UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
FACULDADE DE MEDICINA

Fabiane Affonso Pinheiro

Impacto do *Diabetes Mellitus* Gestacional na funcionalidade dos músculos do assoalho pélvico avaliada pelo US-3D durante a gestação e após o parto

Impact of Gestational Diabetes Mellitus on pelvic floor muscles functionality assessed by 3D-US during pregnancy and long-term postpartum

Tese apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Campus de Botucatu, para obtenção do título de Doutora em Tocoginecologia.

Orientadora: Prof.ª Dra. Angélica Mércia Pascon Barbosa

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Botucatu, 23 de agosto de 2021

Dedicatórias

A **Deus**, o meu grande mestre, autor da minha fé e maior exemplo de amor. Obrigada por enxergar tua grandeza em minha pequenez e pelo teu olhar sempre me acompanhar nessa etapa tão importante. Reconheço que minha história é nada sem o seu amor. Gratidão pelos milagres de todos os dias, pela sua ternura nos momentos difíceis e por suas mãos me sustentarem de pé.

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.

Epígrafe

“Não se inquiete por não ter a resposta da pergunta de hoje. Embora a tenha nascido agora, ela foi construída ao longo da vida. Ela é resultado de vivências, perdas, ganhos, demoras e esperas. Portanto, não se apresse com a resolução. Quem nos mantêm vivos não são as respostas, são as perguntas”

Padre Fábio de Melo

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Lista de abreviações em Português

CEP	Comitê de Ética em Pesquisa
CIDPN	Centro de Investigação do Diabete Perinatal
DM	diabetes mellitus
DMAP	disfunção muscular do assoalho pélvico
DMG	*diabetes mellitus* gestacional
Dra.	doutora
FAPESP	Fundação de Amparo à Pesquisa do Estado de São Paulo
FFC	Faculdade de Filosofia e Ciências
FMB	Faculdade de Medicina de Botucatu
GJ	glicemia de jejum
HL	hiato do levantador
IU	incontinência urinária
IU-EG	incontinência urinária específica da gestação
MAP	músculos do assoalho pélvico
MGH	miopatia hiperglicêmica gestacional
MLA	músculo levantador do ânus
MRA	músculos reto abdominais
Prof.ª	professora
TOTG	teste oral de tolerância à glicose
UNESP	Universidade Estadual Paulista
UNIMAR	Universidade de Marília
US-3D	ultrassonografia tridimensional
US-3DTP	ultrassom tridimensional transperineal

Lista de abreviações em Inglês

%	percentage
3D-TPUS	three- dimension transperineal ultrasound
3D-US	three-dimension ultrasonographic
A1	activity 1
A2	activity 2
AI	anal incontinence
ADA	American Diabetes Association
BMI	body mass index
C	contraction
C1	contraction 1
CI	contractility index
CI1	contractility index 1
cm	centimeter
cm^2	square centimeter
D	distension
D1	distension 1
DI	distensibility index
DI1	distensibility index 1
DM	diabetes mellitus
GDM	Gestational Diabetes Mellitus
GE	General Electric
ICS	International Continence Society
IUGA	International Urogynecological Association
kg	kilograms
LH	levator hiatal
LHarea	Levator hiatal area
M	mobility
M	meter
MHz	megahertz
MI	mobility index
Max	maximum
Min	minimum

OAB	overactive bladder syndrome
OGTT	glucose tolerance test
PDRC	Perinatal Diabetes Research Center
PCR	Perinatal Research Center
PFM	pelvic floor muscles
PFMD	pelvic floor muscle dysfunction
POP	pelvic organ prolapse
PS-UI	pregnancy specific-urinary incontinence
R	rest
R1	rest 1
R_1	rest post-contraction
R_2	rest post-distension
Rb	basal rest
SD	Standard Deviation
SUI	stress urinary incontinence
3D-TPUS	Three-dimensional transperineal ultrasound
UI	urinary incontinence
US	ultrasonographic
US	ultrasound

Sumário

Seção 1

Trajetória Acadêmica

No ano de 1994 iniciei a minha formação acadêmica, ingressando no curso de Fisioterapia pela Universidade de Marília (UNIMAR). Foram 4 anos de dedicação intensa, amadurecimento, e quando tive a certeza que ser Fisioterapeuta tinha sido a minha melhor escolha profissional.

Terminada a graduação, me tornei servidora da Prefeitura Municipal de Assis-SP e desde então venho atuando e adquirindo experiência em diversas áreas da fisioterapia. Entretanto, em 2015, minha amiga e parceira profissional, Prof.ª Dra. Angélica Barbosa (Faculdade de Filosofia e Ciências - FFC – Unesp / Marília – SP), me apresentou a fisioterapia na saúde da mulher, a qual me envolveu inteiramente.

Naquele mesmo ano integrei o grupo de pesquisa “Diabete e Gravidez - Clínico e Experimental” (Faculdade de Medicina de Botucatu - FMB – Unesp), liderado pela Prof.ª Marilza Rudge, e em 2017 obtive o título de Mestra em Ginecologia, Obstetrícia e Mastologia, com a dissertação intitulada: “Ultrassonografia tridimensional da funcionalidade dos músculos do assoalho pélvico de gestantes com diabete melito gestacional”. Tal titulação foi obtida junto ao Programa de Pós-Graduação em Ginecologia, Obstetrícia e Mastologia, atualmente denominado Programa de Pós-Graduação em Tocoginecologia (FMB - Unesp). Paralelamente ao mestrado, finalizei a especialização em Fisioterapia Pélvica - Uroginecologia Funcional pela Faculdade Inspirar (Paraná, Brasil) (Anexo 1), e considero que esses dois títulos foram essenciais para o impulso e continuidade da minha jornada acadêmica.

Em 2017 iniciei o Doutorado e também as atividades de pesquisa financiadas pelo Projeto Temático Fapesp DIAMATER, “*The Diamater Study Group*”, das quais tive o prazer de trabalhar com equipe multidisciplinar e totalmente dedicada a pesquisa. Iniciei o doutorado tendo a Prof.ª Titular Marilza Rudge como orientadora e no final de 2019, transferimos a orientação para Prof.ª Dra. Angélica Barbosa, ocasião que foi credenciada no programa como professora permanente. Ao longo desses 4 anos tenho dado

seguimento ao meu projeto e tive a oportunidade de participar de 5 eventos internacionais, sendo que no 2nd *World Congress on Gynecology & Obstetrics* (Anexo 2), participei como mediadora de *Plenary Forum* e apresentei o trabalho intitulado "*Impact of Gestational Diabetes Mellitus on Pelvic Floor Muscle Contraction: Three-Dimensional Ultrasound*".

Ampliei meus conhecimentos ao realizar 17 cursos complementares, com destaque para 6 deles (Anexo 3), o "*International workshop: 3D ultrasound of female pelvic floor and rectus abdominis muscle*", ministrado pela professora e colaboradora do nosso grupo DIAMATER, PhD Baerbel Junginger (Charitè Universitätsmedizin Berlin, Alemanha); "Exercícios para incontinência urinária por esforço – prática clínica baseada em evidência" oferecido pelo Instituto Cinesioterapia Pélvica Integrada; "*Upgrade* em incontinência urinárias, prolapsos e *hands on* em anatomia", promovido pela Universidade de Campinas e pela Associação Latino Americana do Piso Pélvico; além dos cursos "Exercícios na gestação: da prevenção ao tratamento de disfunções musculoesqueléticas" e "Atuação do fisioterapeuta na preparação do assoalho pélvico para o parto e no trabalho de parto", oferecidos pela Sabrina Baracho – Fisioterapia na Saúde da Mulher. Em 2020 cursei a Formação em Fisioterapia na Função Miccional Feminina: da Evidência Científica a Prática Clínica (Instituto Patrícia Lordêlo).

Foi possível colaborar e ser autora de 9 artigos em periódicos (Anexo 4) de alto impacto e ter 1 artigo desta tese submetido na revista PLOS ONE (Anexo 5). Colaborei em 13 resumos publicados em anais de congressos (Anexo 6). Participei como membro de 4 bancas examinadoras de Trabalhos de Conclusão de Curso (Anexo 7), de graduandas do curso de Fisioterapia da FFC – Unesp / Marília. Em 2019 participei de Edital de Seleção pública para função docente na Fundação Educacional do Municipal de Assis, tendo sido aprovada em 2º lugar na seleção (Anexo 8).

Agradeço imensamente a Deus por mais essa etapa que está se finalizando e também de maneira especial a minha querida amiga Prof.ª Dra. Angélica Barbosa que caminhou comigo até aqui. Os desafios e adversidades são grandes, mas o crescimento profissional e pessoal muito maior. Que eu continue movida na busca pelo conhecimento…sempre!!!!

Seção 2

Contextualização

Avanços do conhecimento sobre o impacto do *Diabetes Mellitus* Gestacional nos Músculos do Assoalho Pélvico

Investigações sobre a tríade *Diabetes Mellitus Gestacional* (DMG), miopatia diabética e incontinência urinária e seus biomarcadores, são realizadas pelo *Grupo de pesquisa Diabete e Gravidez: Clínico e experimental,* desde 2006. O DMG, definido como hiperglicemia identificada pela primeira vez na gravidez(1), mesmo tratado de acordo com padrões internacionais da *American Diabetes Association*(1) institucionalizado no Centro de Investigação do Diabete Perinatal (CIDPN) não foi suficiente para evitar o efeito deletério da hiperglicemia gestacional controlada sobre a Incontinência Urinária Específica da Gestação (IU-EG) e disfunção muscular do assoalho pélvico (DMAP)(2). A procura de marcadores dessa miopatia caracteriza o Projeto Temático (2016/01743-5). O *Conceptual Model* (3), estabelecido da integração entre DMG, IU-EG e miopatia hiperglicêmica tem a funcionalidade dos músculos do assoalho pélvico (MAP) e músculos reto abdominais (MRA) como variáveis moderadoras e precisa ser investigado.

Recomenda-se investigar todas as mulheres, com ou sem fatores de risco, por avaliação dos níveis de glicemia de jejum (GJ) antes da 20ª semana e as que apresentaram GJ elevada no início da gestação pelo Teste Oral de Tolerância à Glicose (TOTG) com sobrecarga de 75g, entre 24-28 semanas gestacional. Prévio a 20ª semana gestacional, o DMG é diagnosticado por GJ ≥ 92 mg/dL e < 126 mg/dL e o DM na gestação por GJ ≥ 126 mg/dL. O diagnóstico do DMG realizado entre a 24ª e 28ª semana, é definido pelos limites do TOTG-75g ou glicose de 1h pós-sobrecarga ≥ 180 mg/dL ou glicose de 2h ≥ 153 mg/dL e < 200 mg/dL(4–6).

O DMG está associado a repercussões maternas, fetais, neonatais e perinatais negativas com maior frequência, quando comparado à gestação normoglicêmica(7). Sua incidência, oscila entre 3 e 7%, e é a complicação médica de maior ocorrência na

gestação(8). O DMG mostrou-se relacionado à deterioração da função muscular fisiológica(8,9), o que denota a existência de conexão entre o metabolismo e a função mecânica dos músculos(7,8,10).

Resultados do CIDPN confirmaram prevalência aumentada da DMAP nas gestantes com DMG(11,12) e dois anos após a cesárea, definindo clara associação entre DMG e DMAP(2,13,14). Na mesma linha, a pesquisa translacional, usando modelos de hiperglicemia leve (induzida ao nascimento) e severa (induzida na prenhez) em ratas *Wistar*, evidenciou interação entre hiperglicemia e alterações morfológicas e estruturais da musculatura estriada periuretral e reto abdominal(15–18).

Os estudos com modelo animal reforçam o achado clínico de alterações musculares, demonstrando que ratas prenhes com diabete moderado (glicemia entre 120 e 300mg/dl) apresentam alterações similares ao diabete grave(17) na Matriz Extracelular e no músculo estriado uretral, como: atrofia, adelgaçamento, aumento de colágeno na área de músculo estriado, aumento de vasos, acúmulo de mitocôndrias, além de gotas de lipídios e grânulos de glicogênio presentes em grande quantidade, colocalização das fibras rápidas e lentas, diminuição de fibras rápidas e a presença de fibrose/deposição de fibras de colágeno, associados com atrofia muscular(6,16).

