Kerley, e áreas em “vidro despolido”, que são visíveis em tomografias computadorizadas. As principais causas são edema pulmonar cardiogênico e pneumonia. Para a investigação, a ultrassonografia pulmonar tornou-se ferramentachave e apresenta curva de aprendizado íngreme. Apenas alguns segundos são necessários para a detecção de padrão B (50, 55).

Duas ou mais regiões positivas bilateralmente são o sinal sonográfico de síndrome intersticial. A mesma também pode ser avaliada quantitativamente através da técnica de análise de 28 zonas pulmonares: em cada uma, o número de linhas B é contado de zero a dez, ou é estimado o percentual de linhas B confluentes ocupando cada espaço intercostal. O termo “padrão B” é o mais apropriado na descrição de múltiplas linhas B em pacientes portadores de síndrome intersticial (57).

Linhas verticais que não apagam as linhas A, frequentemente encontradas de forma isolada, são denominadas linhas Z e não apresentam implicação patológica (50). Um estudo (58) demonstrou presença de linhas B exclusivamente no último espaço intercostal acima do diafragma em 27% de indivíduos saudáveis.

O menor índice de aeração pulmonar é expresso pelas linhas C (figura 5), as quais, em seu grau máximo, mostram ecogenicidade semelhante a de órgãos sólidos como fígado e baço.

Dado o exposto, ultrassonografia torácica oferece a oportunidade única de avaliar a aeração pulmonar regional: linhas A até linhas C, do maior ao menor coeficiente de relação ar-líquido (50, 54, 57).

Outras aplicações da ultrassonografia pulmonar, que incluem a detecção de pneumotórax e de derrame pleural, fogem ao escopo da presente revisão.

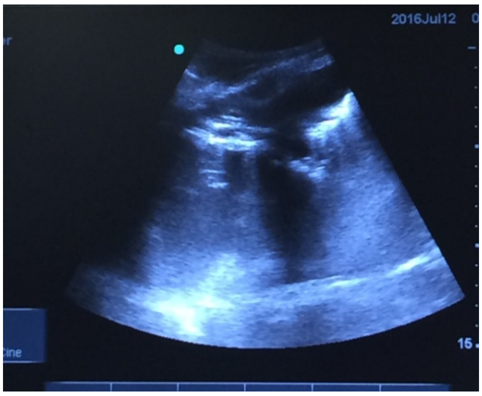

Figura 5. Linhas C: mínimo ou nenhum grau de aeração pulmonar. Nota-se a irregularidade das linhas pleurais e o pequeno derrame pleural superiormente.

1.4 Ultrassonografia e Edema Pulmonar

A primeira demonstração do emprego da ultrassonografia pulmonar para distinguir doença pulmonar obstrutiva crônica (DPOC) e edema pulmonar cardiogênico em indivíduos apresentando dispneia aguda ocorreu em 1998 (59). Mas, sem dúvida, o estudo-chave que impulsionou a disseminação do método na UTI foi publicado em 2008 pelos mesmos autores, Daniel Lichtenstein e Gilbert Mezière: protocolo BLUE, mnemônica aludindo à cianose (60). Os autores realizaram ultrassonografia pulmonar em 301 pacientes críticos em IRpA em até 20 minutos da admissão hospitalar. O diagnóstico final foi estabelecido pela equipe assistente sem levar em consideração os achados ultrassonográficos. A ferramenta apresentou uma acurácia total de 90% para diagnóstico das seis condições que mais comumente levam a IRpA: edema agudo de pulmão, pneumonia, DPOC exacerbada, asma aguda, pneumotórax e tromboembolismo pulmonar. Especificamente para edema pulmonar de etiologia cardiogênica, o valor preditivo negativo foi de 99% para seu diagnóstico. Vale lembrar que os autores tomaram para análise apenas os dados referentes às quatro regiões pulmonares do tórax anterior (zonas 1 e 2 bilateralmente) e documentaram um tempo máximo de 3 minutos para a conclusão do exame.

Cardiologistas também mostraram grande interesse pelo método, particularmente no estudo de portadores de insuficiência cardíaca congestiva (61). Uma coorte italiana de 340 pacientes admitidos em uma clínica de cardiologia observou associação direta entre o número de linhas B e a classe funcional conforme a *New York Heart Association*; a correlação com a fração de ejeção obtida através da ecocardiografia, contudo, foi fraca (62). O mesmo grupo seguiu por até 16 meses 290 indivíduos portadores de dispneia ou dor torácica e concluiu que a contagem de linhas B foi um forte preditor de morte ou eventos cardiovasculares nessa amostra (63). Uma análise semelhante ao protocolo BLUE foi conduzida por Volpicelli *et al.* (64) em 300 pacientes oriundos da sala da emergência, porém submetidos à ultrassonografia em até 48 horas da admissão e detendo-se apenas a síndromes intersticiais. Os autores concluíram que a presença de linhas B em duas ou mais zonas pulmonares era bastante específica para esse diagnóstico, com desempenho muito superior ao da radiografia pulmonar. De acordo com diretrizes internacionais baseadas em evidência (57), o exame ultrassonográfico negativo – ou a ausência de linhas B – é superior ao raio X de tórax convencional para descartar síndrome intersticial. Em uma amostra de 81 pacientes internados por insuficiência cardíaca congestiva, houve correlação positiva entre critérios clínicos de gravidade, escore radiológico, níveis de BNP e contagem de linhas B; as mesmas apresentaram decremento após o tratamento e a subsequente resolução dos sintomas (65).

Pacientes portadores de insuficiência renal crônica em terapia dialítica representam uma população estável que apresenta mudanças significativas de volemia em curtos espaços de tempo. Neste sentido, um grupo de emergencistas norteamericano observou redução expressiva no percentual de linhas B ao longo do procedimento de hemodiálise convencional, examinando 28 zonas pulmonares (66). Esse estudo foi complementado mais recentemente (67), sendo demonstrada associação forte entre o peso acumulado antes da diálise e o percentual de linhas B. Com base nos resultados acima descritos, pode-se afirmar que o emprego da ultrassonografia pulmonar para documentar variações de intensidade de congestão pulmonar que ocorrem em até 30 minutos é absolutamente factível.

Desde as primeiras correlações entre linhas B e síndromes alvéolo-intersticiais (58), muito tem-se documentado acerca da habilidade da ultrassonografia torácica em predizer pressões de enchimento. Uma comparação entre os achados ultrassonográficos e POAP obtida através de cateterismo de artéria pulmonar foi realizada em 102 pacientes em VM (68). Houve boa correlação entre valores baixos de POAP e predominância de linhas A nas zonas 1 e 2 bilateralmente; todavia, a predominância de linhas B foi encontrada em uma grande dispersão de valores. Outro estudo com 20 pacientes em período pós operatório de cirurgia cardíaca (69) demonstrou correlação linear positiva entre um escore de linhas B composto pela análise de 28 zonas, água pulmonar extravascular e POAP. Uma análise observacional, prospectiva e multicêntrica de 73 doentes críticos (70) confirmou dados anteriores de que nem sempre existe associação entre POAP elevada e padrão B à ultrassonografia torácica, e sim uma melhor especificidade entre a detecção do padrão B e de aumento de água pulmonar extravascular evidenciado pelo cateter de PiCCO. Além disso, autores alemães constataram que o emprego de um protocolo simplificado, analisando apenas as quatro regiões torácicas anteriores, também apresenta alta acurácia para diagnóstico de água pulmonar extravascular (71).

A ultrassonografia torácica também tem sido incorporada a protocolos de manejo hemodinâmico do choque séptico. Lichtenstein (72) propôs o protocolo FALLS (*Fluid Administration Limited by Lung Sonography*) a partir da relação que estabeleceu entre a ausência de linhas B e baixos valores de POAP. Esquematicamente, linhas A indicariam fluidorresponsividade, ao passo que o padrão B motivaria a suspensão da administração de fluidos. Muito sujeito a críticas, o próprio autor reconheceu que sua abordagem não é comparável a métodos dinâmicos de avaliação de fluidorresponsividade, tampouco àqueles que avaliam concomitantemente o débito cardíaco (73). O protocolo FALLS não foi avaliado prospectivamente em estudos de intervenção.

1.5 Ultrassonografia Pulmonar e Desmame da Ventilação Mecânica

O uso de ultrassonografia pulmonar à beira do leito é uma ferramenta promissora particularmente quando aliada à ecocardiografia na investigação de causas de falha de desmame. A literatura traz relatos de casos e propostas de árvore de decisão no manejo dessa circunstância através de uma abordagem integrada (74, 75), entretanto ainda não submetidos a análise mais rigorosa em ensaio clínico randomizado.

Em 2012, Soummer *et al.* (76) observaram perda de aeração pulmonar ao exame ultrassonográfico de tórax entre o início e o fim do TRE em indivíduos que, posteriormente, necessitaram de reintubação. Utilizando o "*lung ultrasound score*" mediante análise de 12 zonas torácicas e atribuindo um valor numérico ao grau de arejamento, que no final compunha um escore, o grupo constatou que a razão de verossimilhança positiva de 11,8 (intervalo de confiança: 3,8 – 36,8) de escore maior que 17 para predição de falha de extubação em 100 doentes críticos inicialmente sob VM. Não obstante, nada pôde ser inferido antes da submissão ao TRE, e 25% da amostra apresentou resultados inconclusivos para a predição do desfecho (escores entre 13 e 17). Os autores pontuaram que, já no início do TRE, zonas pulmonares posteriores e inferiores estavam desarejadas e reconheceram que a execução completa da avaliação para o LUS não seria viável em UTIs com grande demanda de trabalho.

2. JUSTIFICATIVA

Considerando o mecanismo de insuficiência cardíaca induzida pelo TRE, indaga-se como pacientes acometidos pela disfunção e que, consequentemente, falham ao teste T possam ser melhor identificados e previamente manejados, de maneira a otimizar o procedimento de desmame. O reconhecimento do potencial de falha, entretanto, não pode implicar atraso demasiado no início do desmame, sob risco de estar-se agregando morbimortalidade ao processo.

A literatura correlaciona BH positivo, falha de extubação e excesso de mortalidade. Não há clareza suficiente, contudo, para se estabelecer uma relação causal entre os fatores. O excesso de líquido corporal coloca o paciente em potencial desvantagem frente à realização do TRE. Dada a imprecisão que permeia os cálculos de BH na prática diária, é possível que esta suposta adversidade possa ser detectada preliminarmente através da radiografia torácica. Além disso, tendo em vista os inúmeros estudos demonstrando superioridade da ultrassonografia pulmonar à beira do leito em termos de acurácia e redução de riscos quando comparada aos métodos de imagem tradicionais, bem como sua capacidade de identificar o comportamento dinâmico da água pulmonar extravascular, formula-se a hipótese de que a ferramenta seja capaz de diagnosticar precocemente um fator que contribua para falha ao TRE e, do mesmo modo, alertar o intensivista para a possibilidade iniciar o processo de desmame antes do que considerava.

3. OBJETIVOS

3.1. Objetivo geral

Avaliar o comportamento dos achados ultrassonográficos pulmonares em pacientes elegíveis para desmame ventilatório em dois momentos: 1) imediatamente antes do início do TRE, ou seja, ainda sob pressão intratorácica positiva; e (2) ao final do TRE, ou seja, sob pressão intratorácica negativa, tanto em caso de falha como de sucesso no mesmo.

3.2. Objetivos específicos

- Verificar se o mecanismo de alterações súbitas de gradiente para retorno venoso e aumento da pós-carga cardíaca é traduzido por incremento significativo de zonas pulmonares com padrão B;
- Avaliar a síndrome intersticial identificada à ultrassonografia e sua possível associação com falha no desmame da VM;
- Estabelecer sensibilidade, especificidade, valor preditivo positivo, valor preditivo negativo e razão de verossimilhança do método para eleição do paciente para o TRE;
- Identificar outros possíveis preditores de falha no TRE;
- Demonstrar a viabilidade da realização do exame ultrassonográfico simplificado à beira do leito, com rapidez, reprodutibilidade e isenção de quaisquer riscos ao paciente.

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5. ARTIGO 1

BEHAVIOR OF LUNG ULTRASOUND FINDINGS DURING SPONTANEOUS BREATHING TRIAL

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The authors have no commercial associations which impact on this work.

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The authors have disclosed no conflicts of interest.

ABSTRACT

Introduction: Changes in respiratory and cardiac load occurring throughout spontaneous breathing trial (SBT) might manifest with dynamic changes in lung ultrasound (LUS).

Methods: Fifty-seven subjects eligible for ventilation liberation were enrolled. Patients with tracheostomy were excluded. LUS assessment of six thoracic zones was performed immediately before and at the end of SBT. B-predominance was defined as any profile with anterior bilateral B-pattern. Patients were followed up to 48 hours after extubation.

Results: Thirty-eight individuals were successfully extubated, 11 failed the SBT and 8 needed reintubation within 48 hours of extubation. At the beginning of T-piece trial, B-pattern or consolidation were already found at lower and posterior lung regions in more than half of the individuals and remained nonaerated at the end of the trial. Loss of lung aeration during SBT was observed only in SBT-failure group (p= 0.07). These subjects also exhibited higher B-predominance at the end of trial (p= 0.019). Prior to weaning procedure, however, we were not capable to discriminate individuals who would fail in SBT, nor who would need reintubation within 48 hours.

Conclusion: Higher loss of lung aeration during SBT might suggest cardiovascular dysfunction and increases in extravascular lung water (EVLW), both induced by weaning. This study should be repeated with an enlarged population.

INTRODUCTION

Weaning process comprises progressive withdrawal from the invasive ventilatory support until removal of the endotracheal tube, and it might represent approximately 42% of the duration of mechanical ventilation (MV) (1-3). In the intensive care unit (ICU), use of multiple respiratory indices to dictate the weaning process have been largely supplanted by the more rapid and predictive spontaneous breathing trial (SBT) (4-6). As soon as the illness that resulted in the need for MV has resolved and basic airway and cardiopulmonary stability criteria are satisfied, most patients are successfully discontinued from the ventilator within 30 to 120 minutes of an SBT. However, some patients fail multiple SBTs and are not extubated. Better assessments of patients before and during an SBT are of paramount importance to predict weaning failure and focus treatment that can reduce the time spent on artificial ventilation.