A remodelação uretral do tecido conjuntivo com perfil de glicosaminoglicanos e organização de fibrilas de colágeno constituíram a primeira linha de evidência entre+ hiperglicemia e lesão do sistema fibromuscular uretral, possivelmente, relacionada à DMAP em gestantes com hiperglicemia(15–18). Isto trouxe reflexões sobre potenciais implicações clínicas e respectivas estratégias terapêuticas na atenção à saúde dessas mulheres.

Estes resultados clínicos e experimentais demonstraram intrínseca relação do binômio DMG e MAP. Os MAP representam elemento crítico de ação no suporte dos órgãos pélvicos como bexiga, útero e junção uretrovesical no mecanismo de fechamento

esfincteriano uretral e anal e na mobilidade do canal vaginal(19–25) e consequente boa qualidade de vida relacionada a estes aspectos(19,21–23).

A contração coordenada e eficaz dos MAP (26) está relacionada à manutenção das funções de micção, evacuação e sexualidade. Por outro lado, MAP disfuncionais podem resultar em sintomas como micção ou defecação prejudicada, dor pélvica e disfunção sexual(27). Além disso, a adequada distensão dos MAP pode favorecer o parto e provavelmente reduzir a incidência de lesões dos músculos elevadores do ânus(28).

A integridade dos MAP pode sofrer alterações tanto anatômicas quanto fisiológicas, nas diferentes fases da vida da mulher, associadas com obesidade e menopausa, mas especificamente na gestação e parto, e sendo mais evidentes na gestação complicada pelo diabetes(2,14,29–31). Mecanicamente, as causas da DMAP tem duas vertentes, alargamento do hiato do levantador e descida do assoalho pélvico abaixo da linha pubococcigeal, sendo a consequência mais comum a incontinência urinária (IU)(32).

Com o objetivo de aprofundar a investigação e identificação de biomarcadores do DMG, miopatia diabética e IU-EG, nos aspectos morfológicos, clínicos, metabólicos, genéticos, imunológicos, moleculares e funcionais, o grupo de pesquisa "Diabetes e gravidez - clínico e experimental" da FMB, em 2017, obteve aprovação do Projeto Temático DIAMATER (Processo Fapesp: 2016/01743-5).: “Coorte prospectiva da tríade hiperglicemia gestacional, “incontinência urinária específica da gestação” e perfil (morfológico, funcional, bioquímico, molecular e ômico) da “miopatia hiperglicêmica gestacional (MHG)” como preditora da incontinência urinária e disfunção muscular do assoalho pélvico (DMAP) 6-12 meses pós-parto; e pesquisa translacional do impacto do *biodevice* de látex de seringueira com células tronco mesenquimais na regeneração muscular pós-parto de ratas diabéticas”.

Resultados clínicos da avaliação dos MAP provenientes do Diamater

demonstraram que na evolução da gestação entre 24-30 e 36-40 semanas, avaliada pela eletromiografia, o grupo DMG apresetnou recrutamento menor dos MAP em relação ao grupo não-DMG, denotando diminuição da atividade elétrica em repouso (p=0,042) e na contração tônica (p=0,044) (33). Estudos que avaliaram a morfologia e a funcionalidade dos MAP pela ultrassonografia tridimensional (US-3D)(34) demonstraram, em avaliação realizada no mesmo intervalo gestacional que as medidas biométricas da morfologia foram diferentes em repouso para o grupo com DMG em relação ao grupo sem DMG, e também alteração na funcionalidade, com menor contratilidade, distensibilidade e mobilidade(35).

Com base nesses fatos, a avaliação da funcionalidade dos MAP é recomendada pela *International Continence Society* (ICS) e *International Urogynecological Association* (IUGA)(36), e pode ser realizada por diversos métodos, incluindo ultrassonografia (US) transperineal(37). O mais importante é que a avaliação dos MAP deve incluir a avaliação da função dos MAP tanto em repouso quanto durante atividades dinâmicas, como contração e distensão(38).

A US é exame realizado com segurança durante a gestação, por não apresentar risco de radiação ou toxicidade por contraste(39–43), e permite o acesso ao plano axial, com a técnica transperineal 3D(44,45), captando imagens diretas da área hiatal do músculo levantador do ânus (MLA)(39–43)(Figura 3). A US-3D é exame universal para avaliar em tempo real(45) a funcionalidade dos MAP, considerando as medidas dos diâmetros do hiato do levantador (HL), durante o repouso, contração e distensão (manobra de Valsalva)(46–55).

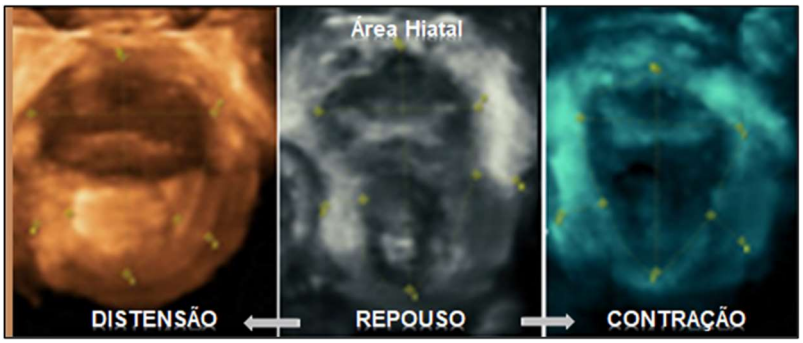

Figure 1 – Imagens da área hiatal do MLA durante repouso, contração e distensão(35).

O MLA é termo usado para descrever os principais MAP e os responsáveis pela continência urinária(23,56). É formado pelos músculos estriados, pubococcígeo, puborretal e ileococcígeo, apresenta forma laminar e preenche o espaço entre o músculo obturador interno lateralmente, o púbis anteriormente e o cóccix posteriormente(44,51). A uretra, a vagina e o canal anal atravessam o MLA(46,57).

A área do HL é delimitada anteriormente pelo púbis e lateral e posteriormente pelo MLA. As medidas da US-3D mais consistentes são obtidas pelo plano definido pela margem inferior da sínfise púbica e o bordo interior do músculo puborretal, na junção anorretal(49).

Durante a evolução da gestação normoglicêmica, aumento de todas as dimensões hiatais tem sido encontrado por meio da US-3D. Esse achado indica que as mudanças nos MAP não são somente decorrentes do parto, mas também de alterações fisiológicas e funcionais(51–56,58,59) durante a gestação(60,61). Esse aumento da distensibilidade do HL pode ter papel no desenvolvimento de DMAP a longo prazo, na vida da mulher.(61)

O conhecimento sobre o impacto do DMG nos MAP durante a gestação tem sido demonstrado pela US-3D, e foi tema da dissertação de mestrado de Fabiane Affonso Pinheiro em 2017(35), contudo a associação direta entre DMG e DMAP ao longo da gestação com acompanhamento após o parto não está totalmente esclarecida. A experiência do Grupo Diamater em avaliar a funcionalidade dos MAP pela US-3D, levou a análise crítica sobre a importância de incluir no protocolo dinâmico de avaliação,

medidas de repouso entre cada atividade dinâmica realizada. Outro aspecto discutido foi a necessidade, de desenvolver fórmulas para serem aplicadas as medidas adquiridas deste protocolo, que fornecessem resultados com os valores absolutos e em índices tanto em valores absolutos quanto em diferença percentual. Desta forma medidas mais fidedignas em relação a funcionalidade podem ser obtidas, incluindo o relaxamento, contratilidade, distensibilidade e mobilidade dos MAP.

Até o momento, nenhum estudo foi encontrado que demonstram proposta para avaliar o desempenho dos MAP com dinâmica e forma sequencial das suas diferentes atividades, bem como com as medidas de descanso intermediários entre todas estas atividades realizadas e fórmulas específicas para sua interpretação. Nesse contexto, analisar o desempenho dos MAP com medidas ultrassonográficas confiáveis, objetivas, visíveis e em tempo real é método alternativo para orientar a prática clínica e científica na avaliação e nos cuidados preventivos e terapêuticos.

A presente Tese inédita integra e se propõe responder perguntas previstas nos objetivos do Projeto Temático Diamater", segue a linha da dissertação desenvolvida pela mesma pós-graduanda e agora com proposta de acompanhamento das gestantes à longo prazo. Tem aprovação do Comitê de Ética em Pesquisa (CEP) para seu desenvolvimento no projeto "guarda-chuva" CAAE: 82225617.0.0000.5411 (Anexo 9). Os objetivos à saber, são: 1) desenvolver estudo de coorte prospectiva das repercussões do DMG na funcionalidade dos MAP avaliada pela US-3D durante a gestação e após o parto; 2) desenvolver protocolo dinâmico de avaliação dos MAP por US transperineal e, 3) interpretar o desempenho dos MAP de gestantes com ou sem IU-EG aplicando diferentes análises pelo PFM-US Diamater's Protocol.

Os resultados desta Tese, estão apresentados em 3 artigos de acordo o respectivo objetivo:

1 - *Pelvic floor muscle dysfunction detected by 3D-US in women with GDM in the third trimester remains in long-term postpartum*

2 - *Dynamic Protocol for Pelvic Floor Muscles Assessment by Transperineal Ultrasound: A New Approach of the Diamater Study Group*

3 - Distinct interpretations of pelvic floor muscle performance assessed through the PFM-US Diamater´s Protocol in pregnant women with and without pregnancy-specific urinary incontinence

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Seção 3

Resumos Expandidos

Resumo da Tese

Pinheiro, F. A. Impacto do *Diabetes Mellitus* Gestacional na funcionalidade dos músculos do assoalho pélvico avaliada pelo US-3D durante a gestação e após o parto 2021. 172f. Tese (Doutorado) – Faculdade de Medicina de Botucatu, Universidade Estadual Paulista, Brasil.

Introdução: Os músculos do assoalho pélvico (MAP) representam elemento fundamental no suporte dos órgãos pélvicos, fornecendo suporte ativo tanto em repouso quanto durante a atividade. A contração coordenada e eficaz da MAP está relacionada à manutenção das funções de micção, evacuação e função sexual. Além disso, distensão adequada dos MAP pode favorecer o parto e provavelmente reduzirá a incidência de lesões nos músculos elevadores do ânus. A disfunção dos músculos do assoalho pélvico (DMAP) é distúrbio que afeta tanto a capacidade de contrair, distender, relaxar, controlar e coordenar os MAP, e está associada a sintomas como à incontinência urinária (IU), incontinência urinária de esforço, síndrome da bexiga hiperativa, prolapso de órgão pélvico, incontinência anal, dor pélvica, disfunção sexual, constipação e resulta em impacto negativo na qualidade de vida. Estudos de pesquisa associaram o *Diabetes Mellitus* Gestacional (DMG) com a DMAP. O DMG é definido como distúrbio de tolerância à glicose com início durante a gravidez e é cada vez mais comum em mulheres, afetando aproximadamente 8,3% das gestações em todo o mundo. A interação entre gravidez e DMG impacta na saúde materna precoce e de longo prazo. O DMG está associado a miopatia diabética, que se refere a alterações funcionais, metabólicas e estruturais que são induzidas pelo *diabetes mellitus* (DM) no músculo esquelético. Estudos clínicos demonstraram que o DMG impacta negativamente na atividade eletromiográfica dos MAP ao longo da gestação e, além disso, também altera a morfologia das estruturas dos MAP quando avaliada pela ultrassonografia tridimensional (US-3D). A DMAP em mulheres com DMG mostrou-se fator de risco independente para Incontinência Urinária Específica na Gestação (IU-EG) e fator de risco para IU dois anos após parto cesárea. Lesão que acomete o músculo reto abdominal durante a gestação também foi relacionada ao DMG. Estudos translacionais mostraram impactos prejudiciais tanto de hiperglicemia leve de longo prazo quanto de hiperglicemia severa de curto prazo no músculo de ratas grávidas uretrais como atrofia, adelgaçamento, desorganização, ruptura das fibras musculares e perda de tipos específicos de fibras de localizações anatômicas normais, denotando conexão entre os níveis de glicemia níveis e estrutura do MAP. Recentemente, protocolo de estudo clínico estabeleceu pesquisa de

biomarcador bem desenvolvida em novo modelo conceitual do papel da integração da tríade DMG, IU-EG e miopatia hiperglicêmica como preditora de IU de longo prazo e DMAP. A avaliação do desempenho dos MAP é recomendada pela *International Continence Society* e *International Urogynecological Association*, e pode ser realizada por ultrassonografia (US) transperineal. A avaliação deve incluir o desempenho dos MAP em repouso e em atividades dinâmicas, como contração e distensão. A ultrassonografia tem sido relatada como método simples, não invasivo, de fácil execução e amplamente utilizado na prática clínica obstétrica como ferramenta de avaliação dos MAP. A técnica é de acesso fácil, sem radiação, desconforto mínimo, tem boa confiabilidade interobservador e interdisciplinar e permite avaliação dinâmica. **Justificativa:** Aprofundar e preencher lacunas do conhecimento sobre a repercussão do DMG e da miopatia diabética na gestação e a longo prazo. Não foram encontrados estudos que investigassem e avaliassem a funcionalidade dos MAP com US-3D durante a gravidez e acompanhamento no pós-parto de longo prazo, de gestantes expostas ao DMG. Também não foram encontrados estudos com proposta de avaliação do desempenho das atividades dos MAP (relaxamento, contração e distensão) de forma dinâmica e sequencial, assim como medidas de repouso intermediárias entre todas essas atividades realizadas e, fórmulas específicas para sua interpretação. Nesse contexto, analisar o desempenho da função dos MAP com medidas ultrassonográficas em tempo real é método dinâmico, valioso, objetivo e alternativo para orientar a prática clínica e científica nos cuidados preventivos e terapêuticos. **Objetivos: 1)** Analisar o efeito do DMG na funcionalidade dos MAP em dois momentos da gestação e no pós-parto avaliados pela US-3D. **2)** Desenvolver modelo dinâmico ultrassonográfico para avaliação do desempenho dos MAP; e propor fórmulas para o cálculo dos índices de repouso, relaxamento, contratilidade, distensibilidade e mobilidade dos MAP. Além disso, desenvolver protocolos baseados no modelo e demonstrar sua aplicação e interpretação. **3)** Interpretar o desempenho dos MAP de gestantes com ou sem IU-EG aplicando diferentes análises pelo PFM-US Diamater's Protocol. **Métodos: 1)** Trata-se de estudo de coorte prospectivo realizado no Centro de Pesquisas em Diabetes Perinatal (PDRC) da Universidade Estadual Paulista (UNESP), Faculdade de Medicina de Botucatu, Brasil. A declaração STROBE foi usada como guia para relatar este estudo. Os dados foram coletados em três momentos: 24-30 e 38-40 semanas de gestação e 6-12 meses pós-parto de março / 2016 a julho/2020. Este estudo foi aprovado pelo Comitê de Ética em Pesquisa (CAAE 82225617.0.0000.5411). As gestantes foram recrutadas para participar

do estudo durante a rotina de rastreio do DMG na 24-30 semanas de gestação no PDRC. Os critérios de inclusão foram gestantes com 24-30 semanas de gestação, 18-40 anos de idade, primigesta, gestação única, normoglicêmica e DMG com tratamento não medicamentoso. Foram excluídas as participantes com DM tipo I ou II, uso de hipoglicemiantes, triagem ou diagnóstico inadequado de DMG, tratamento farmacológico após falha no controle da glicose com modificação do estilo de vida e dieta, gestação anterior, doença do tecido conjuntivo, distúrbios neurológicos, prolapso ou cirurgia de incontinência, distúrbio hipertensivo gestacional ou pré-existente, incapacidade de realizar a sequência de contração dos MAP ou manobra de Valsalva máxima, limitações que impediram a conclusão total ou parcial em qualquer dos momentos de coleta, parto prematuro, morte fetal intrauterina, evolução para parto vaginal, diagnóstico de DM no pós-parto e nova gravidez antes de completar o acompanhamento. O diagnóstico do DMG foi realizado de acordo com os critérios da *American Diabetes Association* (ADA) e quando confirmado estas participantes foram alocadas no grupo DMG. As participantes com resultado negativo foram alocadas no grupo não DMG. As participantes foram submetidas a avaliação dos MAP pela US-3D considerando a área do hiato do levantador, entre 24-30 e depois com 38-40 semanas de gestação e respeitando o critério de ter decorrido no mínimo 10 semanas entre a primeira e a segunda avaliação durante a gravidez. Todas foram também avaliadas no terceiro momento entre 6 e 12 meses pós-parto. Todas as participantes forneceram consentimento informado previamente ao início da coleta de dados. **2)** O modelo foi proposto para avaliar o desempenho dos MAP em suas diferentes atividades por meio da US e desenhado com base na importância de incluir, além da medida de repouso inicial, as medidas de repouso antes e depois de cada atividade realizada. Este conceito permitirá análise ampliada e detalhada do desempenho dos MAP entre os repousos, entre as atividades e repousos, bem como entre atividades semelhantes e/ou opostas. Além disso, consideramos que o modelo PFM-US Diamater's Protocol é dinâmico, pois suas etapas podem ser organizadas de acordo com a necessidade do avaliador, bem como utilizado por pesquisador ou clínico. Adicionalmente, foram desenvolvidas fórmulas para calcular os índices de variação de repouso, relaxamento, contratilidade, distensibilidade e também o índice de variação de atividade entre atividades semelhantes e o índice de mobilidade relacionado à excursão muscular entre atividades opostas. Essas fórmulas podem ser aplicadas para qualquer medida obtida pela ultrassonografia, incluindo a área hiatal do elevador e diâmetro anteroposterior e transverso. Nesse contexto, os índices

podem ser calculados em valores absolutos para medidas lineares (cm) e / ou valores percentuais (%) para medidas de área (cm^2). Vale ressaltar que a versão final do PFM-US Diamater's Protocol foi obtida após revisão de três avaliadores voluntários externos: um com expertise clínica (M.G.O.), um com expertise em pesquisa (C.B.P.) e outro sem expertise em avaliação ultrassonográfica dos MAP (A.A.P.). Para demonstrar a avaliação e a aplicação das fórmulas foi realizado estudo transversal no Centro de Pesquisas da FMB, Botucatu, SP, Brasil. (CAAE 82225617.0.0000.5411) Quinze mulheres caucasianas assintomáticas entre 20-30 anos foram incluídas no tutorial demonstrativo para aplicação e interpretação do US no PFM-US Diamater's Protocol. **3)** Estudo transversal realizado no Centro de Pesquisas Perinatal (CPP) da Universidade Estadual Paulista (UNESP), Faculdade de Medicina de Botucatu, Brasil, pelo Grupo de Estudos Diamater. A coleta de dados foi realizada entre novembro de 2019 a fevereiro de 2020. No total, 49 gestantes foram incluídas nesta análise e distribuídas em dois grupos: mulheres com IU-EG (n = 23) e sem apresentar IU-EG (n = 26). Este estudo foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Medicina de Botucatu, Universidade Estadual Paulista (UNESP), Botucatu, Estado de São Paulo, Brasil (CAAE: 82225617.0.0000.5411). As mulheres foram convidadas a participar durante a sala de espera para rotina do pré natal a partir da 24ª semana de gestação no (CPP) e foi obtido o termo de consentimento livre e esclarecido de todas as participantes incluídas. Os critérios de inclusão foram gestantes maiores de 18 anos, continentes ou incontinentes com início específico na gestação atual. Mulheres com IU pré-gestacional, diabetes conhecido tipo 1, tipo 2 ou DMG e aquelas que se recusaram a participar não foram incluídas neste estudo. Foram excluídas também as participantes que durante a avaliação do assoalho pélvico não conseguiram realizar uma correta contração ou uma manobra de Valsalva máxima dos MAP e aquelas em que as imagens ultrassonográficas apresentaram falha técnica. Foi aplicado um questionário para coletar os seguintes dados: etnia, tabagismo na gravidez, atividade física na gravidez, escolaridade, idade na gravidez, semanas de gestação, índice de massa corporal (IMC) pré-gravidez e na gravidez e também ganho de peso materno. O exame físico foi realizado por uma fisioterapeuta (Pinheiro, FA) com 8 anos de experiência em treinamento e exame dos MAP. Na primeira etapa do exame físico todas as participantes foram orientadas sobre como realizar a seguinte sequência: repouso, contração dos MAP e distensão dos MAP pela manobra de Valsalva. Um experiente investigador (Sartorão Filho, CI) adquiriu as imagens pela ultrassonografia tridimensional transperineal (US-3DTP) dos MAP. O

conjunto de dados de imagem foram obtidos seguindo o PFM-US Diamater' Protocol 1. Para avaliar o desempenho dos MAP em repouso e durante as suas diferentes atividades, 5 imagens diferentes em sequência e cores foram coletadas. Ao final, as imagens foram salvas de forma anônima e analisadas offline em uma ordem aleatória por números de código anônimos. Além disso, fórmulas matemáticas foram aplicadas para calcular os índices de variação da área do hiato do levantador (HL) em valores absolutos (cm^2) e percentuais (%). **Resultados: 1)** 48 participantes foram incluídas na análise final, sendo 20 no grupo DMG e 28 no grupo não-DMG. A comparação entre os grupos em cada momento de avaliação em relação as medidas obtidas pelo US-3D dos MAP, mostrou diminuição em todas as variáveis nos valores absolutos e diminuição na variação da contração e mobilidade no segundo momento no grupo DMG. No pós-parto apresentou diminuição do repouso e da contração nos valores absolutos das medidas quando comparado ao grupo não-DMG. Na presença de efeito de interação dos grupos dentro dos momentos e dos momentos dentro dos grupos em relação às medidas dos MAP demonstrou em repouso que o comportamento do grupo não-DMG no segundo momento foi significativamente maior quando comparado ao primeiro e terceiro momentos. Na distensão, o grupo não-DMG no primeiro momento teve medida menor que o segundo momento, e o primeiro e segundo momentos tiveram medidas significativamente maiores quando comparados ao terceiro momento. No grupo DMG, o segundo momento teve medida significativamente maior quando comparado com o terceiro momento. O grupo não-DMG também apresentou maior medida que o grupo DMG no segundo momento. Na ausência de interação, os grupos foram comparados independentemente dos momentos e momentos foram comparados independentemente dos grupos. Foi observada na contração, medidas menores no não-DMG e segundo momento medidas maiores que primeiro e terceiro momento. A variação entre a contração em repouso demonstrou no grupo não-DMG medida menor do que no grupo DMG e a variação entre distensão em repouso no primeiro e no segundo momento foi significativamente maior do que no terceiro momento. A análise de interação da variação mobilidade apresentou maior medida no grupo não-DMG em relação ao grupo DMG. O primeiro e o segundo momentos tiveram mobilidade maior do que o terceiro momento**. 2)** PFM-US Diamater's Protocol foi desenvolvido e é possível visualizar o modelo no desenho esquemático. A sequência de atividades dos MAP a serem realizadas estão apresentadas em balões e com setas conectando os balões e indicando as fórmulas a serem aplicadas, tanto. em valores absolutos para medidas lineares (cm) quanto em