Cardiac dysfunction is well-established cause of weaning failure (7, 8). Switching a patient from positive pressure ventilation to spontaneous breathing reinstitutes negative inspiratory intra-thoracic pressure, thus increasing venous return, central blood volume, and left ventricular afterload. This normal condition, often an effort test for the patient, can decompensate cardiorespiratory function in case of volume overload and left ventricular systolic or diastolic dysfunction (9). Also, in patients with pre-existing right ventricular disease, increase in weaning-induced right ventricular afterload may occur as a consequence of hypoxemia or worsening of intrinsic positive end-expiratory pressure; then enlarged right ventricle could impede diastolic filling of the left ventricle through a biventricular inter-dependence mechanism (7, 8). SBT–induced increases in extravascular lung water (EVLW) and

B-type natriuretic peptide are reliable alternatives to the pulmonary artery catheter for diagnosing weaning-induced pulmonary edema (10).

Lung ultrasound (LUS) is a basic application of critical ultrasound - a loop associating urgent diagnoses with immediate therapeutic decisions. LUS would be of minor interest if the usual tools (bedside radiography, computed tomography) did not have drawbacks: irradiation, low information content for radiography, need for transportation (11, 12)… B-lines are defined as discrete laser-like vertical hyperechoic reverberation artifacts (previously described as 'comet-tail' or 'lung rockets') that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding. Multiple B-lines are considered the sonographic sign of lung interstitial syndrome (11-13). The so-called B-pattern has been validated to measure EVLW (14-16), and emergency presentations with shortness of breath, patients with known heart failure and fluid overload in the context of chronic hemodialysis have all been studied with LUS (17). LUS has demonstrated sensitivity of 97-100% and specificity of 95% for detecting acute pulmonary edema (13, 18).

Reasons for failure to wean from MV support are often multifactorial and involve a complex interplay between cardiac and pulmonary dysfunction. A recent review suggests the intensivist may productively use ultrasonography to identify impediments to successful extubation (19). To further investigate the relationship between B-lines and MV-weaning, here we report LUS findings of 57 MV-subjects submitted to SBT, immediately before and at the end of procedure.

MATERIALS AND METHODS

Nonconsecutive individuals older than 18 years of age, who had undergone invasive MV for at least 24 hours, were enrolled from a medical-surgical, semiclosed unit in a private hospital, full-time covered by intensivists. Individuals with a tracheostomy were excluded. The research ethic board approved the study and waived the requirement for informed consent. The study was registered as NCT02022839 at clinicaltrials.gov.

Patients were assessed daily for eligibility to weaning according to (1) improvement of underlying condition that led to acute respiratory failure; (2) alert and able to communicate; (3) adequate gas exchange, as indicated by a arterial pressure of oxygen of at least 60mmHg with an inspired fraction of oxygen < 0.40; (4) no significant respiratory acidosis; (5) rapid shallow breathing index equal to or less than 105 cycles per minute per liter; and (6) vasoactive drugs at low and stable doses (norepinephrine doses lower than 0.12μg per kilogram per minute or dopamine equivalent doses).

A Siemens Sonoline G50 ultrasound machine and a 3.5-MHz curved array probe were used for all examinations. The same trained investigator at each time point of the study conducted LUS assessment. Patients were scanned while in supine position. Using a longitudinal view, each intercostal space of upper and lower parts of the anterior, lateral, and posterior regions of the left and right chest wall was carefully examined (figure 1).

Ultrasound evaluations were performed at the following time points: before starting SBT and at its conclusion - either after 30-120 minutes, prior to extubation, or at the appearance of criteria for SBT interruption (*see below*). In order to avoid expeditious examinations in conditions of overwhelming respiratory distress just before reconnecting the patient to the ventilator, we did not described patterns of aeration other than A-line, B-line and C-line – the number of single or confluent B-lines could not be reported. Eventually, LUS findings on four anterior chest zones were mainly analyzed: the intercostal space between the third and fourth ribs and the intercostal space between the sixth and seventh ribs to the left and right of the sternum and between the parasternal and midclavicular line.

SBT failure was defined as inability to tolerate a T-piece trial of spontaneous breathing during 30 to 120 minutes, in which case subjects were not extubated. Breathing trial was interrupted if patient developed signs of respiratory discomfort (respiratory frequency > 35 breaths per minute, arterial oxyhemoglobin saturation < 90%, use of accessory respiratory muscles or paradoxical thoracoabdominal ventilation), tachycardia (heart rate more than 140 beats per minute), hemodynamic instability (systolic blood pressure less than 90mmHg or 20% over basal levels) or change in mental status (drowsiness, coma, anxiety). Extubation failure was defined as need for reintubation within 48 hours after planned removal of the artificial airway.

Demographic data including age, gender, race, comorbidities, severity of illness at the time of ICU admission, reason for the initiation of MV, physiological weaning predictors and fluid balance in the 48 hours preceding SBT were recorded. Presence of diastolic or systolic left ventricular dysfunction (the latter condition defined as ejection fraction < 45%) was documented according to formal echocardiogram report dated up to six months prior to admission.

STATISTICS

Results were expressed as the mean and standard deviation, median and interquartile range, and proportions, as appropriate. The normal distribution of the various parameters was investigated observing the distribution of data and the Shapiro-Wilk test. We used the Fisher exact test to compare proportions. Comparisons among the following three groups: (1) patients successfully extubated (successful SBT and extubation group); (2) patients who failed the T-piece trial (SBT failure group); and (3) patients reintubated within 48 h (extubation failure group) were made through one-way analysis of variance (ANOVA) for continuous variables with normal distribution, and through the Kruskall–Wallis test for variables with nonnormal distribution. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio of B-predominance for prediction of SBT failure and extubation failure were calculated. A p value <0.05 was taken to be statistically significant. Statistical analysis was performed with SPSS Version 20.0.

RESULTS

All included individuals were successfully examined, and no dropouts caused by poor examination conditions occurred. Forty-six subjects (80.7%) successfully completed T-piece trial and were immediately extubated; eight of 57 (14%) required reintubation within 48 hours. The remaining 11 individuals had signs of poor tolerance during SBT and were reconnected to the ventilator. Overall, weaning failure (failed SBT and extubation) occurred in 19 patients (33%). Table 1 shows baseline characteristics of cohort according to outcome. There was a higher prevalence of chronic obstructive pulmonary disease in SBT failure group (54.5 vs 7.9 and 12.5% in successful SBT and extubation group and extubation failure group, respectively). Sepsis of any source constituted main reason for initiate MV in all groups. Thirty-four patients (59.6%) were extubated at first attempt.

At the beginning of T-piece trial, B-pattern or consolidation were already found at lower and posterior lung regions in more than half of the individuals and remained nonaerated at the end of the trial (figure 1). We then hypothesized that a simplified approach on four chest anterior zones would be enough for the specific purpose of our study. Accordingly, we denominated B-predominance as any profile with anterior bilateral B-pattern. This concept allowed a dichotomous approach to the lung.

In SBT failure group, there was slightly statistical trend of increasing of B-predominance during T-piece trial (p= 0.07). These subjects also exhibited higher B-predominance at the end of trial (90% compared to 42.1% and 62.5% in successful SBT and extubation and in extubation failure groups, respectively; p= 0.019). Although not reaching significance (p= 0.26), successful SBT and extubation group started procedure with lower B-predominance (39.5% compared to 63.6% and 50% in, respectively, SBT failure and in extubation failure groups) [table 2].

Table 3 shows values of sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio of B-predominance for prediction of SBT failure and extubation failure outcomes.

DISCUSSION

We presented an analysis of some changes observed in LUS findings before and at the conclusion of SBT and, while acknowledging the low sample size of this study, our results lend credence to the notion that increment of B-pattern on four anterior chest zones in subjects who failed T-piece trial represents cardiac disturbance mechanism. Prior to conduction of T-piece trial, however, we were capable to discriminate neither individuals who would fail in SBT, nor who would need reintubation within 48 hours.

Rapid changes in respiratory and cardiac load occurring throughout SBT might manifest with dynamic changes in LUS that are only visible with real-time scanning. At start of trial we could not demonstrate statistically significant differences in B-predominance among groups, conceivably on account of type II error. During the trial, though, SBT-failure group behave differently, exhibiting higher raises in LUS B-predominance, similarly to other parameters of lung mechanics, hemodynamic performance and global tissue oxygenation (20). Clinical utility of such finding is uncertain, since clinical manifestations of severe respiratory distress were already evident at the moment of its detection.

Initiation of SBT after a period of MV is associated with some loss of lung aeration in critically ill subjects. Using the same LUS score technique (lower scores = better aeration) as Bouhemad *et al.* (21), Soummer *et al.* (22) showed that progressive lung derecruitment during an SBT identified patients likely to fail extubation. At the end of the SBT, patients with LUS score less than 13 had a 9% risk of postextubation failure (4 of 43) whereas those with LUS score more than 17 had an 85% risk of postextubation failure (18 of 21). End SBT LUS score between 13 and 17, seen in

25% of patients, did not allow an accurate prediction of extubation outcome. No conclusion might be derived regarding risk of failed SBT prior T-piece trial.

Our data presented lack of B-predominance accuracy for prediction of need of reintubation within 48 hours. Given our small sample size, it is unclear whether considering the simplified four-region LUS protocol is truly imprecise for such purpose. Even though, considering that extubation failure may eventuate due to causes other than imbalance between cardiorespiratory capacity and load (failure to maintain airway patency due to upper airway edema, excessive secretions, inadequate muscle strength, neurological impairment etc.), behavior of LUS findings during SBT might not portend reintubation rates accurately.

In the lung aeration during SBT study, Soummer *et al.* (22) performed transthoracic echocardiography (TTE) and B-type natriuretic peptide (BNP) measurement before and at the end of the SBT to assess the contribution of cardiac dysfunction to postextubation distress. Although BNP levels were significantly higher and TTE variables significantly different in the postextubation failure group, neither BNP levels nor TTE changes provided clinically useful cutoffs for predicting postextubation distress. While cardiac function is crucial to the weaning process, it is difficult to estimate real incidence of cardiac-related weaning failure, as increases in respiratory load and cardiac load are strongly interrelated; so it is difficult to identify to what extent a cardiac problem is the cause for the failure (7, 8). Cabello *et al.* (23) reported that cardiac-related weaning failure occurred in 42% of cases among 76 patients who failed SBT. Only eight (14%) of patients included in the present study had a history of cardiac failure, thus no inference could be made. Still, an integrated assessment of weaning using bedside LUS and echocardiography, particularly for difficult-to-wean and prolonged-weaning patients, seems promising (19, 24).

Quantification of pulmonary overhydration was not the main scope of our investigation – yet, from a practical point of view, B-pattern indicates an increase in extravascular lung water with an absolute sensitivity (25). An association between the absence of B-lines detected by LUS and a low level of wedge pressure (pulmonary artery occlusion pressure) has been reported; nonetheless, B-predominance is observed in a wide range of pulmonary artery occlusion pressure values, precluding firm conclusions for the need of fluid withdrawal (26). Other observational studies demonstrated a better specificity of the finding of B-pattern in detecting elevated EVLW by transpulmonary thermodilution method (PiCCO system) (15, 16). Enghard *et al.* (14) applied four-region LUS protocol and also found a good correlation with transpulmonary thermodilution measurements. Finally, Dres *et al.* (10) reported a link between SBT-induced increases in EVLW and weaning failure of cardiac origin with a specificity of 100%.

The present study is practical and qualitative, and also highly reproducible. Documenting, for instance, lateral walls, cardiac function, volume of pleural effusion, and vein calipers could provide additional information, to the detriment of simplicity. In this preliminary approach, the authors did not focus on posterior changes since posterior B-lines may indicate gravitational changes. Indeed, reducing scanning just to four anterior chest zones was aimed to facilitate the initial assessment of this subset of patients through a simple, rapid and easy-to-perform method. Within up to 1 minute of LUS examination, researchers were able to acquire valuable information regarding the diagnosis of lung edema. LUS score as presented (21, 22) has utility as a research tool, but may be overly complicated for the frontline intensivist to use in a busy ICU. We did not compare different protocols using, for example, an 8-, 12- or even a 28-

zone approach, so no final conclusions can be drawn regarding the superiority of either one of them.

Our major limitations are the fact that it was done at a single center and the small sample size. LUS examinations were performed only during working hours. The choice of a convenience sample and the small sample size also limit the interpretation and the generalization of the findings. The overall rate of weaning failure was relatively high (33%). The rate of reintubation following extubation (14%) was, however, comparable to what has been reported before (27), as well as the prevalence of simple-weaning (75%) (1-3), indicating that our prospective opportunity sample had same expected pre-test probability of SBT failure that any ordinary, medical-surgical ICU population. Like all techniques of ultrasonography, bedside LUS can be operator-dependent, however, a high intra- and interobserver reproducibility has been reported (21).

CONCLUSIONS

Our study does not allow one to draw a general conclusion, but some important points can be inferred. Scanning of four regions is quite feasible and time-saving, as long as inferior and posterior B-lines may reflect gravitational changes. We hypothesize that higher loss of lung aeration during SBT suggests weaning-induced cardiovascular dysfunction and increases in EVLW.

The observation that SBT-failure subjects display more severely deranged lung mechanics than do successful extubated subjects raises the question of whether derangements might be detectable while patients are receiving full ventilatory support. Usual practice, physiology and well-known causes of weaning failure all support the use of LUS to identify patients who are at high risk for a failed SBT.

However, we do concede that these data need to be confirmed with an enlarged sample population to reduce the considerable data dispersion affecting the study. Thus, we designed a multicenter observational study to evaluate whether LUS findings prior T-piece trial is able to predict the earliest time that an individual might resume spontaneous breathing.