valores percentuais (%) para diferenças entre as medidas. Desta forma, nosso modelo apresenta a possibilidade de calcular a variação de repouso, relaxamento, contratilidade, índices de distensibilidade, índice de variação de atividade e índice de mobilidade. Além disso, quatro protocolos foram desenvolvidos como exemplos do PFM-US Diamater's Protocol, considerando diferentes combinações de atividades dos MAP em repouso, contração e distensão. Desta forma, siglas e números foram substituídos de acordo com cada protocolo proposto. Foram desenvolvidos 4 protocolos demonstrativos seguindo o desenho esquemático do modelo. Os resultados relacionados à aplicação e interpretação do tutorial demonstrativo, de um dos 4 protocolos, dessa amostra hipotética, demonstrou que não houve variabilidade nesta população considerando a análise em valores absolutos, contudo houve variabilidade nos resultados quando considerada a diferença em todas as atividades, nas proporções em diferenças percentuais. Dependendo da atividade realizada e da fórmula aplicada, os resultados podem gerar resultados positivos ou negativos e estão relacionados ao aumento ou diminuição da área do hiato do elevador. **3)** 49 gestantes foram alocadas em um grupo sem IU-EG (n = 26) e em um grupo com IU-EG (n = 23). As informações demográficas da população do estudo, foram semelhantes entre os grupos. A comparação das medidas da área do hiato do levantador (HL) em valores absolutos (cm^2) entre os grupos, mostrou que as variáveis dos MAP (repouso basal, contração, repouso pós-contração, distensão, repouso pós-distensão) foram significativamente maiores no grupo IU-EG. A comparação dos índices de variação da área do HL em valor absoluto (cm^2) entre os grupos, apresentou menor índice de variação do repouso 2 para o repouso 1 e do repouso 2 para o repouso basal no grupo IU-EG, bem como um índice de relaxamento mais negativo após distensão quando em comparação com o grupo sem IU-EG. Realizando os mesmos cálculos com as medidas da área do HL em porcentagem (%), encontramos diferenças mais significativas entre os grupos. O grupo IU-EG apresentou menor índice de variação do repouso 2 ao repouso 1, índice de variação mais negativo do relaxamento após distensão, menor índice de mobilidade da distensão à contração e da contração à distensão, menor índice de distensibilidade em relação ao repouso basal e menor índice de variação do repouso 2 ao repouso basal quando comparado ao grupo sem IU-EG. A comparação intragrupos da área do HL em valor absoluto (cm^2) nos três momentos de repouso (repouso basal, repouso 1- pós-contração e repouso 2- pós-distensão) apresentou menor medida de área de HL em repouso basal e repouso 1 (pós -contração) em comparação ao repouso 2 (pós-distensão) no grupo sem IU-EG e

medição de repouso basal maior do que o repouso 1 no grupo IU-EG. Por fim, a comparação da área do HL em valor absoluto (cm^2) entre os grupos e para os três momentos de repouso demonstrou que, no grupo sem IU-EG, todas as medidas de repouso da área do HL (repouso basal, repouso 1 e repouso 2 foram significativamente menores em relação ao grupo IU-EG. **Conclusão: 1)** A disfunção da musculatura do assoalho pélvico no final da gestação e pós-parto de longo prazo, determinada pela US-3D, está relacionada ao Diabetes Mellitus Gestacional. **2)** PFM-US Diamater's Protocol foi desenvolvido com sucesso para avaliar o desempenho dos MAP pela ultrassonografia. O tutorial demonstrativo sobre como aplicar e interpretar diferentes índices de desempenho dos MAP também foi demonstrado por meio de um dos quatro protocolos de avaliação. **3)** Gestantes com IU-EG apresentaram diferente desempenho dos MAP avaliados pelo US-3DTP. A interpretação dessas diferenças é distinta dependendo das fórmulas aplicadas. Os resultados do índice de variação em porcentagem demonstraram diferenças em mais variáveis quando comparados ao índice de variação em valores absolutos. Os resultados obtidos por meio deste estudo indicam que gestantes com IU-EG apresentam maior área do HL em todas as atividades avaliadas, bem como pior desempenho para relaxamento, contração e distensibilidade dos MAP.

Palavras-Chaves: Assoalho pélvico; contração; *diabetes mellitus* gestacional; músculo do assoalho pélvico; gravidez; ultrassonografia.

Thesis Abstract

Pinheiro, F. A. Impact of Gestational Diabetes Mellitus on pelvic floor muscles functionality assessed by 3D- ultrasonography during pregnancy and long-term postpartum - 2021. 172p. Thesis (Doctorate) - Botucatu Medical School (FMB), São Paulo State University (UNESP), Brazil.

Introduction: The pelvic floor muscles (PFM) represent a critical element in supporting the pelvic organs, providing active support both at rest and during activity. The coordinated and effective contraction of PFM is related to the maintenance of urination, evacuation and sexuality. In addition, adequate distention of the PFM can favor childbirth and is likely to reduce the incidence of injuries to the levator ani muscles. Pelvic floor muscle dysfunction (PFMD) is a disorder that affects the ability to control and coordinate PFM, associated with urinary incontinence (UI), stress urinary incontinence, overactive bladder syndrome, pelvic organ prolapse, anal incontinence, pelvic pain, sexual dysfunction and constipation results in a negative impact on the quality of life. Research studies have associated Gestational Diabetes Mellitus (GDM) with PFMD. The GDM is defined as glucose tolerance disorder begins during pregnancy and is increasingly common in women, affecting approximately 8.3% of pregnancies worldwide. The interaction between pregnancy and GDM impacts on early and long-term maternal health. GDM is associated with "diabetic myopathy", which refers to functional, metabolic and structural changes in skeletal muscle that are induced by diabetes mellitus (DM). Clinical studies have shown that GDM negatively impacts the electromyographic activity of PFM throughout pregnancy. In addition, it also changes the morphology of PFM structures when assessed by three-dimensional ultrasonographic (3D-US). PFMD in women with GDM proved to be an independent risk factor for Pregnancy Specific-Urinary Incontinence (PS-UI) and a risk factor for UI two years after cesarean section. Injury that affects the rectus abdominis muscle during pregnancy was also related to GDM. Translational studies have shown harmful impacts of both long-term mild hyperglycemia and severe short-term hyperglycemia on the muscle of pregnant rat’s urethra such as atrophy, thinning, disorganization, rupture of muscle fibers and loss of specific types of fibers from normal anatomical locations, denoting connection to normal anatomical locations and PFM structure. Recently, a clinical study protocol established well-developed biomarker research in a new conceptual model of the role of the integration of the triad GDM, PS-UI and hyperglycemic myopathy as a predictor of long-term UI and PFMD. The performance assessment of PFM by transperineal ultrasonography (US) is

recommended by the International Continence Society (ICS) and International Urogynecological Association (IUGA). The assessment should include the performance of PFM at rest and in dynamic activities, such as contraction and strain. Ultrasonography has been reported as a simple, non-invasive, easy to perform and widely used method in obstetric clinic as a tool for assessing PFM. This technique is readily available, lack of ionizing radiation, minimal discomfort, has good interobserver and interdisciplinary reliability and allows dynamic assessment. Justification: Deepening and filling knowledge gaps about the long-term repercussion of GDM and hyperglycemic myopathy is essential. Previously, no studies were investigated and assessed the functionality of PFM with 3D-US during pregnancy and long-term postpartum follow-up of pregnant women exposed to GDM. There were also no studies with a proposal to evaluate the performance of PFM activities (contraction and distension) in a dynamic and sequential way, as well as intermediate rest measurements between all these activities performed and specific formulas for their interpretation. In this context, analyze the function of MAP performance with ultrasound measurements in real time is a dynamic method, valuable, and objective alternative to guide clinical practice and science in preventive and therapeutic care. **Aims: 1)** To analyze the effect of GDM on the PFM functionality at two-time points of gestation and in the long-term postpartum assessed by 3D-US. **2)** To develop dynamic ultrasonographic model to assess the MAP performance; and propose formulas for calculating the rest, relaxation, contractility, distensibility and mobility indexes of PFM. Also, to develop protocols based on the model and demonstrate its application and interpretation. **3)** To interpret the PFM performance of pregnant women with or without PS-UI applying different analyzis by the PFM-US Diamater's Protocol. **Methods: 1)** This is a prospective cohort study conducted at the Perinatal Diabetes Research Center (PDRC) of São Paulo University State (UNESP), Botucatu Medical School, Brazil. The STROBE statement was used as a guide to report this study. Data were collected at three times: 24-30 and 38-40 weeks of gestation and 6-12 months postpartum during March 2016 to July 2020. This study was approved by the Research Ethics Committee (CAAE 82225617.0.0000.5411) of Botucatu Medical School, São Paulo University State (UNESP), Brazil. Pregnant women were recruited to participate in the study during the routine screening of GDM at 24-30 weeks of gestation at the PDRC. Inclusion criteria were pregnant women with 24-30 weeks of gestation, 18-40 years of age, first pregnancy, singleton pregnancy, non-GDM and GDM with non-pharmaceutical treatment. Participants with previous type I or II DM, use of hypoglycemic agents, inadequate

screening or diagnosis of GDM, pharmacological treatment after failure to control glucose with lifestyle and diet modification, previous gestation, connective tissue disease, neurological disorders, prolapse or incontinence surgery, gestational or pre-existing hypertensive disorder, inability to perform the sequence of PFM contraction or maximum Valsalva maneuver, limitations that prevented complete or partial completion at any of the collection times, premature birth, intrauterine fetal death, evolution to vaginal delivery, diagnosis of postpartum DM and new pregnancy before completing follow-up were excluded. The diagnosis of GDM was performed according to the criteria of the American Diabetes Association (ADA), when confirmed these participants were allocated to the GDM group. Participants with negative results were allocated to the non-GDM group. The participants underwent PFM assessment by 3D-US between 24-30 and then at 38-40 weeks of gestation, respecting the criterion of having passed at least 10 weeks between the first and the second assessment during pregnancy. All were evaluated at the third moment between 6 and 12 months postpartum. All participants provided informed consent prior to the start of data collection. **2)** The model was proposed to assess the performance of PFM in their different activities through 3D-US and designed based on the importance of including, in addition to the baseline rest measurement, the rest measurements before and after each activity performed. This concept will allow an expanded and detailed analysis of PFM performance between rests, activities and during rest, as well as between similar and / or opposite activities. In addition, we consider that the model PFM-US Diamater's Protocol is dynamic, since its steps can be organized according to the assessor needs, as well as used by either a researcher or clinician. In addition, formulas have been developed to calculate the rest variation, relaxation, contractility, distensibility indexes and also the activity variation index between similar activities and the mobility index related to muscle excursion between opposite activities. These formulas can be applied for any ultrasonographic measurement, including levator hiatal area and anteroposterior and transverse diameter. In this context, the indexes can be calculated in absolute values for linear measurements (cm) and / or percentage values (%) for area measurements (cm^2). It is worth noting that the final version of the PFM-US Diamater's Protocol was obtained after revision from three external volunteer assessors: one with clinical expertise (M.G.O), one with research expertise (C.B.P) and another without expertise in PFM ultrasonographic assessment (A.A.P). To demonstrate the evaluation and application of the formulas, a cross-sectional study (CAAE 82225617.0.0000.5411) was carried out at the PDRC of FMB-UNESP, Botucatu, SP,

Brazil. Fifteen asymptomatic Caucasian woman aged 20-30 years were included in the demonstrative tutorial for applying and interpreting the US in the PFM-US Diamater's Protocol. **3)** A cross-sectional study was conducted at the Perinatal Research Center (PRC), São Paulo State University (UNESP), Botucatu Medical School, Brazil, by the Diamater Study Group. The data collection was performed from November 2019 to February 2020. In total, 49 pregnant women were included in this analysis and distributed into two groups: PS-UI (n=23) and non- PS-UI (n=26). This study was approved by the Institutional Ethical Committee of Botucatu Medical School, São Paulo State University (UNESP), Botucatu, São Paulo State, Brazil (CAAE: 82225617.0.0000.5411). The women were invited to participate during the waiting room for routine from 24 weeks of gestation at PRC and the informed consent to participate document from all participants included was obtained. The inclusion criteria were pregnant women over 18 years old, continent or incontinent with specific onset in the current pregnancy. Women with pre-pregnancy UI, known type 1, type 2 diabetes or GDM and them who refused to participate were not included in this study. The participants that during the pelvic floor assessment were not able to perform a correct PFM contraction or a maximal Valsalva maneuver as well as the ones in which ultrasound images presented technical failure was excluded. A questionnaire was also applied to collect the following data: ethnicity, smoking in pregnancy, physical activity in pregnancy, education level, age in pregnancy, weeks of gestation, body mass index (BMI) pre-pregnancy and in pregnancy and also maternal weight gain . A physical examination was conducted by a physical therapist (Pinheiro, FA) with 8 years of experience on PFM training and examination. In the first physical examination step all participants were instructed about how to perform the following sequence: rest, PFM contraction and PFM distension by Valsalva maneuver. An experienced investigator (Sartorão Filho, CI) acquired the PFM three-dimensional TPUS (3D-TPUS) images. Imaging data sets were taken following the PFM-US Diamater's Protocol 1. To evaluate the PFM performance at rest and during different activities, 5 different images in sequence and colors were collected. At the end, the images were saved anonymously and analyzed offline in a random order by anonymous code numbers. Furthermore, mathematical formulas were applied to calculate the indexes of Levator Hiatal (LH) area variation in absolute (cm^2) and percentage (%) values. **Results: 1)** 48 participants were included in the final analysis, 20 in the GDM group and 28 in the non-GDM group. Comparison between groups in each time point of Levator Hiatal area (LHarea) measurements of PFM showed decrease in all variables in absolute values and

decrease in contraction and mobility in variation at second time point in GDM group. Long-term postpartum showed decrease in rest and contraction in absolute values when compared to non-GDM group. In the presence of the interaction effect of the groups within time points and time points within the groups in relation to the LHarea measurements, it demonstrated in rest that the behavior of the non-DMG group at second time point was significantly larger when compared to the first and third time points. In distension, the non-DMG group at the first time point had a smaller measurement than the second moment, and the first and second time points had significantly larger measurements when compared to the third time point. In the DMG group, the second time point had a significantly larger measurement when compared to the third time point. The non-DMG group also showed a larger measurement than the DMG group in the second time point. In the absence of interaction, the groups were compared independently of the time points and time points were compared independently of the groups. It was observed in the contraction, smaller measurements in the non-DMG and larger measurements in the second time point when compared to the first and third time points. The variation between contraction at rest showed a smaller measurement in the non-DMG group than in the DMG group and the variation between distension at rest in the first and second time points was significantly larger than in the third time point. The interaction analysis of the variation mobility had a larger measurement in non-GDM than the GDM group. First and second time points had larger mobility than third time point. **2)** PFM-US Diamater's Protocol was developed and it is possible to view the model in the schematic drawing. The sequence of PFM activities to be performed are presented in balloons and with arrows connecting the balloons and indicating the formulas to be applied, both in absolute values for linear measurements (cm) and in percentage values (%) for proportional differences between measurements. In this way, our model presents the possibility to calculate the rest variation, relaxation, contractility, distensibility indexes, activity variation index and mobility index. In addition, four protocols were developed as examples of the PFM-US Diamater's Protocol, considering different combinations of PFM activities at rest, contraction and distension. In this way, acronyms and numbers were replaced according to each proposed protocol. Four demonstrative protocols were developed following the schematic design of the model. The results related to the application and interpretation of the demonstrative tutorial of one of the 4 protocols, of this hypothetical sample, demonstrated that there was no variability in this population considering the analysis in absolute values, however there was variability in the results when considering the

difference in all activities, in proportions in percentage differences. It is worth mentioning that depending on the activity performed and the formula applied, the results can generate positive or negative results. The negative results are related to the decrease in the hiatal area and the positive results are related to the increase in the levator hiatal area. **3)** 49 pregnant women were allocated in a non-PS-UI (n=26) group and in a PS-UI (n=23) group. The demographic information of the study population, being all baseline characteristics were similar between groups. The comparison of Levator Hiatal (LH) area measurements in absolute values (cm^2) between groups, showed that PFM variables (basal rest, contraction, rest post-contraction, distension, rest post-distension) were significantly greater on the PS-UI group. The comparison of LHarea variation indexes in absolute value (cm^2) between groups, presented lower variation index from rest 2 to rest 1 and from rest 2 to basal rest in PS-UI group, as well as a more negative relaxation index after distension when compared to the non-PS-UI group. Performing the same calculations with LHarea measurements in percentage (%), we found more significant differences between groups. The PS-UI group presented lower variation index from rest 2 to rest 1, more negative variation index of relaxation after distension, lower mobility index from distension to contraction and from contraction to distension, lower distensibility index in relation to basal rest and lower variation index from rest 2 to basal rest when compared to the non-PS-UI group. Comparison intragroups of the LHarea in absolute value (cm^2) at the three rest-time points (basal rest, rest 1- post-contraction and rest 2- post-distension) presented smaller LHarea in basal rest and rest 1 (post-contraction) compared to rest 2 (post-distension) in non-PS-UI and basal rest measurement greater than rest 1 in PS-UI group. Lastly, the comparison of the LHarea in absolute value (cm^2) between groups and for the three rest-time points demonstrated that in the non-PS-UI group, all LHarea rests measurements (basal rest, rest 1 and rest 2) were significant lower in relation to the PS-UI group. **Conclusion: 1)** Pelvic floor muscle dysfunction in end of pregnancy and long-term postpartum, determined by 3D-US, is related to Gestational Diabetes Mellitus. **2)** PFM-US Diamater's Protocol was successfully developed to assess the PFM performance by ultrasonography. The demonstrative tutorial on how to apply and interpret different PFM performance indexes was also demonstrated using one of the four assessment protocols. **3)** Pregnant women with PS-UI presented different PFM performance evaluated by 3D-TPUS.The interpretation of these differences is distinct depending of the formulas applied. The results of variation index in percentage demonstrate differences in more variables when compared to variation index in absolute

values. The results obtained through this study indicate that pregnant women with PS-UI present greater LHarea in all assessed activities as well as worse performance for PFM relaxation, contraction and distensibility.

Key words: Pelvic floor; contraction; gestational diabetes mellitus; pelvic floor muscle; pregnancy; ultrasonography.

Seção 4
Artigos

Artigo 1

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Title Page

Pelvic floor muscle dysfunction detected by 3D-US in women with GDM in the third trimester remains in long-term postpartum

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Abstract

Aim: To analyze the effects of gestational diabetes mellitus (GDM) on pelvic floor muscles (PFM) function in two time points of gestation and following in the long-term postpartum when evaluated by tridimensional ultrasonography (3D-US)

Method: An observational prospective cohort study was conducted at the Research Center of Botucatu Medical School including 20 pregnant women with GDM and 28 non-GDM pregnant women. Ultrasound measurements of the levator hiatal area (LHarea) were taken at rest, during PFM contraction, distension and mobility at three time points: 24-30 and 38-40 weeks of gestation and 6-12 months postpartum.

Results: The comparison between groups at first time point showed that non-GDM and GDM groups had no significant differences in all LHarea measurements. At second time point GDM group showed smaller measurements in relation to rest LHarea (*P*=0.024) and distension LHarea (*P*=0.000) and showed larger LHarea (*P*=0.045) at contraction in relation to the non-GDM group. The percentage variation in contraction/rest LHarea (*P*=.0.001) and mobility LHarea (*P*=0.000) showed significantly smaller variation compared to non-GDM group. At third time point the GDM group had larger measurements in relation to rest LHarea (*P*=0.022) and in contraction LHarea (*P*=0.006) compared to non-GDM group. It was demonstrated also in rest (*P*<0.001) and distension (*P*<0.001) an interaction effect. In the analysis of contraction there was no interaction effect, so the groups and time points were compared independently. The non-GDM group had a smaller measurement than the GDM (*P*=0.001) and in second time point presented larger measurement than first and third time point (*P*=0.003). The variation from contraction to rest had in non-GDM group a smaller measurement than the GDM group (*P*=0.003) and also first and second time points were significantly larger (*P*<0.001) than third time point. The variation mobility between distension and contraction demonstrate that non-GDM group had a larger measurement than the GDM group (*P*=0.006) and first and second time point had larger mobility than third time point (*P*=0.010).

Conclusions: Pelvic floor muscle dysfunction, considering contraction, distension and mobility, at 3D-US detected in third trimester of GDM exposure remains in long-term postpartum.

KEYWORDS

gestational diabetes mellitus, pelvic floor muscle, pregnancy, 3D transperineal ultrasonographic, contraction, Valsalva maneuver

1 INTRODUCTION

Pelvic floor muscle dysfunction (PFMD) is a disorder that affects ability to contract, distend, relax, control and coordinate pelvic floor muscles (PFM)(1–4), results negative impact on quality of life (5–7) and is associated with symptoms urinary incontinence, stress urinary incontinence, overactive bladder syndrome, pelvic organ, anal incontinence, pelvic pain, sexual dysfunction and constipation(8–11).

Research studies associated Gestational Diabetes Mellitus (GDM) with PFMD(12–15). A decrease vaginal pressure squeeze (16) showed to be an independent risk factor for Pregnancy Specific-Urinary Incontinence (PS-UI) and a risk factor for UI two-years after the Cesarean section(16). A injury that impairs rectus abdominis muscle during the prenatal period was also related with GDM(14,15,17,18). Translational studies, showed detrimental impacts either long-term mild or short-term severe hyperglycemia on urethral pregnant rats muscle as atrophy, thinning, disorganization, rupture of muscle fibers, and loss of specific fiber types from normal anatomical locations, denoting a connection between glycemic levels and PFM structure(17,18).

GDM is defined as a glucose tolerance disorder with on set during pregnancy(19) and is increasingly more common in women(20), affecting approximately 8.3% of pregnancies worldwide(21).The interaction effect between pregnancy and GDM impacts on early and long-term maternal health(22). GDM is also associated with the term "diabetic myopathy" characterized by reduced physical capacity, strength, and muscle mass, is a relatively understudied complication of diabetes mellitus (DM), but is believed to directly influence the rate of co-morbidity development (23,24).

To date, there is a lack of studies monitoring the changes in PFM functionality in postpartum period of pregnant women who were exposed to GDM. Clinical studies demonstrated that GDM impacts negatively on PFM electromyography activity on

gestation progress(15) and furthermore also alters the morphology of pelvic floor structures when assessed by tridimensional ultrasonographic (3D-US)(14). However, no studies were found that investigated and evaluated the PFM functionality with 3D-US during pregnancy and followed up in long-term postpartum.

Ultrasonographic has been reported as a simple, non-invasive, easy to perform and widely used method in clinical obstetric as an assessment tool for the PFM(25). The technique is readily available, lack of ionizing radiation, minimal discomfort(26), has good interobserver and interdisciplinary reliability, and allows PFM dynamic assessment(27).

The aim of the present study was to analyze the effects of GDM exposure on the PFM functionality in rest, contraction, distension and mobility, in two time points of gestation and followed in the long-term postpartum evaluated at 3D-US.

2 METHODS

The STROBE(28) statement was used as a guide to report this study. This was a observational prospective cohort study performed at the Perinatal Diabetes Research Center (PDRC), São Paulo State University (UNESP), Botucatu Medical School, Brazil by the Diamater Study Group. Data were collected during three times points: 24-30 and 38-40 weeks of gestation and at 6-12 months postpartum from March/2016 to July/2020. This study was approved by the Institutional Review Board (CAAE 82225617.0.0000.5411).

Pregnant women were recruited to participate of the study during the waiting room for routine GDM screening at 24-28 weeks of gestation at PDRC. The inclusion criteria were pregnant women at 24-30 weeks of gestation, 18-40 years of age, at first pregnancy, singleton pregnancy, non-GDM and GDM with non-pharmacological treatment were included. Participants who had previous known type I or II DM, use of hypoglycemic drugs, inadequate screening or diagnosis of GDM, pharmacological treatment after failing

to achieve glucose control with lifestyle and diet modification, connective tissue disease, neurological disorders, prolapse or anti-incontinence surgery, gestational or preexisting hypertensive disorder were not included. Inability to perform the sequence and correct PFM contraction or a distension by maximal Valsalva maneuver, limitations that prevented full or partial completion in any time point of this study, preterm birth, intrauterine fetal death, evolution to vaginal delivery, DM diagnosis postpartum and new pregnancy status before completing the postpartum follow-up were excluded.

During the first contact the result from the fasting plasma glucose to compose the groups were not known, so it promoted a first time point blinded assessment and pregnant who underwent fasting ≥92 mg/dL were allocated to the GDM group as recommended by the ADA criteria(29). The participants who had lower values assigned the non-GDM group. Participants included in first time point of gestation were scheduled to blinded assessment in second time point at 38-40 weeks gestation, as criterion the minimum time elapsed of 10 weeks between first and second evaluation during pregnancy. They were reassessed in third time point among 6 and 12 months postpartum. All participants provided written informed consent prior data collection.