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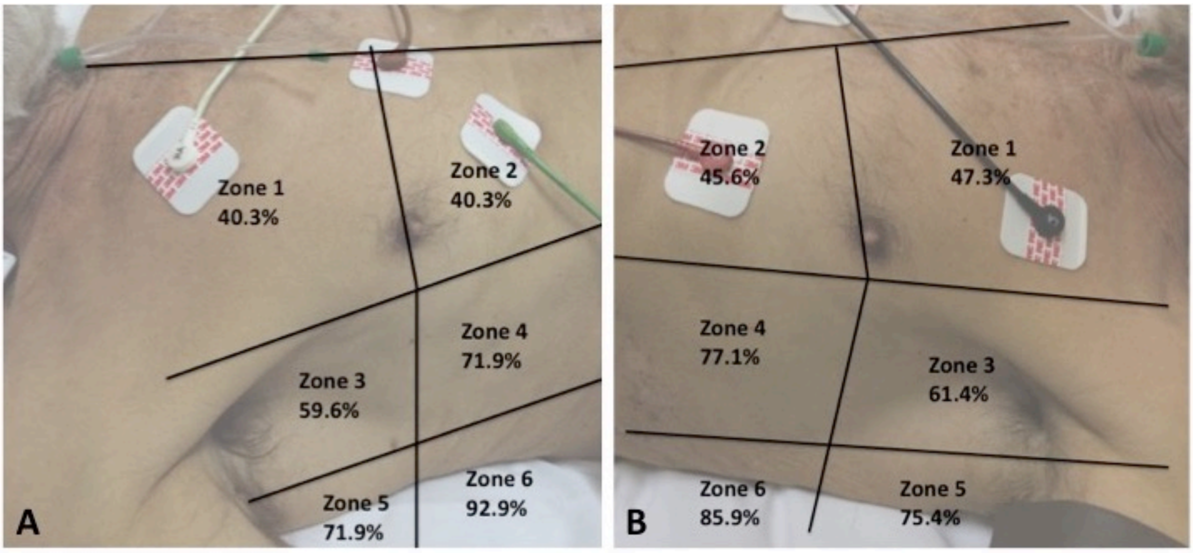

Figure 1. Prevalence of B-pattern and consolidation in 12 zones before spontaneous breathing trial (SBT) in all 57 individuals. A: right side B: left side.

Table 1. Characteristics of the Study Cohort

Patients Characteristics (n = 57)	Successful SBT and extubation (n= 38)	SBT failure (n= 11)	Extubation failure (n= 8)	p Value
Age (years)	70.6 ± 15.6	70.9 ± 22.7	82.7 ± 16.9	0.17
Female Sex	16 (42.1)	6 (54.5)	3 (37.5)	0.72
APACHE II (points)	20 ± 6.8	22.6 ± 8.8	22.3 ± 4.4	0.47
SOFA score (points)	5.5 ± 2.9	7.6 ± 5.7	6.5 ± 4.4	0.26
BMI (kg/m^2)	26.9 ± 5.6	23.7 ± 2.7	25.4 ± 7	0.26
RSBI (f/VT)	61.4 ± 21.73	71.1 ± 17.1	53 ± 17.8	0.44
MV duration (days)	5 (3 - 8.2)	7 (4 - 13)	5.5 (2.2 - 15.2)	0.50
48 hour-fluid balance prior to SBT (mL)	511.9 ± 3080.45	1821.5 ± 2720.29	747.50 ± 2958.95	0.45
Co-morbidities				
COPD	3 (7.9)	6 (54.5)	1 (12.5)	0.04
EF < 45%	3 (7.9)	2 (18.2)	0 (0)	0.37
LV diastolic dysfunction	11 (61.1)	2 (50)	6 (100)	0.18
Ischemic coronary disease	8 (21.1)	0 (0)	3 (37.5)	0.91
RRT	9 (23.7)	3 (27.3)	2 (25)	1.00
Ascitis	2 (5.3)	2 (18.2)	0 (0)	0.25
Reason for Mechanical Ventilation				
Respiratory Sepsis	5 (13.2)	5 (45.5)	1 (12.5)	0.06
Non Respiratory Sepsis	14 (36.8)	1 (9.1)	1 (12.5)	0.13
CHF	6 (15.8)	0 (0)	2 (25)	0.21
Coma	8 (21.1)	1 (9.1)	2 (25)	0.69
Postoperative ARF	1 (2.6)	0 (0)	0 (0)	1.00
COPD/Asthma	0 (0)	0 (0)	1 (12.5)	0.15
Pulmonary Embolism	1 (2.6)	0 (0)	0 (0)	1.00
ARDS	2 (5.3)	2 (18.2)	0 (0)	0.25
Simple Weaning	30 (78.9)	9 (81.8)	4 (50)	0.17

Data are presented as median (interquartile range), mean±SD or n(%).

SBT: spontaneous breathing trial. APACHE II: Acute Physiology and Chronic Health Evaluation II. SOFA: Sequential Organ Failure Assessment. BMI: body mass index. RSBI: rapid shallow breathing index. MV: mechanical ventilation. COPD: chronic obstructive pulmonary disease. EF: Ejection fraction. LV: left ventricular. RRT: renal replacement therapy. CHF: congestive heart failure. ARF: acute respiratory failure. ARDS: acute respiratory distress syndrome.

Table 2. B-predominance prior to spontaneous breathing trial and at the end of trial according to weaning groups

B-predominance	Successful SBT and extubation (n= 38)	SBT failure (n= 11)	Extubation failure (n=8)	p Value**
Before SBT	15 (39.5%)	7 (63.6%)	4 (50%)	p= 0.36
End of SBT	16 (42.1%)	9 (90%)	5 (62.5%)	p= 0.019
p Value*	p= 0.4	p= 0.07	p=0.27	

Data are presented as n (%).

SBT: spontaneous breathing trial

* For comparison between before SBT and end of SBT

** For comparison among weaning groups at each moment

Table 3. Performance of B-predominance as a screening test for weaning prediction

Time of assessment	Outcome	Sensitivity	Specificity	PPV	NPV	PLR	NLR
Before SBT (n= 57)	*SBT failure (n= 11)*	0.64 (0.32 – 0.88)	0.59 (0.43 – 0.73)	0.27 (0.12 - 0.48)	0.87 (0.52 - 0.88)	1.54 (0.87 - 2.70)	0.62 (0.27 - 1.40)
Before SBT (n= 57)	*SBT failure and extubation failure (n= 19)*	0.58 (0.34 - 0.79)	0.60 (0.43 – 0.75)	0.42 (0.24 – 0.63)	0.74 (0.55 – 0.87)	1.47 (0.85 – 2.54)	0.69 (0.40 – 1.22)
End of SBT (n= 46)*	*Extubation Failure (n= 8)*	0.62 (0.26 – 0.90)	0.58 (0.40 – 0.73)	0.24 (0.09 -	0.88 (0.68 – 0.97)	1.48 (0.77 – 2.85)	0.65 (0.26 – 1.64)

Data are expressed as estimated value (95% confidence interval)
** Excluding failed SBT cases (not extubated)*

SBT: spontaneous breathing trial. PPV: positive predictive value. NPV: negative predictive value. PLR: positive likelihood ratio. NLR: negative likelihood ratio

6. ARTIGO 2

48-HOUR FLUID BALANCE DOES NOT PREDICT SUCCESS OF A SPONTANEOUS BREATHING TRIAL

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The authors have no commercial associations which impact on this work.

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The authors have disclosed no conflicts of interest.

Ana Carolina Peçanha Antonio conceived and drafted the paper. Cassiano Teixeira, Augusto Savi and Marcelo Basso Gazzana contributed substantially to the conception and design. Cassiano Teixeira and Marli Knorst revised the draft for important intellectual content. Ana Carolina Peçanha Antonio and Priscylla Souza Castro collected data. All of the authors gave final approval of the version to be published.

ABSTRACT:

Purpose: Both delayed and premature liberation from mechanical ventilation (MV) are associated with increased morbimortality, and fluid balance (FB) could negatively influence extubation outcomes. We sought to determine the impact of FB in the 48 hours prior to spontaneous breathing trial (SBT) on weaning outcomes in a mixed intensive care unit (ICU) population.

Methods: A prospective, observational study in two adult medical-surgical ICUs. All enrolled patients met eligibility criteria for weaning from MV. SBT failure (SBTF) was defined as inability to tolerate a T-piece trial during 30 to 120 minutes. Demographic, physiologic, FB in the preceding 48 hours of SBT (fluid input minus output over the 48-h period), lung ultrasound findings, and outcomes data were collected.

Results: A total of 250 SBTs; SBTF eventuated in 51 (20.4%). Twenty-nine patients (11.6%) had chronic obstructive pulmonary disease (COPD) and forty (16%) were intubated due to respiratory sepsis. One hundred eighty-nine patients (75.6%) were extubated at first attempt. Comparing to SBT success (SBTS) individuals, SBTF patients were younger (median 66 vs 75 years, p= 0.03), had higher duration of MV (median 7 vs 4 days, p< 0.0001) and higher prevalence of COPD (19.6 vs 9.5%, p= 0.04). There were no statistically significant differences in 48 hour-FB prior to SBT between groups (SBTF: 1201.65 ± 2801.68 mL vs SBTS: 1324.39 ± 2915.95 mL). However, in COPD subgroup, we found significant association between positive FB in the 48 hours prior to SBT and SBTF (odds ratio = 1.77 [1.24 – 2.53], p= 0.04).

Conclusions: Fluid balance should not delay SBT indication since it did not predict greater probability of SBTF in medical-surgical critically ill population. Notwithstanding, avoiding positive FB in COPD patients might improve weaning outcomes.

KEYWORDS: respirator weaning; fluid balance; chronic obstructive pulmonary disease; cardiac failure

INTRODUCTION

Imprecise definition of weaning from mechanical ventilation (MV) prevents the rigor of research in this area, as well as interpretation of the findings (1). Both delayed and premature discontinuation of MV have been associated with increased mortality (36%) (2), assuming that reintubation is not related to upper airway obstruction (3). Early identification of patients who are able to breathe spontaneously results in a shorter duration of MV and lower complication rates (4). Ventilator-associated pneumonia incidence is estimated to be 1-3% each day on MV (5).

Switching a patient from positive pressure ventilation to spontaneous breathing reestablishes negative inspiratory intra-thoracic pressure, thus increasing venous return (left ventricular [LV] preload), central blood volume, and LV afterload. This normal condition, often an effort test for the patient, can decompensate cardiorespiratory function in case of volume overload and LV systolic or diastolic dysfunction (6). Also, in patients with pre-existing right ventricular (RV) disease, increase in weaning-induced RV afterload may occur as a consequence of hypoxemia or worsening of intrinsic positive end-expiratory pressure (PEEP), especially in chronic obstructive pulmonary disease (COPD) population (7). In addition to simultaneous raise in systemic venous return, higher RV afterload may lead to a marked RV enlargement during weaning, thus impeding the diastolic filling of the left ventricle through a biventricular inter-dependence mechanism.

Previous authors (8-10), in observational studies of weaning procedures, found correlation between higher fluid balance (FB) and extubation failure. However, there was considerable diversity in terms of populations evaluated, weaning and extubation protocols and outcomes analyzed. Furthermore, spontaneous breathing trial (SBT) events were not discriminated among outcomes. A randomized controlled trial (RCT) showed that fluid management guided by brain natriuretic peptide (BNP) plasma concentrations reduced time to weaning (11), despite similar FB between groups on the day of extubation. Empirically and unnecessary administration of diuretics in every ready-to-wean patient has become more and more frequent, even though extra-cardiac causes are responsible for weaning failure in at least 50% of cases and roughly 70% of patients are successfully extubated at first attempt (simple weaning). Moreover, uncontrolled diuretic therapy may have potentially harmful effects, such as serious electrolyte disturbances and microatelectasis related to bronchiolar obstruction by dry bronchial secretions (7).

So, we therefore hypothesized that FB value should not delay the decision to submit the ordinary MV-patient to SBT, since it cannot accurately predict the earliest time that an individual might resume spontaneous breathing. The objective of our study was to assess prospectively the variables associated with spontaneous breathing trial failure (SBTF) in a heterogeneous group of MV-patients.

MATERIALS AND METHODS

Between January 2011 and March 2013, nonconsecutive patients older than 18 years of age, who had undergone invasive MV for 24 hours, were enrolled from mixed ICUs in two private hospitals. Patients with a tracheostomy were excluded. The research ethic board at each center approved the study and waived the requirement for informed consent. The study was registered as NCT02022839 at clinicaltrials.gov.

Patients were assessed daily for eligibility to weaning according to (1) improvement of underlying condition that led to acute respiratory failure; (2) alert and able to communicate; (3) adequate gas exchange, as indicated by arterial pressure of oxygen of at least 60mmHg with an inspired fraction of oxygen < 0.40; (4) rapid shallow breathing index (RSBI) equal to or less than 105 cycles per minute per liter; and (5) vasoactive drugs at low and stable doses (norepinephrine doses lower than 0.12μg per kilogram per minute or dopamine equivalent doses).

The main outcome of interest was SBTF, defined as inability to tolerate a T-piece trial of spontaneous breathing during 30 to 120 minutes, in which case patients were not extubated. Breathing trial was interrupted if patient developed signs of respiratory discomfort (respiratory frequency > 35 breaths per minute, arterial oxyhemoglobin saturation < 90%, use of accessory respiratory muscles or paradoxical thoracoabdominal ventilation), tachycardia (heart rate more than 140 beats per minute), hemodynamic instability (systolic blood pressure less than 90mmHg or 20% over basal levels) or change in mental status (drowsiness, coma, anxiety).

Demographic data including age, gender, race, comorbidities, severity of illness at the time of ICU admission, reason for the initiation of MV, physiological weaning predictors, last chest X-ray findings available before SBT and FB in the 48 hours preceding SBT were recorded. Presence of diastolic or systolic LV dysfunction (the latter condition defined as ejection fraction < 45%) was documented according to echocardiogram report dated up to six months prior to admission. Diagnosis of COPD was based on history, physical examination, chest X-ray and previous pulmonary function tests.