The following demographic information during the first time point (24-30 weeks of gestation) in a private office at PDRC were obtained: maternal age, ethnicity, education level, smoking in pregnancy, physical activity, pre-pregnancy and 24-30 weeks of gestation body mass index (BMI). Maternal weight gain was obtained at second time point (38-40 weeks of gestation). Newborn weight, physical activity, smoking and BMI in third time point, at 6-12 months postpartum was obtained. Clinical data about glycemic control between time points were collected in medical records.

The ultrasonographic procedures followed the literature recommendations of Dietz(30) and is considered a reliable technique that can be learned in a short period of time and could be incorporated easily into examinations of the pelvic floor(31). 3D-US

transperineal was performed at first time point, 24-30 weeks of gestation, at second time point, 38-40 weeks of gestation, and at third time point, 6-12 months postpartum. Prior to the 3D-US examination, all participants were instructed by a physiotherapist (FAP) with 6 years of experience on PFM training and examination on how to perform the sequences of PFM rest, contraction and distension by Valsalva maneuver. An experienced investigator (CISF) on 3D-US transperineal acquired the imaging data of the PFM. A GE Voluson I system with a RAB 2-6RS (2-6 MHz) curved array 3D transducer (GE Healthcare, Zipf, Austria) was used and all PFM ultrasonographic examination was performed with the participants in supine position and with empty bladder. The probe was covered with a condom and placed on the perineum in the sagittal plane. The field of view angle was set to its maximum of 70° in the sagittal plane and 85° in the coronal plane(32). The images were saved anonymously and different colors in the following sequence were applied to identify each PFM function: 1) a gray image at rest, with no PFM movement and acquired to be used as a standard basal measurement to calculate the variation from rest to functional activity; 2) a blue image at maximal voluntary PFM contraction; 3) and a sepia image at maximal distension obtained during Valsalva maneuver.

The technique of PFM contraction was explained by this verbal prompt: "Please squeeze your pelvic muscle, as though you were trying to hold in gas and as forcefully as possible, maintain the contraction as long as possible"(33). A PFM contraction was considered correct by observing the best cranial shift of the levator ani muscle(34,35) and when the investigator felt inward pressure or upward traction on the examining finger in the vagina(36). Accessory contractions of the abdominal, adductor and gluteal muscles(35), hip movements and expulsion movements were discouraged and rectified(36). To PFM distension, the maximal Valsalva maneuver was performed, instructing the participants to do a forced expiration and to push as during delivery(37) for

at least 6 seconds(38). A correct distension was confirmed by a caudodorsal displacement of the levator ani muscle(38).

Participants were verbally instructed to keep their PFM relaxed while the examiner acquired three consecutive images at rest. PFM contraction and distension were also done three times and the set with the best image data was chosen for analysis(39). The 3D-US images were analyzed in random order offline by anonymous code numbers generated by the software, by one investigator blinded to group allocation and background data. Analysis of the levator hiatal area (LHarea) dimension was carried out using the 4D View program, version 14, Ext. 3 (GE Healthcare). For test-retest analyses, the ultrasonographic data of ten women were randomly selected and analyzed offline by a second investigator (BJ) six months after the final examination. BJ was blinded to group allocation and background data. The delivery time, mode and obstetric management of all participants were not affected by the study.

The LHarea measurement was used to evaluate the functionality of PFM in contraction, distension and mobility. It plays an important role in obstetric and gynecological practice, is associated with progress in labor and seems to play a major role in pelvic floor dysfunction(40). The LHarea was measured as the area enclosed by the inner border of the pubic symphysis ventrally, and the inner surface of the puborectalis sling laterally, and caudally in the plane of minimal hiatal dimensions during distension obtained by maximal Valsalva maneuver(41).

The measurement of LHarea dimension was obtained and the results for the GDM group were compared to non-GDM group at each of the three-time points (24-30 weeks, 38-40 weeks of gestation and 6-12 months postpartum) and between them. Contraction and distension were analyzed considering the resting state and determined by the difference of measurements between contraction or distension in relation to rest. Contraction (C) was calculated by subtracting the LHarea measurement of contraction

from the LHarea measurement at rest (R) (CR=100*(LHarea C-LHarea R)/LHarea R). The smaller value obtained for contraction, the greater PFM contraction capacity. Distension (D) was determined by subtracting the LHarea measurement of distension from the LHarea measurement at R (DR = 100*(LHarea D-LHarea R)/LHarea R). The larger value obtained for distension, the greater PFM distension capacity. In order to analyze PFM complete muscle excursion capacity, we established the term 'mobility' (M) and was considered for this, the variation of the dimensions from contraction to distension and determined by the formula (DC = 100*(LHarea D-LHarea C)/LHarea C). The larger value obtained the greater mobility. These formulas were applied and calculated in absolute values (cm^2) and percentage values (%) for the variation in all LHarea measurements.

The association between DMG and variables was analyzed by non-parametric tests Mann–Whitney U, Chi-square and Fischer's exact. ANOVA models with repeated measures were adjusted to explain the LHarea as a function of the non-GDM and GDM groups throughout the observation time points. If the hypothesis of sphericity was rejected by the Mauchly test, the interaction effect and main effects of the model were tested using the Greenhouse-Geisser test. In the presence of a significant interaction effect, the groups were compared within the time points and the time points were compared within the groups using Bonferroni correction. In the absence of interaction effect, the groups were compared independently with the time points and time points were compared independently with the groups. Differences were considered statistically significant if $P<0.05$. Analyses were performed with SPSS Statistics 22.0 software.

3 RESULTS

During the study period, a total of 434 pregnant women were selected however 330 were not considered eligible to participate of the study. From this population, 104 were recruited

to participate of the study and 77 gave written informed consent to complete the baseline assessment at 24-30 weeks of gestation. During the three time points there was an exclusion of participants according to the exclusion criteria and in the final analysis, 48 participants were included, 20 in the GDM group and 28 in the non-GDM group. The figure 1 shows the number of women examined in each group and the reasons for non-participation. No differences in background variables were found between those in each group who completed the study and those who did not (*data not shown*).

Baseline participants characteristics are presented in table 1. The significant difference was in the fasting plasma glucose at first time point (24–30 weeks of gestation), newborn weight at birth and BMI at 6-12 months postpartum (Table 1).

Comparison between groups in each time point of LHarea measurements of PFM on rest, contraction, distension and mobility, in absolute values (cm^2) and variation (%) are presented in table 2. At first time point (24-30 weeks of gestation) the non-GDM and GDM groups had no significant differences in LHarea measurements. At second time point (38-40 weeks of gestation), the LHarea showed significant differences in all variables in absolute values, GDM group showed smaller measurements in relation to rest LHarea (*P*=0.024) and distension LHarea (*P*=0.000) and showed larger LHarea (*P*=0.045) at contraction in relation non-GDM group. The percentage variation in contraction/rest LHarea (*P*=.0.001) and mobility LHarea (*P*=0.000) showed significantly smaller variation compared to non-GDM group. At third time point (6-12 months postpartum) the GDM group had larger measurements in relation to rest LHarea (*P*=0.022) and in contraction LHarea (*P*=0.006), in other words, less shortening, compared to non-GDM group.

Interaction effect analysis and comparison between groups independently time points and time points independently groups, considering the LHarea measurements of PFM on rest, contraction, distension and mobility in absolute values (cm^2) and variation

(%), was demonstrated in table 3 and figure 2.

It was demonstrated in rest (P<0.001) and distension (P<0.001) interaction effect. In relation to rest the non-DMG group at second time point was significantly larger when compared to the first and third time points. In relation to distension the non-GDM group had smaller measurement in first time point when compared to second time point, and first and second time point had significantly larger measurements when compared to third time point.

In the analysis of contraction there was no interaction effect, so the groups and time points were compared independently. The non-GDM group had a smaller measurement than the GDM (P=0.001), regardless of the time point. Second time point presented larger measurement than first and third time point (P=0.003), regardless of the groups.

The variation between contraction at rest had no interaction effect, so the groups and time points were compared independently. The non-GDM group had a smaller measurement than the GDM group (P=0.003), regardless of the time point. Regardless of groups, there was no significant difference between time points.

The variation between distension at rest had no interaction effect, so the groups and time points were compared independently. There was no significant difference between non-GDM and GDM groups. First and second time point were significantly larger (P<0.001) than third time point, regardless of groups.

There was no interaction effect in variation mobility, that is, between distension and contraction, so the groups and time points were compared independently. The non-GDM group had a larger measurement than the GDM group (P=0.006), regardless of the time point. First and second time point had larger mobility than third time point (P=0.010).

4 DISCUSSION

4.1 Principal findings

The most important findings of the observational prospective cohort study were that the GDM group had a negative impact on the expected physiological PFM function in pregnancy and postpartum. GDM induces a decrease in rest, distension and mobility and increase contraction in LHarea measurements. These findings suggest a relation between abnormalities in PFM functionality and GDM exposure.

4.2 Clinical implications

The study links GDM to poor physiological PFM function in the third trimester of pregnancy and during the postpartum period. The study findings hold that women with GDM have a higher risk of experiencing a low-quality life during pregnancy and postpartum period when compared to women with no GDM. Notably, scientific evidence reveals that UI increases significantly during and after pregnancy in women with GDM. Specifically, GDM weakens the muscle strength of PFM(15,16). A similar study conducted on rats established that the urethral muscle pressure decreases with GDM hence worsening UI (42).

A new and interesting finding of our study is that a decreased of PFM function, considering contraction, distension and mobility ability, at 3D-US detected in third trimester of GDM exposure remains in long-term postpartum and may play a role in the development of pelvic floor dysfunction in later life. Therefore, GDM is a primary health concern among women during pregnancy and the postpartum period.

The cohort study established no significant differences in LHarea variables of rest, contraction, mobility, and distention between the GDM and non-GDM groups at 24–30-week gestation**.** The findings indicate that GDM has some effect on the physiology of PFM towards the end of the pregnancy and postpartum. A similar study (14) noted that

GDM alters the pelvic floor structure. Another study(43), observes that GDM reduces the energy inducted into the striated and smooth urethral muscles besides weakening the urethral sphincter resulting in urinal incontinence.

The LHarea variables at 38-40 weeks gestation showed significant differences at rest, contraction, mobility, and distension in GDM and non-GDM groups. Specifically, rest (P=0.024), distention (P=0.000) mobility LHarea (P=0.000) variables showed smaller measurements in GDM groups compared to the non-GDM group. Conversely, in the GDM group, contraction LHarea (P=.0.045) displayed larger measurements when compared to the non-GDM groups. The finding indicates that women with GDM, due to morphological alterations of the PFM, experience lower muscle contraction than in non-GDM women. Existing scientific evidence suggest that structural changes of the pelvic floor muscle of pregnant women with GDM is responsible for the changes (15,17,18,44). In this respect, the study surmises that time is a significant factor when evaluating the effect of GDM on PFM. The maternal and fetal physiological changes as the pregnancy progress to term could explain the findings between 38th and 40th-week gestation and demonstrated that the US-3D evaluation method can sufficiently detect the effect of GDM on PFM during the late third trimester of pregnancy.

Likewise, significant contraction measurements in GDM groups compared to non-GDM groups are indicators of damaged pelvic floor muscles during pregnancy and lasting 6-12 months postpartum. The finding is consistent with existing studies that GDM causes inadequate pelvic muscle squeeze pressure and incontinence during and after pregnancy. Therefore, the study findings confirm previous research findings on the physiological effects of GDM on PFM.

The study also analyzed the interaction effect of rest, contraction, distention, and mobility variables at first, second, and third-time points measured in absolute values (cm^2). Notably, the rest measurements were significant in all second-time points than in

first and second-time points in the non-GDM group. On the other hand, the study established that the distension variable was greater during the period between 38th and 40th-week gestation than in periods between 24th -30th week and in postpartum in non-GDM groups.