FB was routinely recorded on report sheet and was defined as total inputs minus total outputs, tallied at midnight daily. Losses through urinary, gastrointestinal or other drainage tubes were subtracted from all fluids, nutrition, medications and blood products administered, whatever the route of administration.

STATISTICS

On the basis of results of the study of Upadya *and cols.* (8), which observed a 1500mL FB higher in failure compared to success group in the 48 hours prior to extubation, we estimated that 250 patients would have 91% power to show same difference, at a two-sided alpha level of 0.05.

Results were expressed as the mean and standard deviation, median and interquartile range, and proportions, as appropriate. The normal distribution of the various parameters was investigated observing the distribution of data and using the Kolmogorov-Smirnov test. We used the Student t test or the Mann-Whitney U test to compare continuous variables, and the χ^2-test or the Fisher exact test to compare proportions, as appropriate. The primary end point was also analyzed in the three predefined subgroups: COPD, LV systolic dysfunction (defined as ejection fraction < 45%) and isolated LV diastolic dysfunction. Receiver operating characteristic (ROC) curves were generated for thoses subgroups, comparing their ability to discriminate spontaneous breathing trial success (SBTS) and SBTF patients according to FB values. Finally, all patients were divided into categories according to FB in the 48 hours prior to SBT using arbitrary steps of 1 liter, analogously to Frutos-Vivar *and cols.* (10).

RESULTS

We obtained complete data in 250 weaning procedures. Overall, SBTF occurred in 51 (20.4%). Table 1 shows the baseline characteristics of the study cohort according to outcome. Patients who were successfully extubated were older (median 75 vs 66 years, *p*= 0.03) and had been intubated for a shorter duration (MV median 4 vs 7 days, *p*< 0.0001). There was also a lower prevalence of COPD in SBTS group (19.6 vs 9.5%, p= 0.04).

FB in the 48 hours preceding SBT was similar between groups (1324.39 ± 2915.95 mL vs 1201.65 ± 2801.68 mL [p= 0.52] for, respectively, SBTS and SBTF patients) [Figure 1]; and using arbitrary steps of 1000mL, the prevalence of SBTF demonstrated a random distribution (Figure 2).

The subgroup analysis in patients with COPD, LV systolic dysfunction and isolated LV diastolic dysfunction is shown in Table 2. An area under the ROC curve of 0.70 (0.50-0.89) was found in COPD patients with a cut off of 0 mL to SBTF. Therefore, comparing individuals with 48h FB above and under 0 mL cut off value according to SBT outcomes resulted in significant association between positive FB in the 48 hours preceding SBT and SBTF in this subgroup (odds ratio = 1.77 [1.24 – 2.53], p= 0.04), as presented on figure 3. The area under the ROC curve was 0.59 and 0.50 for LV systolic dysfunction and isolated LV diastolic dysfunction, respectively.

DISCUSSION

In a heterogeneous cohort of mechanically ventilated patients candidates to SBT, we found no association between FB in the preceding 48 hours and SBT outcomes. Patients with COPD, however, might derive some benefit in terms of not allowing positive FB, probably due to heart-lung interaction issues.

In spite of relationship between failure to wean from MV and positive FB, there is no clear evidence of principle of cause and effect, and outcomes employed are diverse among studies (weaning, extubation or both combined). A central question for clinicians is whether extubation failure is simply a marker of poor prognosis or instead contributes to induce a poor prognosis (12). A retrospective analysis of Vasopression in Septic Shock Trial (VASST) demonstrated that mortality increases with positive FB in a linear manner independent of severity of illness or shock, and this dose-response correlation was found out at only 12 hours after study enrollment(13). Whether FB independently affects outcome or it is just a confounder, a marker of severity of illness, remains unclear, but clearly aggravating FB by using the wrong tools and the wrong endpoints should not take place in the context of current knowledge.

Inaccuracies in monitoring and recording fluid therapy in daily practice are a growing issue in intensive care setting, owing to lack of agreement with standardized body weight measurements (14-16). All of the studies neglected to consider nutritional aspects, and some did not take into account the sensible or insensible fluid losses. Average daily and cumulative FB were arithmetically incorrect in about one-third of cases (15). We could even question the clinical importance or significance of changes in total body water, as the volume load of specific compartments (intravascular volume, cardiac preload, extravascular lung water) is probably more relevant.

Upadya *et al* (8) examined 87 patients who underwent 205 breathing trials (T-piece or pressure support) between 2002 and 2003 and verified that negative FB in the preceding 24 hours, 48 hours and the net negative cumulative balance were associated with weaning success. There was high percentage of COPD patients in the sample (46%) and only 44% was classified as simple-to-wean patients. Although administration of diuretics was associated with negative FB, it was not associated with weaning outcomes. A prospective study of 40 trauma and surgical patients who were at least 60 years old (9) also proposed a direct relationship between negative FB and weaning success; nevertheless, weaning failure group already had a FB significantly higher at entry into the study. Frutos-Vivar *et al* (10) published a representative cohort study of 900 patients searching for risk factors predicting extubation failure following a SBT and concluded that reintubated patients were more likely to have a positive FB in the 24 hours prior to extubation. Finally, a randomized controlled trial showed that fluid management guided by BNP plasma concentrations reduced time to weaning (11), a benefit observed predominantly in patients with LV systolic dysfunction in subgroup analysis, in spite of not significant difference in FB between usual care and intervention group on extubation day.

A comparison of our study design to the others mentioned above is shown on Table 3. Note our higher prevalence of simple weaning, as described in literature, and use of SBTF as outcome instead extubation failure. We chose SBTF as principal outcome since we aimed to predict the earliest time that a patient might resume spontaneous breathing. Moreover, the exact reason for extubation failure often escapes identification. Reintubation is usually performed because of an apparently new episode of respiratory distress, which may be related to primary respiratory failure, congestive heart failure, aspiration, ineffective cough with airway secretion build-up, or upper airway obstruction. Other reasons for reintubation include the onset of new sepsis, surgical complications, acute coronary syndrome, and neurological impairment. This multiplicity of causative factors contributes to explain the clinical difficulties raised by extubation and the persistent uncertainties about the pathophysiology of extubation failure (1).

Limitations of our study were observational design, with all its intrinsic methodologic flaws, and small sample size with high prevalence of elder population and lower prevalence of COPD comparing to others similar studies. Also, there is potential for inaccuracy and lack of precision of clinical data retrieved from daily flow sheets.

On January 28th 2013, we received 10 patients rescued from Kiss nightclub fire in Santa Maria, Rio Grande do Sul, Brazil. They were between 17 and 23 years old, all had smoke inhalation injury, and six of them failed at T-piece test at least once. By excluding those patients, there would be no statistically difference in age (p= 0.209) nor in FB (p= 0.523) between SBTF and SBTS groups.

In conclusion, FB may not predict SBT outcomes in a mixed medical-surgical ICU population.

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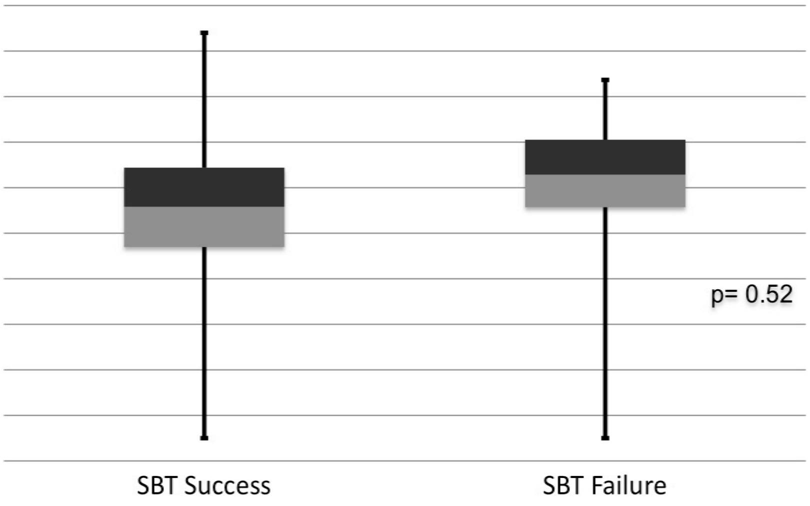
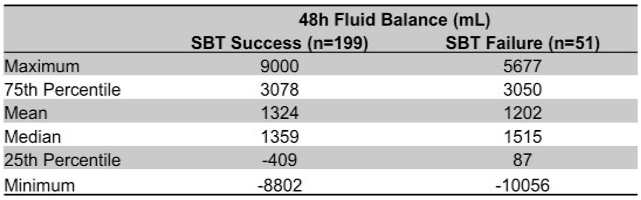
Table 1. Characteristics of the study cohort

Patients Characteristics (n = 250)	SBT Success (n= 199)	SBT Failure (n= 51)	p Value
Age (years)	75 (60-83)	66 (47-81)	0.03
Female gender (%)	42.2	45.1	0.71
APACHE II (points)	20.8 ± 6.9	21.8 ± 7.8	0.25
SOFA score (points)	5 (3-9)	5 (2-9)	0.9
BMI (kg/m^2)	25 (23-30)	25 (23-29)	0.82
RSBI (f/VT)	58.3 ± 24.3	58.4 ± 24	0.89
MV duration (days)	4 (2-6)	7 (4-11)	<0.001
Co-morbidities			
COPD	19 (9.5)	10 (19.6)	0.04
EF < 45%	19 (9.5)	6 (11.8)	0.64
LV diastolic dysfunction	73 (65.8)	15 (51.7)	0.16
Ischemic coronary disease	36 (18.1)	5 (9.8)	0.15
RRT	34 (17.1)	13 (25.5)	0.17
Presence of ascitis	7 (3.5)	3 (5.9)	0.44
Reason for MV			
Respiratory sepsis	31 (15.6)	9 (17.6)	0.72
Non respiratory sepsis	52 (26.1)	12 (23.5)	0.7
CHF	20 (10.1)	2 (3.9)	0.17
Coma	39 (19.6)	6 (11.8)	0.2
Postoperative ARF	15 (7.5)	4 (7.8)	0.94
COPD/Asthma	2 (1)	2 (3.9)	0.14
Pulmonary Embolism	6 (3)	1 (2)	0.68
ARDS	10 (5)	5 (9.8)	0.2
Simple weaning	151 (75.9)	38 (74.5)	0.61
XR pleural effusion	60 (30.2)	17 (33.3)	0.66
XR pulmonary edema	56 (26.6)	18 (35.3)	0.22
Vasopressor	39 (19.6)	5 (9.8)	0.1
Vasodilator	13 (6.5)	3 (5.9)	0.87

Data are presented as median (interquartile range), mean±SD or n(%).

SBT: spontaneous breathing trial. APACHE II: Acute Physiology and Chronic Health Evaluation II. SOFA: Sequential Organ Failure Assessment. BMI: body mass index. RSBI: rapid shallow breathing index. MV: mechanical ventilation. COPD: chronic obstructive pulmonary disease. EF: Ejection fraction. LV: left ventricular. RRT: renal replacement therapy. CHF: congestive heart failure. ARF: acute respiratory failure. ARDS: acute respiratory distress syndrome. XR: chest X-ray.





	48h Fluid Balance (mL)	
	SBT Success (n=199)	SBT Failure (n=51)
Maximum	9000	5677
75th Percentile	3078	3050
Mean	1324	1202
Median	1359	1515
25th Percentile	-409	87
Minimum	-8802	-10056

Figure 1. 48-hour fluid balance according to weaning outcomes.

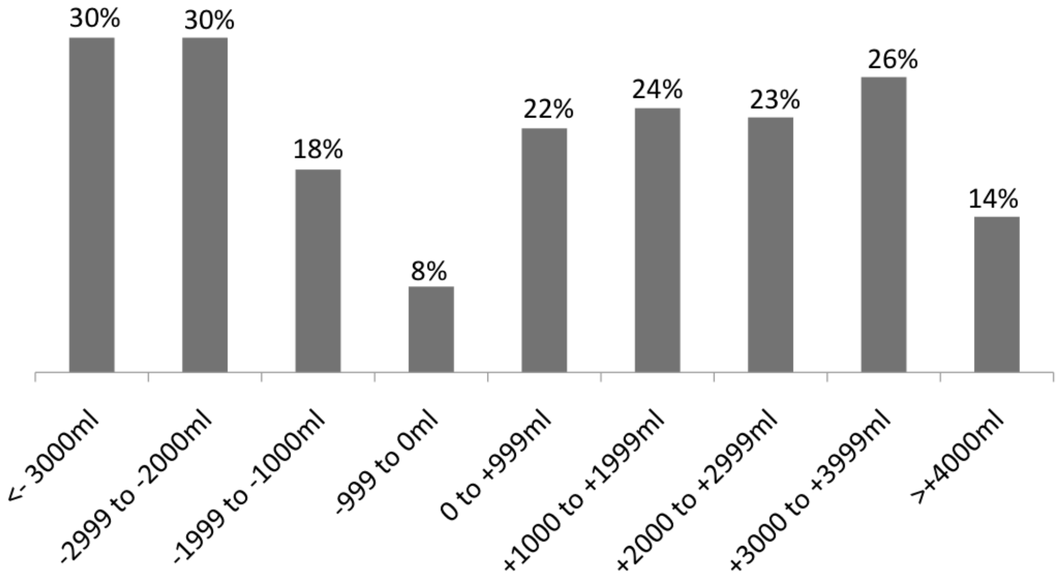


Figure 2. Prevalence of weaning failure by fluid balance category. Patients were divided into categories using arbitrary steps of 1000 mL.

Table 2. Fluid balance and outcomes according to specific subgroups

	SBT Success (n)	SBT Failure (n)	*p* Value
EF < 45%	1096 ± 3062 mL (19)	1804 ± 1264 mL (6)	0.13
LV diastolic dysfunction	1241 ± 2782 mL (73)	996 ± 1899 mL (15)	0.15
COPD	1091 ± 2195 mL (19)	2399 ± 1533 mL (10)	0.32

EF: Ejection fraction, LV: left ventricular, COPD: chronic obstructive pulmonary disease, SBT: spontaneous breathing trial.