Regarding contraction measurements, the GDM groups showed different values than the non-GDM groups across all the time points. Irrespective of the study group, the second time point posted significantly different contraction values. A previous study on non-GDM women established that factors like muscle resistance and greater anterior posterior pelvic diameter offered insight into contractility (48). Therefore, a decrease contractility of PFM in GDM diagnosed women means that the muscle has lost its function due to diabetic myopathy hence affecting its ability (18,45). At rest, levator ani muscles produce the best starting point for measuring the muscle stretch (46)(47). Particularly, distension at rest for the 24th-30th week and 38th -40th weeks gestation had larger values than during postpartum. The research attributes the finding by repercussions caused by GDM.

The study further established that variation mobility arising from the difference between distention and contraction of the PFM was larger for the non-GDM group than the GDM group. Arguably, GDM is the cause for PFM weakening leading to poor mobility. For instance, women without GDM experienced greater PFM contracted from the rest point than in pregnant women with GDM (18,46). The finding implies that women with no GDM experienced near-normal pelvic floor muscle functionality during pregnancy and in the postpartum period. A similar study conducted on rats(47) established that pregnant rats with DM had decrease in fast fiber muscles and increase in collagens. Therefore, pregnant women with GDM experience poor PFM functionality leading to frequent incidences of pelvic floor dysfunctions(48,49).

Studies found showed increased of Hiatal dimensions in third trimester of non-GDM

pregnant women, however in opposite, our study showed that in GMD pregnant women Hiatal dimensions decreased (46,50–52).

In non-GDM pregnant women was identified a smaller levator hiatus area at rest and during distension at mid and late pregnancy, and less shortening of the levator ani muscle during muscle contraction at 37 weeks of gestation, are associated with major levator ani muscle defects(46). In this present study we observed that GDM group has significantly less shortening of the LAM when compared to non-GDM group.

A possible explanation for these findings may be that GDM pregnancy-related factors, affect PFM function. However, more studies are needed to confirm this observation.

4.3 Strengths and limitations

We must consider some limitations of this study. At 24-30 weeks of gestation was the first maternal evaluation considered as baseline. Ideally, all pregnant women should have been assessed before pregnancy to ensure that there was no previous GDM interference. The calculation of the power of this sample considering the type I error of 0.05, estimated that the test power was 0.564 and for the analysis of interaction effect, 0.497, therefore, it is suggested that further studies and analyzes be carried out to evaluate the interaction effect and compare groups. For analyzes between time points, 0.805 of the sample's power was estimated, which supports the results obtained.

Nevertheless, this study is the first report assessments that allowed us to evaluate impacts since the GDM diagnosis through the end of the pregnancy and continuing at long-term postpartum. The examiner who analyzed the ultrasonographic data sets and images was blinded and the results were reviewed by a second investigator. In addition, this study has translational characteristics, since the design was based on previous studies of pregnant diabetic women and rats. The findings of this study should be

considered as providing possible biomarkers of PS-UI of GDM women in order to confirm gestational diabetic myopathy as a potential cause of the illness.

5 CONCLUSIONS

Gestational Diabetes Mellitus causes pelvic muscle dysfunction in pregnancy, especially third trimester and in postpartum period. GDM affects the ability of the pelvic floor muscles in contraction, distension and mobility, fully during pregnancy and after birth. During rest, US-3D approach may not provide accurate evaluation of the effect of GDM on all PFM. As the pioneer study on the effect of GDM on PFM using US-3D at two points in pregnancy and postpartum, the paper recommends that more studies be done on the subject.

6 RESEARCH IMPLICATIONS

The adverse effect reported can be relationship with IU development between other pelvic floor dysfunctions in life later. Further similar studies are necessary to evaluate preventive and therapeutic strategies during and after GDM exposure.

THE DIAMATER STUDY GROUP

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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***List of Abbreviations*:**
PFMD pelvic floor muscle dysfunction
PFM pelvic floor muscle
GDM gestational diabetes mellitus
DM diabetes mellitus
3D-US three dimension ultrasonographic
PDCR perinatal diabetes research center
BMI body mass index
CI contractility index
Cm^2 square centimeter
% percentage
R_b basal rest
DI distensibility index
MI mobility index

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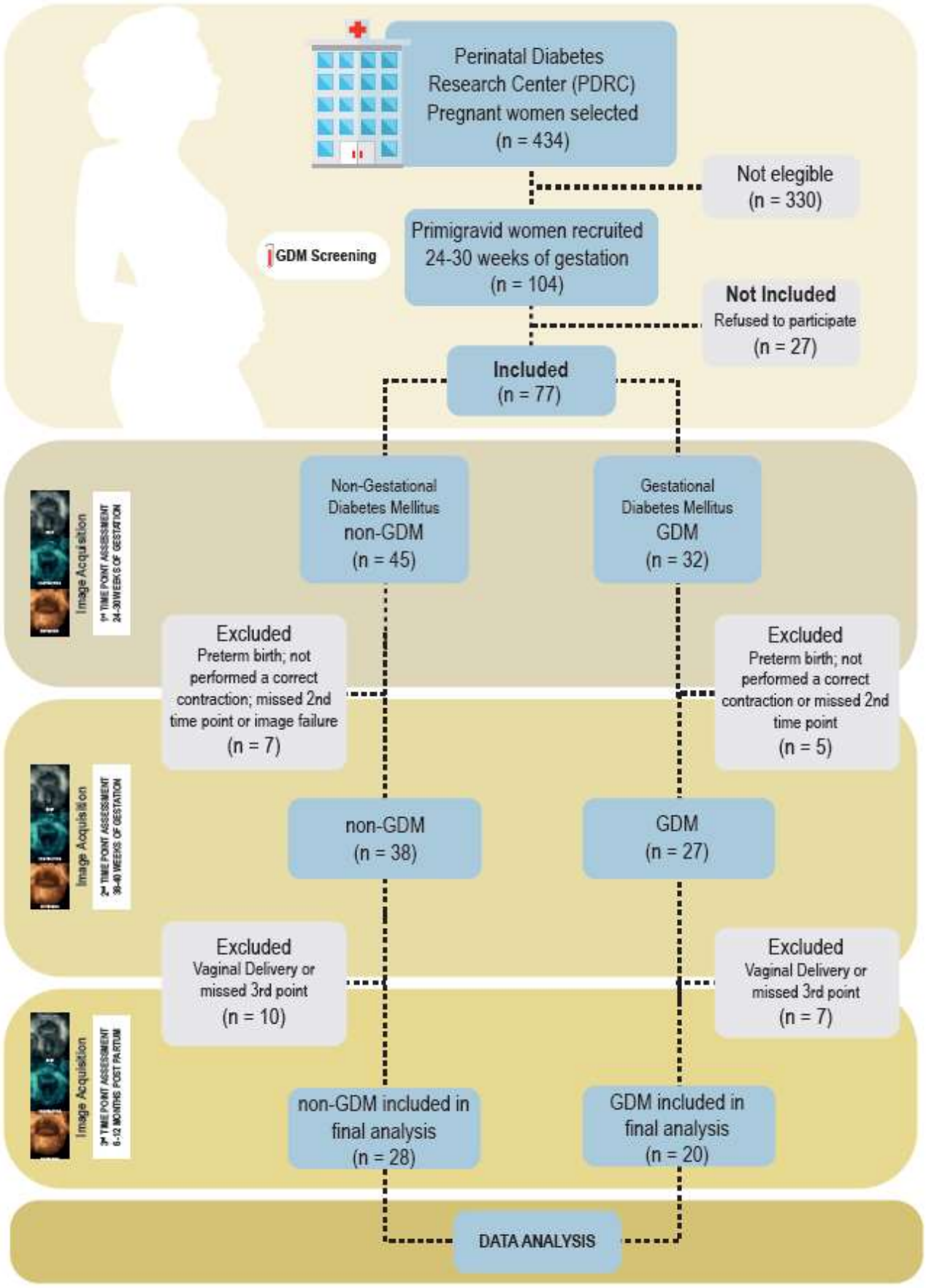

Figure 1 - Flowchart for cohort derivation showing the number of participants and the reasons for loss to follow-up.

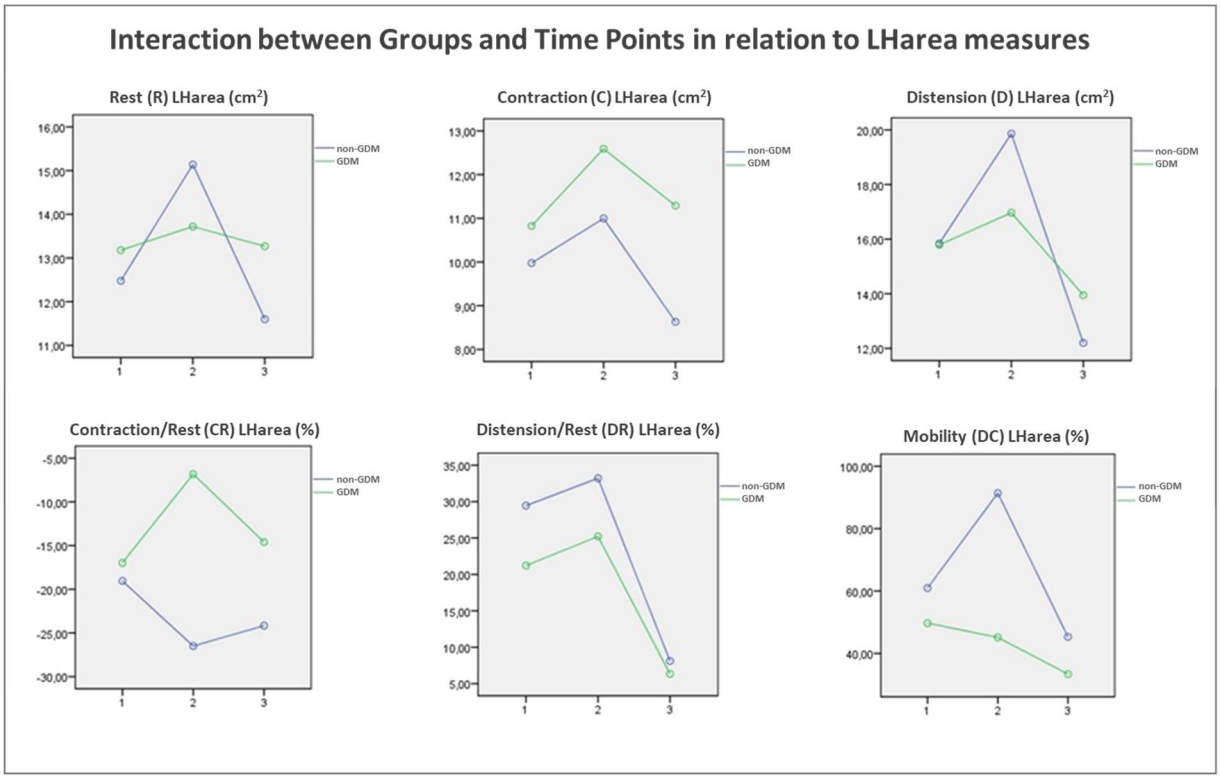

Figure 2 – Interaction effect between groups and time points in relation to Levator Hiatal area (LHarea) measurements**.**

Table 1 – Variables of the study population.