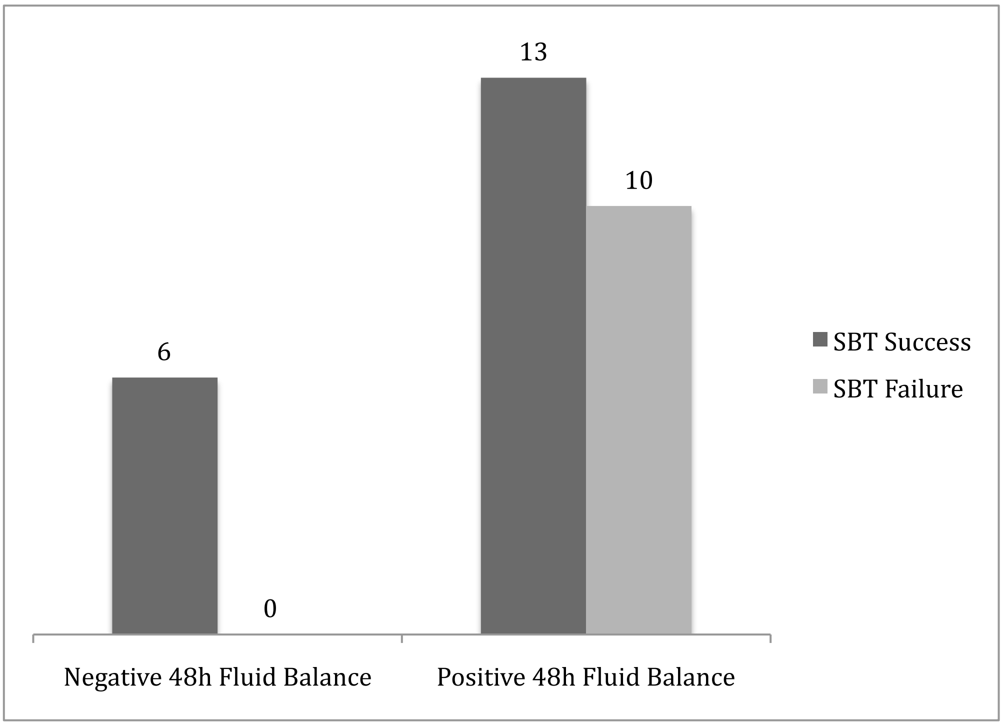


Figure 3. Association between positive fluid balance in the 48 hours preceding spontaneous breathing trial (SBT) and SBT failure in chronic obstructive pulmonary disease (COPD) patients.

Table 3. Comparison of studies

	Antonio *et al*, 2013	Upadya *et al*, 2005	Frutos-Vivar *et al*, 2006	Dessap *et al*, 2012
Sample size	250	205	900	302
Study design	Observational	Observational	Observational	RCT
Method of weaning	T-tube	PSV or T-tube	T-tube, PSV, CPAP, Flow-by	AWS
Outcome	SBT failure	Extubation failure	Extubation failure	Time to extubation
APACHE II	21	17	37	NA
Age (median)	72 years-old	66 years-old	58 years-old	66 years-old
COPD	11.6%	46%	NA	26%
LV dysfunction	39.6%	69%	NA	14,5%
Simple weaning	75.9%	45%	NA	NA
MV duration (median)	4 days	3 days	5 days	6 days
BNP levels	NA	NA	NA	↓ in weaning success patients

PSV: pressure-support ventilation. CPAP: continuous positive airway pressure. AWS: automated weaning system. SBT: spontaneous breathing trial. APACHE II: Acute Physiology and Chronic Health Evaluation II. MV: mechanical ventilation. COPD: chronic obstructive pulmonary disease. EF: Ejection fraction. LV: left ventricular. BNP: brain natriuretic peptide. NA: not available.

7. ARTIGO 3

RADIOLOGICAL SIGNS OF PULMONARY CONGESTION DO NOT PREDICT FAILED SPONTANEOUS BREATHING TRIAL

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The authors have no commercial associations which impact on this work.

Conflict of Interest:

The authors have disclosed no conflicts of interest.

ABSTRACT

Introduction. Both delayed and premature liberation from mechanical ventilation are associated with increased morbi-mortality. Inspiratory fall in intra-thoracic pressure during spontaneous breathing trial may precipitate cardiac dysfunction through abrupt increase in venous return and in left ventricular afterload. We aimed to determine the relationship between radiological signs of pulmonary congestion prior to submission to spontaneous breathing trial and weaning outcomes in a mixed critically ill population.

Methods. A *post hoc* analysis of a prospective cohort study designed to investigate the potential role of lung ultrasound in predicting weaning outcomes in an adult medical-surgical intensive care unit. All enrolled individuals met eligibility criteria for liberation from mechanical ventilation. Tracheostomized subjects were excluded. The primary endpoint was spontaneous breathing trial failure, defined as inability to tolerate a T-piece trial during 30 to 120 minutes, in which case subject was not extubated. An attending radiologist applied a radiological score on interpretation of digital chest x-rays performed before spontaneous breathing trial - the most recent available exam was analyzed.

Results. There was a total of 170 T-piece trials; trial failure eventuated in 28 (16.4%). One hundred thirty-three subjects (78.3%) were extubated at first attempt. Radiological score was similar between spontaneous breathing trial failure and success subjects (median 3 [2 - 4] vs 3 [2 - 4], p= 0.15), meaning only interstitial lung congestion for both groups. Receiver operating characteristic curves analysis demonstrated fail accuracy (area under curve = 0.58) of chest x-rays findings of congestion prior to T-piece trial for discrimination between failure and success

individuals. There was no correlation between fluid balance in the 48 hours preceding T-piece trial and radiological score (ρ= -0.13).

Conclusions. Radiological findings of pulmonary congestion should not delay spontaneous breathing trial indication since they did not predict greater probability of weaning failure in medical-surgical critically ill population.

INTRODUCTION

Weaning process comprises progressive withdrawal from the invasive ventilatory support until removal of the endotracheal tube. It might represent approximately 42% of the duration of mechanical ventilation (MV) (1-3). MV is associated with significant complications that are time-dependent in nature, with a longer duration of intubation resulting in higher incidence of complications, including ventilator-associated pneumonia and increased mortality (4, 5). On the other hand, overly impetuous ventilator withdrawal attempts carry their own hazards. Indeed, a failed extubation is associated with an 8-fold higher odds ratio for nosocomial pneumonia and a 6–12-fold increased mortality risk (6). The clinical challenge then is to balance aggressiveness with safety.

Weaning-induced cardiac dysfunction is recognized as an important cause of weaning failure (7). During SBT, abrupt inspiratory fall in intra-thoracic pressure tends to increase the systemic venous return pressure gradient and to decrease the left ventricular (LV) ejection pressure gradient with a resulting increase in LV filling pressure. A marked increase in work of breathing may increase cardiac work and myocardial oxygen demand (7, 8).

Chest x-ray (CXR) is commonly used to detect pulmonary edema. Radiographic signs that suggest accumulation of fluid in the lung interstitium or alveolar space include vascular redistribution, septal lines (Kerley’s A and B lines), interlobar septal thickening, peribronchial cuffing, bilateral opacities in a ‘batwing’ pattern, air bronchogram and pleural effusion. In pulmonary edema due to heart failure, the heart size is often enlarged (9, 10). Some experts recommend routine checking of chest x-rays (CXR) before submission to spontaneous breathing trial

(SBT) in order to confirm "disease reversal", to discard fluid overload and thus to define eligibility (2, 11-13). However, these criteria have been neither defined nor prospectively evaluated in a randomized controlled trial. Furthermore, CXR accuracy is significantly limited by acquisition techniques and clinical issues that override standardization procedures, especially in the intensive care unit (ICU) (9, 10).

Large clinical trials from 1990s clearly showed that clinicians frequently did not appreciate in a timely fashion that ventilator withdrawal is possible. As most patients were extubated on the same day weaning was initiated (75%), it presumably could have been started earlier. Misconceptions and "slow" weaning procedures were responsible for delaying overall withdrawal process (14, 15).

Shochat *and cols* (16) proposed a radiological score (RS) to evaluate lung fluid content in subjects who developed acute heart failure after acute myocardial infarction. In this prospective single center register, the novel score could assess lung edema severity along with its changes overtime, and it also correlated significantly with clinical status of individuals.

We believed CXR findings of lung edema lack reasonable predictive power to discriminate between SBT-success and SBT-failure individuals; therefore, radiological signs of pulmonary congestion should not delay the decision to initiate SBT. The objective of our study was to assess prospectively whether radiological signs of pulmonary congestion prior to submission to SBT correlated with weaning outcomes in a heterogeneous group of mechanically ventilated subjects.

MATERIALS AND METHODS

Between January 2011 and March 2013, nonconsecutive subjects older than 18 years of age, who had undergone invasive MV for at least 24 hours, were enrolled from a medical-surgical, semiclosed unit in a private hospital, full-time covered by intensivists. Individuals with a tracheostomy were excluded. The research ethic board approved the study and waived the requirement for informed consent. This study was a *post hoc* analysis of a prospective cohort study designed to investigate the potential role of lung ultrasound in predicting weaning outcomes. The research was registered as NCT02022839 at clinicaltrials.gov.

Subjects were assessed daily for eligibility to weaning according to (1) clinical improvement of underlying condition that led to acute respiratory failure; (2) alert and able to communicate; (3) adequate gas exchange, as indicated by a arterial pressure of oxygen of at least 60mmHg with an inspired fraction of oxygen < 0.40; (4) no significant respiratory acidosis; (5) rapid shallow breathing index (RSBI) equal to or less than 105 cycles per minute per liter; and (6) vasoactive drugs at low and stable doses (norepinephrine doses lower than 0.12μg per kilogram per minute or dopamine equivalent doses).

Staff and assistant physicians ordered digital CXRs on a heterogeneous pattern. Confirmation of disease resolution is a typical reason for prescription of CXRs in our center, notably during MV. CXRs were performed in the anterior-posterior view and semi-upright position. For every ready-to-wean subject, a sole attending radiologist was asked for interpret blindly the most recent available radiographic film, usually obtained at the preceding one to 24 hours, according to RS suggested by Shochat (16). Then, staff team, unaware of CXR findings, coordinated ventilator discontinuation through T-piece trial.

Each selected radiological sign of lung congestion was ascribed a predetermined value (table 1) with resulting RS as the sum of sign values, such a way that the larger is the increase in lung fluid content, the higher would be the RS value reflecting this accumulation. Even so, one single adjustment had to be done in RS: abnormal cardiothoracic ratio was considered 60% given semi-upright position of image acquisition (17). Examples of CXRs demonstrating findings of lung edema are presented on figure 1A-B.

Primary outcome in this *post hoc* analysis was SBT failure, defined as inability to tolerate a T-piece trial of spontaneous breathing during 30 to 120 minutes, in which case subjects were not extubated. Breathing trial was interrupted if subject developed signs of respiratory discomfort (respiratory frequency > 35 breaths per minute, arterial oxyhemoglobin saturation < 90%, use of accessory respiratory muscles or paradoxical thoracoabdominal ventilation), tachycardia (heart rate more than 140 beats per minute), hemodynamic instability (systolic blood pressure less than 90mmHg or 20% over basal levels) or change in mental status (drowsiness, coma, anxiety). There were no secondary endpoints for this study.

Demographic data including age, gender, race, comorbidities, severity of illness at the time of ICU admission, reason for the initiation of MV, physiological weaning predictors and fluid balance (total inputs minus total outputs) in the 48 hours preceding SBT were recorded. Presence of diastolic or systolic LV dysfunction (the latter condition defined as ejection fraction < 45%) was documented according to formal echocardiogram report dated up to six months prior to admission. Diagnosis of

COPD was based on history, physical examination, CXR and previous pulmonary function tests, if available.

STATISTICS

Shochat *and cols* (16) observed a mean raise of 4.8 points in RS in individuals who developed overt acute heart failure during hospitalization, whose mean baseline values were 0.6. Hence, our final sample of 170 subjects available for analysis of the primary outcome had 99% power to detect same difference between SBT-success and SBT-failure group, at a two-sided alpha level of 0.05.

Results were expressed as the mean and standard deviation, median and interquartile range, and proportions, as appropriate. The normal distribution of the various parameters was investigated observing the distribution of data and using the Kolmogorov-Smirnov test. We used the Student t test or the Mann-Whitney U test to compare continuous variables, and the $\chi 2$-test or the Fisher exact test to compare proportions, as appropriate. Receiver operating characteristic (ROC) curve was generated based on prediction results of RS and SBT outcomes. Spearman correlation coefficient between fluid balance and RS was also determined. Analyses were performed with the use of SPSS software, version 20.0 (IBM).

RESULTS

We obtained complete data in 170 weaning procedures. Overall, SBT failure occurred in 28 (16.4%). Table 2 shows baseline characteristics of cohort according to outcome. Patients who were successfully extubated had been intubated for a shorter duration (MV median 4 vs 6 days, p= 0.003). One hundred thirty-three patients (78.3%) were extubated at first attempt. Sepsis of any source constituted main reason for initiate MV in approximately 40% of all individuals in both groups. Around 11% of individuals were intubated owing to congestive heart failure and the same amount had pre-existing diagnosis of systolic LV dysfunction.

RS was similar between SBT failure and success subjects (median 3 [2 - 4] vs 3 [2 - 4], p= 0.15), corresponding to interstitial lung congestion. ROC curves analysis demonstrated fail accuracy (area under curve [AUC] = 0.58, p= 0.2) of CXRs prior to T-piece trial for discrimination between SBT failure and success individuals (figure 2). There was no correlation between fluid balance in the 48 hours before SBT and RS (ρ= -0.13, p= 0.1).

DISCUSSION

In a heterogeneous cohort of mechanically ventilated patients candidates to SBT, we found no association between radiological signs of pulmonary congestion indicated by RS and SBT outcomes. Our study suggests that incorporating radiological estimation of lung edema in readiness criteria for MV withdrawal potentially retards it, as long as SBT success ensued in condition of interstitial pulmonary congestion. To the extent of our knowledge, this is the first report encompassing such topic.

Rationale behind hindering SBT due to radiological signs of pulmonary congestion might be the belief that individuals could not pass T-piece trial unless they would be “dry” again, given cardio-respiratory interactions under negative pressure that promote augments both in LV preload and afterload. However, myriad of changes in respiratory mechanics and in cardiovascular system related to weaning failure do not become evident until clinical manifestations of distress, which promptly demand test interruption or reintubation (1). Similarly, weaning indexes have shown inconsistent performance of failure prediction (3, 18). Fluid balance also did not predict SBT outcomes in a slightly larger mixed medical-surgical ICU population, perhaps being more relevant for COPD individuals as we published previously (19). An observational study of one hundred patients immediately before T-piece trial demonstrated that baseline brain natriuretic peptide (BNP) values – a surrogate marker of congestive heart failure - were moderately elevated exclusively in SBT failure individuals whom eventually failed owing to cardiac dysfunction (20). Empirically and unnecessary administration of diuretics in every ready-to-wean patient has become more and more frequent, even though extra-cardiac causes are responsible for weaning failure in at least 50% of cases and roughly 70% of patients are successfully extubated at first attempt (simple weaning). Moreover, uncontrolled diuretic therapy may have potentially harmful effects, such as serious electrolyte disturbances and microatelectasis related to bronchiolar obstruction by dry bronchial secretions (8). A retrospective paper suggesting that chest tube drainage of transudative pleural effusions hastened liberation from MV have been retracted (21).

Indeed, a multicenter randomized trial on computerized weaning provided evidence that physicians are too slow in screening patients for weanability – with the artificial-intelligence-operated ventilator, the delay inherent in diagnostic triggering was bypassed, and there was reduction in duration of MV without increases in reintubation rates (22).

An observer agreement study examined the extent to which intensive care physicians and a radiologist could agree on whether a chest radiograph had diffuse bilateral infiltrates for diagnosis of acute respiratory distress syndrome (ARDS) and concluded that intensivists without formal consensus training can achieve moderate levels of agreement (23). Accordingly, in real clinical practice, expert radiological opinion is not immediately available, and preventing weaning process based upon poor interpretation might be even more questionable. As staff physicians in our study were not aware of most recent CXR images, we were not able to prove the hypothesis mentioned above.

A systematic review (24) highlighted the safety of abandoning routine CXRs in favor of a more restrictive approach. Arguments for adopting a restrictive approach included variable interpretation of CXRs depending on clinician and patient factors, low incidence of clinically unsuspected abnormalities, potential harm arising from unnecessary treatment of minor or false positive findings, cost, radiation exposure and adverse events arising from repositioning of the patient to obtain the CXR (25). Likewise, importance of negative CXR findings on workflow, efficiency, and clinical decision-making may be overestimated. A study collecting the opinions of experienced ICU physicians regarding the appropriateness of performing routine CXRs in various situations encountered in adult ICUs showed there was not a consensus regarding utility of obtaining a routine CXR before extubation (26).

It should be pointed out that our study consisted of relatively small number of patients and absolute number of failure events, high prevalence of elderly patients and low prevalence of systolic LV dysfunction. Nonetheless, our sample had same expected pre-test probability of SBT failure that ordinary, medical-surgical ICU population. Our original study focused on lung ultrasound assessment of ready-to-wean subjects. As a secondary analysis, we did not standardize the moment of CXR acquisition, so not all exams had been performed immediately before SBT but rather within a period of until 24 hours prior to test. At the beginning of this research, limited bedside lung ultrasound expertise as well as lack of any research grant forced us to close enrolment on weekends.

Other limitations also include observational design, with all its intrinsic methodological flaws, and absence of highest numerical scores of radiological signs of lung edema, which might whether imply lesser overall severity or reflect pointlessness in requiring CXR to advance weaning process. Our ready-to-wean population showed modest median values of RS. In the original Shochat paper (16), a RS of 4 or more represented overt acute heart failure in 95% of patients reaching this level. Hence, it seems unlikely an individual presenting a higher RS score to be eligible for SBT.

We decide on SBT failure as principal outcome since we aimed to predict the earliest time that a patient might resume spontaneous breathing. Moreover, the exact reason for extubation failure often escapes identification. Reintubation is usually performed because of an apparently new episode of respiratory distress, which may be related to primary respiratory failure, congestive heart failure, aspiration, ineffective cough with airway secretion build-up, or upper airway obstruction. Other reasons for reintubation include the onset of new sepsis, surgical complications, acute coronary syndrome, and neurological impairment (1).

Radiological score presented by Shochat *and cols* (16) was chosen by virtue of its comprehensive analysis of dynamic changes, good correlation with severity of lung edema, utilization of lung impedance as gold-standard method, and sensitivity for detection of subtle radiological signs of pulmonary congestion. Currently, RS is the only method available proposing quantitative assessment of CXR in terms of lung fluid content. In that cohort, high intra- (κ 0.86, p= 0.0001) and inter-observer correlations (κ 0.82, p= 0.0001) of RS interpretation were found. However, its main drawbacks are lack of assessment in ICU population – although it included patients admitted to a coronary care unit -, unicentric design and absence of large-scale validation. Therefore, for the sake of generability of our findings, RS must be much more explored.

CONCLUSION

In conclusion, since radiological signs of pulmonary congestion demonstrated by RS did not predict greater probability of failed SBT in this medical-surgical critically ill population, we inferred that no CXR reports should be used to preclude hemodynamically stable, sufficiently oxygenated patients from performing an SBT.

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Table 1. Radiological score (RS). Severity of pulmonary edema was determined as follows: RS of 0–1 for a normal chest X-ray (CXR), 2–4 for interstitial lung congestion, and RS values of 5–6, 7–8 and 9–10 signified mild, moderate and severe alveolar edemas, respectively. *See reference 14.*

Roentgenological Sign	Value
Lung vessels redistribution—no	0
Lung vessels redistribution—yes	1
Width of cardiac silhouette (60%)—no	0
Width of cardiac silhouette (□60%)—yes	1
Peribronchial cuffing—no	0
Peribronchial cuffing—yes	1
New pleural effusion—no	0
Unilateral	1
Bilateral	2
Kerley A or/and B or/and C line	
None	0
Uncertain	1
Definite	2
No lung opacity	0
Lung opacity	1
Lung ground-glass opacity	2
Lung batwing edema	3

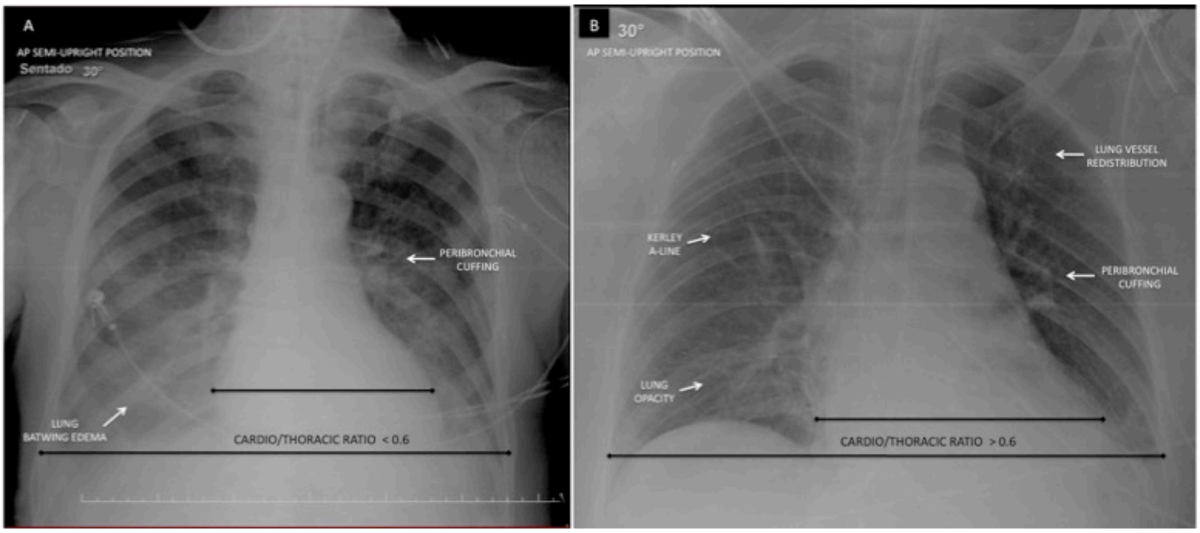


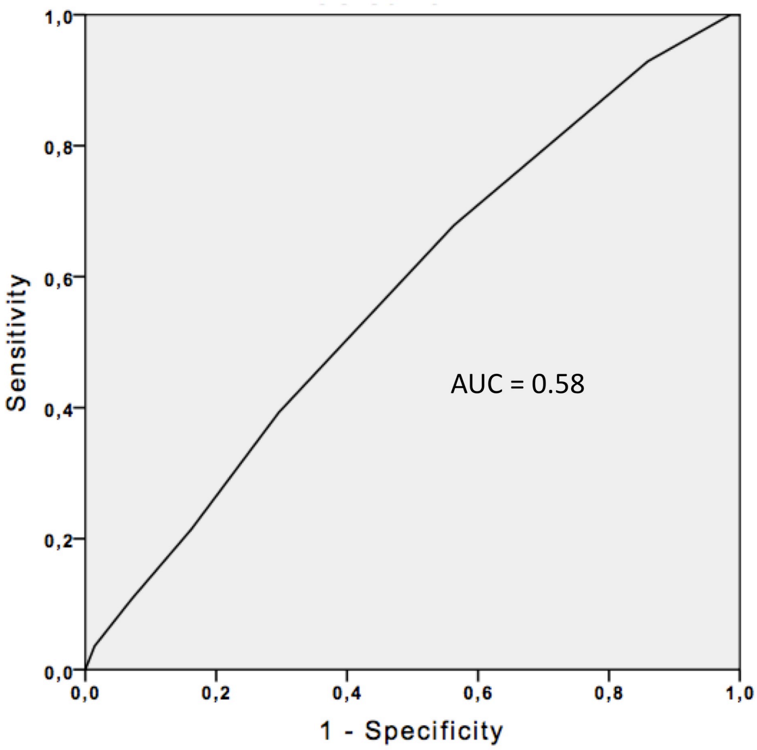
Figure 1. Chest X-ray (CXR) showing peribronchial cuffing and lung batwing edema in a 68-year-old female patient, compounding a radiological score (RS) of 4 (A). CXR exhibiting cardiothoracic ratio higher than 60%, peribronchial cuffing, lung vessel redistribution, Kerley A-line and lung opacity in a 57-year-old male patient, resulting in a RS of 5 (B). According to RS criteria, the former represents interstitial lung congestion, whereas the latter might be characterized as mild alveolar edema (*reference 14*).

Table 2. Characteristics of the study cohort

Patients Characteristics (n = 170)	SBT Success (n= 142)	SBT Failure (n= 28)	*p* Value
Age (years)	76 (66-84)	67 (52-80)	0.15
Female gender (%)	62 (43.7)	13 (46.4)	0.79
APACHE II (points)	21 ± 6.9	23 ± 7.8	0.16
SOFA score (points)	5 (3-9)	5 (2-10)	0.50
BMI (kg/m^2)	25 (23-28)	25 (23-29)	0.97
RSBI (f/VT)	53 (41-75)	52 (36-71)	0.94
MV duration (days)	4 (2-6)	6 (4-11)	0.003
48 hour-fluid balance prior to SBT (mL)	1219 ± 2912	1838 ± 1896	0.48
Co-morbidities			
COPD	14 (9.9)	5 (17.9)	0.32
EF < 45%	15 (10.6)	4 (14.3)	0.52
LV diastolic dysfunction	55 (38.7)	8 (28.6)	0.30
Ischemic coronary disease	28 (19.7)	4 (14.3)	0.50
RRT	23 (16.2)	7 (25.0)	0.28
Presence of ascitis	3 (2.1)	2 (7.1)	0.19
Reason for MV			
Respiratory sepsis	25 (17.6)	6 (21.4)	0.63
Non respiratory sepsis	32 (22.5)	5 (17.9)	0.58
CHF	18 (12.7)	1 (3.6)	0.16
Coma	29 (20.4)	4 (14.3)	0.45
Postoperative ARF	7 (4.9)	2 (7.1)	0.63
COPD/Asthma	2 (1.4)	2 (7.1)	0.13
Pulmonary Embolism	6 (4.2)	1 (3.6)	1.00
ARDS	10 (7.0)	4 (14.3)	0.25
Simple Weaning	108 (76.1)	25 (89.3)	0.27
Vasopressor infusion during T-piece trial	27 (19.0)	4 (14.3)	0.55
Vasodilator infusion during T-piece trial	11 (7.7)	2 (7.1)	1.00

Data are presented as median (interquartile range), mean±SD or n(%).

SBT: spontaneous breathing trial. APACHE II: Acute Physiology and Chronic Health Evaluation II. SOFA: Sequential Organ Failure Assessment. BMI: body mass index. RSBI: rapid shallow breathing index. MV: mechanical ventilation. COPD: chronic obstructive pulmonary disease. EF: Ejection fraction. LV: left ventricular. RRT: renal replacement therapy. CHF: congestive heart failure. ARF: acute respiratory failure. ARDS: acute respiratory distress syndrome.



	SBT success	SBT failure
Radiological Score	3 (2 – 4)	3 (2 – 4)

Figure 2. Receiver operating characteristic (ROC) curve for radiological score (RS) prediction of spontaneous breathing trial (SBT) failure. Area under the curve (AUC) for RS is 0.58 (p= 0.2), meaning poor classification.

8. ARTIGO 4

LUNG ULTRASOUND IS NOT HELPFUL IN DECISION-MAKING PROCESS PRIOR TO SPONTANEOUS BREATHING TRIAL

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The authors have no commercial associations which impact on this work.

Conflict of Interest:

The authors have disclosed no conflicts of interest.

ABSTRACT

Introduction: Lung ultrasound (LUS) is increasingly becoming a diagnostic tool in the critical care setting. B-pattern is an artifact composed by multiple B-lines and correlates with interstitial edema. A randomized controlled trial concluded that bedside thoracic ultrasound could predict post extubation distress through changes in lung aeration during weaning procedure; however, it could not screen patients before submission to spontaneous breathing trial (SBT).

Methods: We conducted a 2-year prospective, multicenter, observational study in two adult medical surgical ICUs in Southern Brazil. All enrolled patients met eligibility criteria for ventilation liberation. Patients with tracheostomy were excluded. LUS was performed immediately before SBT. B-predominance was defined as any profile with anterior bilateral B-pattern. The primary outcome was SBT failure, defined as inability to tolerate a T-piece trial during 30 to 120 minutes, in which case patients were not extubated.

Results: From 2011 to 2013, 250 weaning procedures were evaluated. SBT failure occurred in 51 (20.4%). Patients succeed at SBT and were extubated at first time in 75.9% of cases. B-predominance was a very weak predictor for SBT failure, showing 47% sensitivity, 64% specificity, 25% positive predictive value, and 82% negative predictive value.

Conclusion: B-pattern detected by a simplified LUS protocol should not preclude hemodynamically stable, sufficiently oxygenated patients from performing an SBT.

Keywords: ventilator weaning; pulmonary edema; ultrasonography; clinical decision-making

INTRODUCTION

Liberation from mechanical ventilation remains one of the most challenging aspects of caring for critically ill patients. Although lifesaving as long as needed, prolonged mechanical ventilation is associated with increased morbi-mortality associated with age, the severity of preexisting and current disease processes, and ventilator plus interface (endotracheal or tracheostomy) associated complications (1, 2). Large clinical trials from 1990s clearly showed that clinicians frequently did not appreciate in a timely fashion that ventilator withdrawal is possible. It has been demonstrated that up to 80% of patients can safely abandon ventilatory support immediately (3, 4). Contrasting with successful extubation, failed planned or unplanned extubation was followed by marked clinical deterioration, suggesting a direct and specific effect of extubation failure and reintubation on patient outcomes (5). The clinical challenge then is to balance aggressiveness with safety (6, 7).

Lung ultrasound (LUS) has several advantages over conventional radiological means for assessing lung aeration: it is reliable and accurate, highly reproducible, noninvasive, and easily repeatable at the bedside (8, 9). Probably with the widest implications for weaning management, the simplicity of the technique makes it available to the majority of critical care physicians. Multiple B-lines are considered the sonographic sign of lung interstitial syndrome, the so-called B-pattern (8-10). Presence or absence of B-lines is a useful tool for ruling in or ruling out pulmonary edema and alveolar interstitial syndrome in the acute setting (10, 11) and there is evidence of real time matching of B-line quantity with changes in extravascular lung water and total body water (12-15). Correlation between pulmonary artery occlusion pressure and B-lines in critically ill patients would suggest it is a useful surrogate of left sided filling pressures and has a role in guiding fluid filling and resuscitation (12, 16, 17).

Weaning-induced cardiac dysfunction is recognized as an important cause of weaning failure (18). Switching a patient from positive pressure ventilation to spontaneous breathing reestablishes negative inspiratory intra-thoracic pressure, thus increasing venous return (left ventricular preload), central blood volume, and left ventricular afterload (18, 19). Cabello *et al.* (20) reported that cardiac-related weaning failure occurred in 42 % of cases among 76 difficult-to-wean patients. Spontaneous breathing trial (SBT)–induced increases in extravascular lung water and B-type natriuretic peptide are reliable alternatives to the pulmonary artery catheter for diagnosing weaning-induced pulmonary edema (21).

Soummer *et al.* (22) demonstrated that progressive lung de-recruitment during an SBT may accurately identify patients likely to fail extubation. We previously inspected LUS behavior during SBT (23). Considering B-predominance as any profile with anterior bilateral B-pattern, we reported slightly statistical trend of increasing of B-lines during T-piece trial (p= 0.07) in those individuals who failed SBT and, even though not reaching significance, subjects who were successfully extubated started weaning procedure with lower B-predominance.

In the last 20 years, from physiology to epidemiology, it seems that every imaginable factor with any potential to influence patients' ability to recover spontaneous breathing has been studied, and a large body of sometimes contradictory evidence has led to very different conclusions (24-26). Thus, it is often unclear which factors should be considered in the decision-making process. As far as we know, no study has addressed the potential role of LUS findings in discriminating individuals who are likely to fail to wean, so that either premature unsuccessful trials of spontaneous breathing or undesirable delays could be avoided. Our preceding research (23) lacked sufficient power to detect any significant effects. The objective of the present study was to assess prospectively whether B-pattern at LUS congestion prior to submission to SBT correlated with weaning outcomes in a heterogeneous group of mechanically ventilated subjects.

MATERIALS AND METHODS

Between January 2011 and March 2013, nonconsecutive subjects older than 18 years of age, who had undergone invasive MV for 24 hours, were enrolled from two medical-surgical, semiclosed units in private hospitals in Southern Brazil, full-time covered by intensivists. Individuals with a tracheostomy were excluded. The research ethic board at each center approved the study and waived the requirement for informed consent. The study was registered as NCT02022839 at clinicaltrials.gov.

Patients were assessed daily for eligibility to weaning according to (1) improvement of underlying condition that led to acute respiratory failure; (2) alert and able to communicate; (3) adequate gas exchange, as indicated by a arterial pressure of oxygen of at least 60mmHg with an inspired fraction of oxygen < 0.40; (4) no significant respiratory acidosis; (5) rapid shallow breathing index equal to or less than 105 cycles per minute per liter; and (6) vasoactive drugs at low and stable doses (norepinephrine doses lower than 0.12μg per kilogram per minute or dopamine equivalent doses).

LUS was performed by a trained investigator using a 2- to 4-MHz convex probe as previously described (9, 10, 12, 27). Patients were scanned while in semi-recumbent or supine position, immediately before starting SBT. We divided the anterior surface of thorax into four areas, corresponding to the intercostal spaces between the third and fourth ribs and between the sixth and seventh ribs; the probe was inserted at the center of each, making four points of investigation per lung with dichotomous answer, requiring less than 1 minute (figure 1). Any profile with anterior bilateral B-pattern was denominated B-predominance, which defines interstitial syndrome (9). We did not describe patterns of aeration other than A-line, B-line and C-line – the number of single or confluent B-lines was not reported.

The main outcome of interest was SBT failure, defined as inability to tolerate a T-piece trial of spontaneous breathing during 30 to 120 minutes, in which case subjects were not extubated. Breathing trial was interrupted if patient developed signs of respiratory discomfort (respiratory frequency > 35 breaths per minute, arterial oxyhemoglobin saturation < 90%, use of accessory respiratory muscles or paradoxical thoracoabdominal ventilation), tachycardia (heart rate more than 140 beats per minute), hemodynamic instability (systolic blood pressure less than 90mmHg or 20% over basal levels) or change in mental status (drowsiness, coma, anxiety). There were no secondary endpoints for this study.

Demographic data including age, gender, race, comorbidities, severity of illness at the time of ICU admission, reason for the initiation of mechanical ventilation, physiological weaning predictors and fluid balance (total inputs minus total outputs) in the 48 hours preceding SBT were recorded. Presence of diastolic or systolic LV dysfunction (the latter condition defined as ejection fraction < 45%) was documented according to formal echocardiogram report dated up to six months prior to admission. Diagnosis of COPD was based on history, physical examination, CXR and previous pulmonary function tests, if available.

STATISTICS

Results were expressed as the mean and standard deviation, median and interquartile range, and proportions, as appropriate. The normal distribution of the various parameters was investigated observing the distribution of data and using the Kolmogorov-Smirnov test. We used the Student t test or the Mann-Whitney U test to compare continuous variables, and the χ^2-test or the Fisher exact test to compare proportions, as appropriate. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio of B-predominance for prediction of SBT failure were calculated. A p value <0.05 was taken to be statistically significant. Statistical analysis was performed with SPSS Version 20.0.

RESULTS

We obtained complete data in 250 weaning procedures. Overall, failed SBT occurred in 51 (20.4%). Table 1 shows the baseline characteristics of the study cohort according to outcome. Patients who were successfully extubated were older (median 75 vs 66 years, $p= 0.03$) and had been intubated for a shorter duration (MV median 4 vs 7 days, $p< 0.0001$). There was also a lower prevalence of COPD in SBT success group (19.6 vs 9.5%, $p= 0.04$).

On January 28th 2013, we received 10 patients rescued from Kiss nightclub fire in Santa Maria, Rio Grande do Sul, Brazil. They were between 17 and 23 years old; all had smoke inhalation injury, and six of them failed at T-piece test at least once. By excluding those patients, there would be no statistically difference in age (p= 0.209) between SBT success and failure groups.

B-predominance was observed in 95 cases, but only 24 subsequently failed SBT. Likewise, 27 subjects who did not succeed on SBT had showed no bilateral B-pattern prior to submission to T-piece trial. Therefore, B-predominance finding was a very weak predictor for SBT outcome (table 2).

Contrary to what one might expect, individuals who exhibited B-predominance also had lower fluid balance in the 48 hours prior to weaning procedure (966 [1167.7 – 3050] mL vs 1588 [100 – 3100] mL, p= 0.043). Dispersion of values is shown in figure 2.

DISCUSSION

In a heterogeneous cohort of mechanically ventilated patients candidates to SBT, LUS finding of B-predominance on a simplified four-zone protocol did not have the potential to alter decision to initiate weaning procedure. Our data suggests that incorporating ultrasonographic estimation of lung edema in readiness criteria for MV withdrawal potentially retards it.

Both global and regional assessment of lung de-recruitment provided useful insights into the etiology of the weaning failure in a case report (28). Yet, given the predictable negative physiological effects of pulmonary edema and large pleural effusion on lung mechanics, it is reasonable to consider whether checking for B-predominance might be helpful to optimize the patient's condition before SBT and increase the chances of successful extubation. Nevertheless, in deciding the correct timing of an SBT, LUS should not lower extubation rate at the expense of increased risk of ventilator-associated complications by postponing extubation (1, 2).

Myriad of changes in respiratory mechanics and in cardiovascular system related to weaning failure do not become evident until clinical manifestations of distress, which promptly demand test interruption or reintubation (29). While cardiac function is crucial to the weaning process, it is difficult to estimate real incidence of cardiac-related weaning failure, as increases in respiratory load and cardiac load are strongly interrelated; so it is difficult to identify to what extent a cardiac problem is the cause for the failure (18, 19). Holding SBT up to B-pattern waning, due to belief that individuals could not pass T-piece trial unless they would be "dry" again, has the potential to delaying overall withdrawal process. Fluid balance values did not predict SBT outcomes in a slightly larger mixed medical-surgical ICU population, perhaps being more relevant for selected individuals as we published previously (30). Moreover, a systematic review and metanalysis was unable to identify any evidence to support or refute the use of pleural drainage to promote liberation from MV (31) . Likewise, importance of negative chest x-rays findings on weaning decision-making may be overestimated (32). B-line artefacts may also be affected by other dynamic changes, such as the application of positive end expiratory pressure and the respiratory cycle (33).

One may wonder whether it is really pertinent to predict results of a simple and safe test such as a SBT, rather than performing it. There is no definitive evidence that a carefully monitored, but unsuccessful, trial of spontaneous breathing is detrimental to weaning outcome. To the contrary, in a study of 1067 patients undergoing daily screens, only a single major complication (0.1%) could be possibly attributed to a failed SBT (34). Therefore, in our opinion, there is no real need to perform LUS simply in order to avoid proceeding to SBT in individuals already eligible to it.

While we were still in the process of gathering data for the present study, Soummer *et al.* (22) published their paper demonstrating that LUS predicts extubation failure with some accuracy by identifying global and regional lung de-recruitment. However, the authors could not anticipate 14 failures on 60-minute T-piece trial: LUS score before SBT was not different between groups. The rationale behind this study is that most patients who fail extubation are unable to maintain aeration of the lungs, either because their lungs have a greater tendency to collapse or because their respiratory muscles lack the endurance necessary to optimally expand their lungs. No assumption might be made regarding brain natriuretic peptide levels or transthoracic echocardiography changes predicting postextubation distress.

Correlation between low fluid balance in the 48 hours preceding SBT and B-predominance seems to be completely spurious. There was overlap in a wide range of values. Furthermore, inaccuracies in monitoring and recording fluid therapy in daily practice are a growing issue in intensive care setting, owing to lack of agreement with standardized body weight measurements (35-37). Average daily and cumulative fluid balance were arithmetically incorrect in about one-third of cases (36). We could even question the clinical importance or significance of changes in total body water, as the volume load of specific compartments (intravascular volume, cardiac preload, extravascular lung water) is probably more relevant. Instead, B-pattern indicates an increase in extravascular lung water with an absolute sensitivity (12, 13, 15, 38).

In critically ill patients the assessment can be qualitative, since the ultrasound finding of acute conditions is usually well defined and clear. Also, a more rapid anterior two-region scan may be sufficient to rule out interstitial syndrome in cardiogenic acute pulmonary edema. (9, 10, 27). In a preliminary report (23), we postulated that a simplified approach on four chest anterior zones would be enough for the specific purpose of our study, since B-pattern or consolidation found at lower and posterior lung regions was likely to indicate gravitational changes. Such four-zone protocol has been successfully applied for other purposes elsewhere (10, 13, 16, 39). Indeed, reducing scanning just to four anterior chest zones is aimed to facilitate the initial assessment of this subset of patients through a simple, inexpensive, safe, rapid and easy-to-perform method – i.e. a screening test. Within up to 1 minute of LUS examination, researchers were able to reliably identify B-pattern. The counting approach (22, 40) can be imprecise when considering single scanning sites, has utility as a research tool, but may be overly complicated for the frontline intensivist to use in a busy ICU. No conclusions could be drawn regarding more precise quantification of interstitial syndrome neither different protocols using, for instance, an 8-, 12- or even a 28-zone approach and their relationship to SBT outcomes.

We chose SBT failure as principal outcome since we aimed to predict the earliest time that a patient might resume spontaneous breathing. Furthermore, the exact reason for extubation failure often escapes identification. Reintubation is usually performed because of an apparently new episode of respiratory distress, which may be related to primary respiratory failure, congestive heart failure, aspiration, ineffective cough with airway secretion build-up, or upper airway obstruction. Other reasons for reintubation include the onset of new sepsis, surgical complications, acute coronary syndrome, and neurological impairment. This multiplicity of causative factors contributes to explain the clinical difficulties raised by extubation and the persistent uncertainties about the pathophysiology of extubation failure (29).

Limitations of our study were observational design, with all its intrinsic methodologic flaws, and small sample size. LUS examinations were performed only during working hours. The choice of a convenience sample also limits the interpretation and the generalization of the findings. The prevalence of simple-weaning (75.6%) indicates that our prospective opportunity sample had same expected pre-test probability of SBT failure that any ordinary, medical surgical ICU population (29, 41, 42). Before generalizing the results of the present study, a multicenter randomized interventional study is required to assess the impact of an algorithm based on LUS findings weaning rate, length of stay, and in ICU mortality.

LUS evaluation of pulmonary aeration in the context of weaning from ventilatory support has some limitations. The ultrasound is a surface imaging technique and not a panoramic tool. Lung pathology that is surrounded by aerated lung will not be visible, as aerated lung blocks transmission of ultrasound. Such limitation is seldom relevant in the critically ill patient because diseases characteristic of critical care medicine usually extend to the visceral pleural surface and are therefore visible with ultrasonography (43). Like all techniques of ultrasonography, bedside LUS can be operator-dependent, however, a high intra- and interobserver reproducibility has been reported (40).

CONCLUSION

B-pattern detected by a simplified LUS protocol should not preclude hemodynamically stable, sufficiently oxygenated patients from performing an SBT. Likelihood ratios are not high enough to serve as “stand alone” criteria for clinical decision-making.

Perhaps, LUS may be helpful in defining a mechanism for weaning failure and for guide intervention that may increase the success of the next attempt, particularly when integrated to echocardiography.

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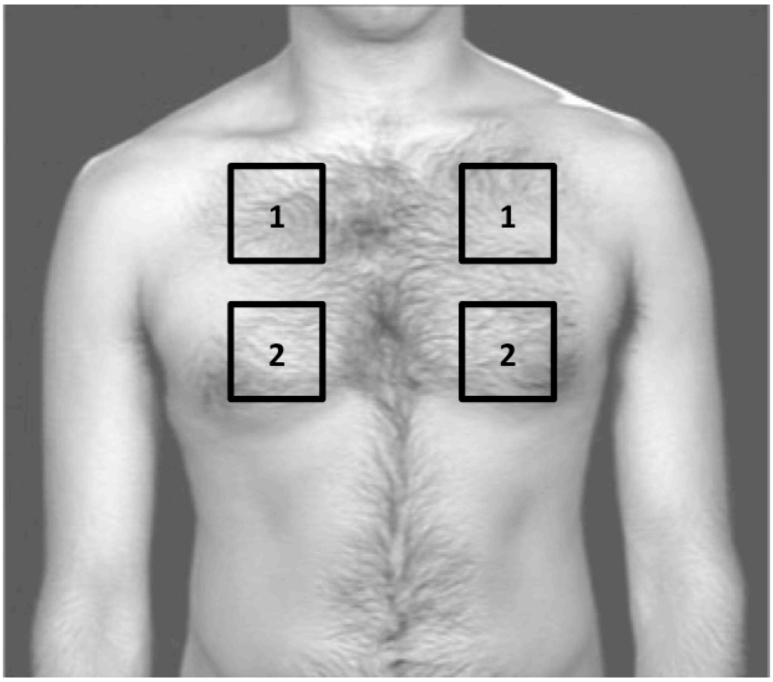

Figure 1. Scheme of the four parasternal views corresponding to the intercostal spaces between the third and fourth ribs and between the sixth and seventh ribs used to investigate B-pattern.

Table 1. Characteristics of the study cohort

Patients Characteristics (n = 250)	SBT Success (n= 199)	SBT Failure (n= 51)	p Value
Age (years)*	75 (60-83)	66 (47-81)	0.03
Female gender (%)	42.2	45.1	0.71
APACHE II (points)	20.8 ± 6.9	21.8 ± 7.8	0.25
SOFA score (points)	5 (3-9)	5 (2-9)	0.9
BMI (kg/m^2)	25 (23-30)	25 (23-29)	0.82
RSBI (f/VT)	58.3 ± 24.3	58.4 ± 24	0.89
MV duration (days)	4 (2-6)	7 (4-11)	<0.001
Co-morbidities			
COPD	19 (9.5)	10 (19.6)	0.04
EF < 45%	19 (9.5)	6 (11.8)	0.64
LV diastolic dysfunction	73 (65.8)	15 (51.7)	0.16
Ischemic coronary disease	36 (18.1)	5 (9.8)	0.15
RRT	34 (17.1)	13 (25.5)	0.17
Presence of ascitis	7 (3.5)	3 (5.9)	0.44
Reason for MV			
Respiratory sepsis	31 (15.6)	9 (17.6)	0.72
Non respiratory sepsis	52 (26.1)	12 (23.5)	0.7
CHF	20 (10.1)	2 (3.9)	0.17
Coma	39 (19.6)	6 (11.8)	0.2
Postoperative ARF	15 (7.5)	4 (7.8)	0.94
COPD/Asthma	2 (1)	2 (3.9)	0.14
Pulmonary Embolism	6 (3)	1 (2)	0.68
ARDS	10 (5)	5 (9.8)	0.2
Smoke inhalation injury*	4 (2)	6 (11.7)	0.006
Simple weaning	151 (75.9)	38 (74.5)	0.61
CXR pleural effusion	60 (30.2)	17 (33.3)	0.66
CXR pulmonary edema	56 (26.6)	18 (35.3)	0.22
Vasopressor infusion during T-piece trial	39 (19.6)	5 (9.8)	0.1
Vasodilator infusion during T-piece trial	13 (6.5)	3 (5.9)	0.87
48 hour-fluid balance prior to T-piece trial (mL)	1324.39 ± 2915.95	1201.65 ± 2801.68	0.52

Data are presented as median (interquartile range), mean±SD or n(%).

**Individuals intubated due to smoke inhalation injury were between 17 and 23 years old and were more likely to fail SBT, explaining imbalanced age between groups. See text for further details.*

SBT: spontaneous breathing trial. APACHE II: Acute Physiology and Chronic Health Evaluation II. SOFA: Sequential Organ Failure Assessment. BMI: body mass index. RSBI: rapid shallow breathing index. MV: mechanical ventilation. COPD: chronic obstructive pulmonary disease. EF: Ejection fraction. LV: left ventricular. RRT: renal replacement therapy. CHF: congestive heart failure. ARF: acute respiratory failure. ARDS: acute respiratory distress syndrome. CXR: chest X-ray.

Table 2. Performance of B-predominance as a screening test for outcome prediction of spontaneous breathing trial

Sensitivity	Specificity	PPV	NPV	PLR	NLR
0.47 (0.33 – 0.61)	0.64 (0.57 - 0.70)	0.25 (0.17 - 0.35)	0.82 (0.75 - 0.88)	1.32 (0.93 - 1.86)	0.82 (0.63 - 1.07)

Data are expressed as estimated value (95% confidence interval)

PPV: positive predictive value. NPV: negative predictive value. PLR: positive likelihood ratio. NLR: negative likelihood ratio

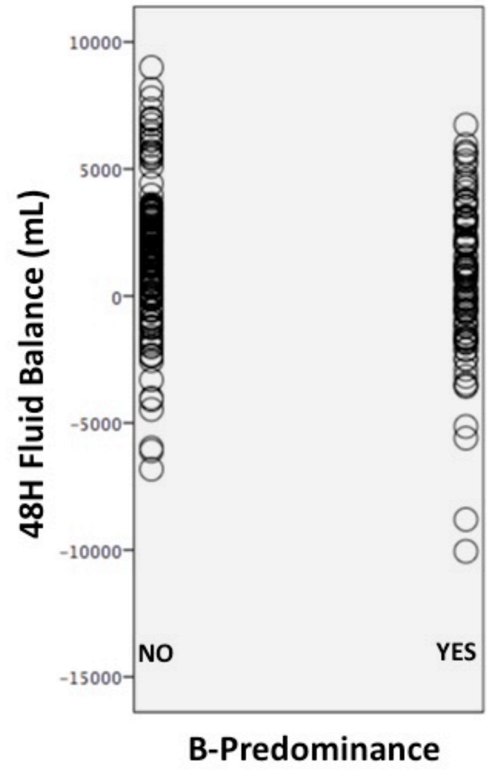

Figure 2. Range of values of fluid balance in the preceding 48 hours of spontaneous breathing trial (SBT) according to finding of B-predominance on lung ultrasound (LUS). Median value of fluid balance was statistically significant lower in the B-predominance group, though showing a wide range of values (966 [1167.7 – 3050] mL vs 1588 [100 – 3100] mL, p= 0.043).

9. CONCLUSÕES

- Alterações de pré e pós-carga cardíaca, precipitadas pela redução abrupta da pressão intratorácica quando do TRE, causam aumento de água pulmonar extravascular. O dinamismo desta repercussão foi evidenciado pela ultrassonografia pulmonar à beira do leito em curto espaço de tempo, traduzindo-se pelo surgimento de predominância de padrão B, ou seja, síndrome intersticial. Observou-se prevalência de padrão B bilateralmente maior que 50% nas zonas pulmonares 3, 4, 5 e 6 quando os pacientes ainda se encontravam em VM. Presumivelmente, esse achado corresponde a alterações gravitacionais, aliadas à reposição volêmica a que tais pacientes estão expostos cumulativamente ao longo de vários dias de permanência dentro da UTI.
- Muito embora o grupo de pacientes que apresentou falha ao TRE tenha demonstrado maior prevalência de predominância B ao final do teste, não foi possível antever a falha através da ultrassonografia pulmonar, isto é, antes que sinais e sintomas clínicos de insuficiência respiratória indicassem a interrupção do procedimento. Também não foi possível reproduzir achados de um estudo observacional anterior que correlacionou perda de aeração pulmonar ao final do TRE a e falha de extubação dentro de 48 horas. Tanto o protocolo simplificado, a avaliação não quantitativa e o pequeno tamanho amostral podem estar implicados. Adicionalmente, a heterogeneidade dos motivos que levaram à reintubação pode ter prejudicado a suposta correlação: não raro a VM foi reinstituída em função do surgimento de novos eventos, tais

como acidente vascular isquêmico, sepse nosocomial, tosse ineficaz ou necessidade de intervenção cirúrgica.

- O desempenho global da ultrassonografia pulmonar para predizer falha no TRE foi muito fraco, demonstrando sensibilidade, especificidade, valor preditivo positivo e valor preditivo negativo de apenas 47%, 64%, 25% e 82%, respectivamente. O valor de somente 1,32 para razão de verossimilhança positiva significa que o achado de síndrome intersticial ou predominância B à ultrassonografia pulmonar em um paciente candidato ao desmame não eleva sua probabilidade pós-teste de falha a patamares suficientemente discriminativos e, portanto, não deve representar uma contraindicação para o TRE.
- Não obstante algumas diretrizes de especialistas recomendem buscar BH negativo e considerar a radiografia de tórax na avaliação de elegibilidade para o desmame, tais variáveis mostraram influência nula no desempenho desta amostra de doentes críticos clínico-cirúrgicos ordinários. Especula-se que pacientes portadores de DPOC, todavia, possam obter alguma vantagem com o BH negativo – um estudo com maior poder amostral é necessário para confirmar ou refutar tal hipótese. BH e presença de síndrome intersticial (predominância B) apresentaram associação inversa. Supõe-se que esse resultado seja espúrio dada a consistente relação demonstrada entre síndrome intersticial identificada pela ultrassonografia pulmonar e conteúdo de água pulmonar extravascular, o que ratifica conclusões de estudos anteriores que levantaram inúmeros problemas pela utilização do BH na prática diária.

- O emprego de um protocolo ultrassonográfico simplificado, de fácil e rápida aplicação, foi capaz de evidenciar as alterações de interação coração-pulmão supracitadas.

10. CONSIDERAÇÕES FINAIS

O presente estudo foi conduzido com o intuito de ser pragmático, reproduzindo o mais fielmente possível o dia a dia dentro da UTI. Assim, empregou-se uma ferramenta inovadora, de crescente utilização, aplicada a uma amostra de pacientes com apenas um critério de exclusão. A simplificação do protocolo ocorreu justamente para que qualquer intensivista com um mínimo de treinamento e conhecimento teórico consiga colocá-lo em prática.

Dentro das tendências mundiais de "*Choosing wisely*" e "*Less is more*", considera-se que resultados negativos também sejam de grande valia para a construção do conhecimento. Nos últimos anos surgiram citações do quanto o emprego sistemático da ultrassonografia à beira do leito elevou o número de diagnósticos e tratamentos, sem ter sido observado qualquer incremento na qualidade assistencial. Antes de criticar esta tecnologia, é preciso considerar de que maneira a mesma vem sendo aplicada. Assim, a administração sistemática de diuréticos a todo paciente apto para o desmame mas com achado de predominância B à ultrassonografia, por exemplo, pode apenas agregar paraefeitos e aumentar o tempo de VM.

Ao término da coleta e análise desses dados, naturalmente muitas incertezas ainda restam. Se a ultrassonografia pulmonar não auxilia na melhor eleição de pacientes gerais para o TRE, o mesmo não se pode afirmar com relação aos indivíduos classificados como desmame difícil ou prolongado, os quais classicamente requerem maior número de intervenções para o sucesso do desmame. Para esse grupo, já se levanta hipótese de que um TRE mais prolongado, ao menos maior que 30 minutos, seja mais apropriado na avaliação de sua capacidade de se manter livre de

VM. Planeja-se um ensaio clínico randomizado testando-se diferentes durações do teste T para pacientes portadores de desmame difícil e prolongado, e novamente será avaliado o desempenho da ultrassonografia pulmonar para predizer falha.