Variable	non-GDM (n=28)	GDM (n=20)	*P**
Ethnicity			.707
Caucasian	24 (85.2)	16 (80.0)	
Other	4 (14.8)	4 (20.0)	
Smoking in pregnancy	0 (0.0)	0 (0.0)	1.000
Smoking postpartum	0 (0.0)	0 (0.0)	1.000
Physical activity in pregnancy	7 (25.9)	5 (25.0)	.943
Physical activity postpartum	4 (14.8)	1 (5.0)	.377
Education level–min. High School	26 (96.3)	20 (100.0)	1.000
Diabetes postpartum	0 (0.0)	0 (0.0)	.176
Age (years)[1]	27.00 (20.00-40.00)	29.00 (21.00-40.00)	.281
BMI (kg/m^2) pre-pregnancy	25.81 (18.52-48.44)	28.00 (21.01-36.70)	.383
BMI (kg/m^2) [1]	26.45 (20.03-33.31)	30.31 (17.18-38.40)	.072
BMI (kg/m^2) [2]	29.47 (21.94-38.62)	32.74 (24.98-37.80)	.093
BMI (kg/m^2) [3]	26.12 (19.38-35.42)	28.85 (17.35-37.81)	.029
Weeks of Gestational[1]	26.50 (22.00-28.00)	27.10 (25.00-28.00)	.965
Weeks of Gestational[2]	38.00 (36.00-39.00)	37.20 (36.00-38.40)	*.271*
Maternal weight gain (kg) [2]	9.80 (0.70-17.7)	9.30 (3.00-14.9)	.401
Postpartum time	9,00 (6.00-12.00)	10.50 (6.00-12.00)	.076
Newborn weight at birth (grams)	2865 (3000–3990)	3350 (2800–3950)	.017
Fasting plasma glucose (mg/dL)[1]	81.00 (65.00-88.00)	95.90 (92.50-99.00)	.000

Non-GDM, non-gestational diabetes mellitus group; GDM, gestational diabetes mellitus group; BMI, body mass index; 1 Evaluation at 24-30 weeks of gestation. 2 Evaluation at 38-40 weeks of gestation. 3 Evaluation at 6-12 months postpartum. Data are the median (minimum, maximum) or n (%). *Based on Mann–Whitney U, Chi-square and Fischer's exact.

Table 2 - Comparison of levator hiatal (LH) area measurements of pelvic floor muscle (PFM) on rest, contraction, distension and mobility, in absolute values (cm^2) and variation (%), between the gestational diabetes mellitus (GDM) and non-GDM (non-GDM) groups in each time point (24-30 weeks of gestation, 38-40 weeks of gestation and 6-12 months postpartum).

Variable	First time point 24-30 weeks of gestation			Second time point 38-40 weeks of gestation			Third time point 6-12 months postpartum		
	non-GDM	GDM	*P*	non-GDM	GDM	*P*	non-GDM	GDM	*P*
	Mean time ± SD			Mean time ± SD			Mean time ± SD		
Rest (R) LHarea (cm^2)	12.48±3.00	13.18±2.20	0.382	15.14±2.07	13.72±2.05	0.024	11.60±2.59	13.20±2.06	0.022
Contraction (C) LHarea (cm^2)	9.98±2.30	10.83±2.18	0.207	11.00±2.26	12.59±3.04	0.045	8.63±1.83	11.29±4.34	0.006
Distension(D) LHarea (cm^2)	15.84±3.47	15.79±2.20	0.954	19.86±2.44	16.9±2.08	0.000	12.20± 2.00	13.95±4.27	0.067
Contraction/Rest CR) LHarea (%)*	-2.50±1.48	-2.35±2.37	0.795	-4.14±2.70	-1.13±3.33	0.001	-2.97±2.07	-1.98±4.09	0.282
Distension/Rest (DR) LHarea (%)**	3.36±2.25	2.61±1.96	0.238	4.72±2.78	3.25±2.06	0.052	0.60±2.29	0.68±4.29	0.934
Mobility (DC) LHarea (%)***	5.87±2.40	4.97±2.07	0.185	8.87±3.30	4.38±3.07	0.000	3.57±1.94	2.66±4.97	0.389

non-GDM, non-gestational diabetes mellitus group; GDM, gestational diabetes mellitus group; SD, standard deviation; LHarea, levator hiatal area; cm^2, centimeter square; %, percentage; * calculated by (CR=100*(LHarea C-LHarea R)/LHarea R); **calculated by (DR = 100*(LHarea D-LHarea R)/LHarea R); ***calculated by (DC = 100*(LHarea D-LHarea C) /LHarea C). Data are in mean and standard deviation. Based on Mann–Whitney U test.

Table 3 - Interaction effect and comparison between groups (non-GDM and GDM) independently time points and time points (24-30 weeks of gestation, 38-40 weeks of gestation and 6-12 months postpartum) independently groups, considering the LHarea measurements of pelvic floor muscle (PFM) on rest, contraction, distension and mobility in absolute values (cm^2) and variation (%).

Variables	non-GDM (n=28)			GDM (n=20)			ANOVA repeated measures		
	1st time point	2nd time point	3rd time point	1st time point	2nd time point	3rd time point	*P* Interaction	*P* Group	*P* Time points
	Mean time ± SD			Mean time ± SD					
Rest (R) LHarea (cm^2)	12.48±0.52	15.14±0.40	11.60±0.46	13.18±0.60	13.72±0.46	13.27±0.53	< 0.001	0.588	< 0.001
Contraction (C) LHarea (cm^2)	9.98±0.43	11.00 ±0.50	8.63±0.60	10.83±0.50	12.59±0.59	11.29±0.70	0.246	0.001	0.003
Distension(D) LHarea (cm^2)	15.84±0.58	19.86 ±0.44	12.20±0.61	15.79±0.67	16.97±0.51	13.95±0.71	< 0.001	0.455	< 0.001
Contraction/Rest (CR) LHarea (%) *	-19.05±2.40	-26.49 ±4.00	-24.17±4.23	-16.98±2.79	-6.82±4.65	-14.60±4.92	0.080	0.003	0.781
Distension/Rest (DR) LHarea (%) **	29.45±3.58	33.21 ±3.99	8.11±4.79	21.21±4.16	25.21±4.64	6.34±5.57	0.657	0.140	< 0.001
Mobility (DC) LHarea (%) ***	60.97±4.91	91.36±11.97	45.31±6.40	49.72±5.70	45.13±13.91	33.38±7.44	0.087	0.006	0.010

non-GDM, non-gestational diabetes mellitus group; GDM, gestational diabetes mellitus group; SD, standard deviation; LHarea, levator hiatal area; cm^2, centimeter square; %, percentage; * calculated by (CR=100*(LHarea C-LHarea R)/LHarea R); **calculated by (DR = 100*(LHarea D-LHarea R)/LHarea R); ***calculated by (DC = 100*(LHarea D-LHarea C) /LHarea C). Means and standard deviation according to groups and time points of observation and comparisons by ANOVA for repeated measures ANOVA models with repeated measures were adjusted to explain the LHarea as a function of the non-GDM and GDM groups throughout the observation time points. When the hypothesis of sphericity was rejected by the Mauchly test, the interaction effect and main effects of the model were tested using the Greenhouse-Geisser test.

Artigo 2

Brief Report elaborado de acordo com as normas de publicação da revista PLOS ONE para a qual foi submetido. (Anexo 5)
Qualis A2 Med III – FI: 2,74 https://journals.plos.org/plosone/s/journal-information

Title Page

Dynamic Protocol for Pelvic Floor Muscles Assessment by Transperineal Ultrasound: A New Approach of the Diamater Study Group

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Abstract

Background: To develop an ultrasonographic (US) dynamic protocol, the PFM-US Diamater's Protocol, for the assessment of pelvic floor muscles (PFM) performance; and to propose formulas for the calculation of PFM's resting, relaxation, contractility, distensibility and mobility indexes. Also, to develop PFM assessment protocols based on PFM-US Diamater's Protocol and demonstrating its application and interpretation in a hypothetical sample.

Methods: The protocol was designed based on the importance of including, in addition to the baseline rest measurement, the rest measurements before and after each performed activity. A cross-sectional study was conducted at Research Center of Botucatu Medical School, Botucatu, SP, Brazil. Fifteen asymptomatic Caucasian women between 20-30 years were included to composite the database with measurements of five hypothetical participants in the demonstrative tutorial for application and interpretation of the PFM-US Diamater's Protocol.

Results: PFM-US Diamater's Protocol was developed to be used both in clinical or research practices using transperineal ultrasound, being adapted according to the assessor needs. The protocol was designed and presented in schematic drawing with balloons representing different PFM activities. Connecting the balloons, arrows indicate the formulas to be applied, in absolute values for linear measurements (cm), area measurements (cm^2) and in percentage values (%) for proportional differences between measurements. Based on these specific activities, formulas for PFM indexes calculations were suggested. Four suggestions of protocols were presented in this study, combining different performances like PFM resting, contraction and distension. The application of the proposal protocol on a hypothetical sample, demonstrated that the results obtained from different formulas were different, since no significant variability was found when used a formula based on absolute values in opposition to the percentage values.

Conclusions: PFM-US Diamater's Protocol was successfully developed for assessing PFM performance by ultrasound. The demonstrative tutorial on how to apply and interpret different PFM performances indexes were also demonstrated through one of the four assessment protocols.

Keywords: Pelvic floor; Physical therapy; Muscle contraction; Rehabilitation; Ultrasonography; Valsalva maneuver

Background

Pelvic floor muscles (PFM) represent a critical element in pelvic organ support, providing active support both at rest and during activity(1,2). A coordinated and effective PFM contraction(3) is related to the maintenance of micturition, evacuation and sexuality functions. On the other hand, a dysfunctional PFM can result in symptoms such as impaired voiding or defecation, pelvic pain, and sexual dysfunction(1,4,5). Additionally, an adequate PFM distensibility may favor labor delivery and will probably reduce the incidence of levator ani muscles injuries(6,7).

Based on these facts, the assessment of PFM performance is recommended by the International Continence Society and International Urogynecological Association(8), which can be performed by several methods, including transperineal ultrasound(9). The most important thing is that PFM assessment must include the evaluation of PFM function at rest as well as during dynamic activities, like contraction and distension(10).

To date, no studies have been found that show us a proposal for assessing the performance of the PFM in a dynamic and sequential way of its different activities as a whole, as well as with intermediate rest measure between all these activities performed and specific formulas for their interpretation. In this context, analyzing the PFM performance with reliable, objective, visible and real-time ultrasonography measurements is an alternative method for the guidance of clinical and scientific practice in preventive and therapeutic care.

Therefore, this study attempted to develop an US dynamic protocol based on the experience of the Diamater Study Group for the assessment of PFM performance during different activities and to propose formulas for the calculation of PFM resting, relaxation, contractility, distensibility and mobility indexes.

Methods

Measures and procedures

PFM-US Diamater's Protocol development

The Diamater is a group of interdisciplinary researchers who study biomarkers involved in female pelvic floor myopathy using different PFM assessment methods for a comprehensive knowledge of PFM static and dynamic functions.

Based on this, the PFM-US Diamater's Protocol was proposal to evaluate the performance of PFM in their different activities, using a two, three or four-dimensional transperineal ultrasound assessment. Additionally, mathematical formulas were developed to calculate the rest variation, relaxation, contractility, distensibility indexes and also the activity variation index between similar activities and mobility index related to the muscle excursion between opposite activities. These formulas can be applied for any ultrasonographic measurement, including levator hiatal area and anteroposterior / transverse diameters, for example. In this context, indexes can be calculated in absolute values for linear measurements (cm) and area measurements (cm^2), and/or percentage values (%) for all levator hiatal dimensions' measurements.

The protocol was designed based on the importance of including, in addition to the baseline rest measurement, the rest measurements before and after each performed activity. This concept will allow an expanded and detailed analysis of the PFM performance between rests, between activities and rest as well as between similar and/or opposed activities (contraction and distension). In addition, we consider that the PFM-US Diamater's Protocol is dynamic, since its steps can be organized according to the assessor needs, as well as it can be used by either a researcher or clinician.

It is worth noting that the final version of the PFM-US Diamater's Protocol was obtained after revision from three external voluntary assessors: one with clinical

expertise (M.G.O.), one with research expertise (C.B.P) and another without expertise in PFM ultrasound assessment (A.A.P).

Protocols based on PFM-US Diamater's Protocol

Demonstrative protocols based on the PFM-US Diamater's Protocol were proposed in this cross-sectional study, considering the combination of different PFM activities, that is, rest, contraction (tonic and phasic)(3) and distension (Valsalva maneuver or Straining)(10).

PFM-US Diamater's Protocol application and interpretation demonstrative tutorial

The STROBE statement was used as a guide to report this study. In order to demonstrate the application and interpretation of the PFM-US Diamater's Protocol, data were collected from a reference sample following one of the protocols developed in this study. The data collection was performed at the Research Center of Botucatu Medical School / UNESP / São Paulo, Brazil, from November 2019 to February 2020. Fifteen asymptomatic Caucasian women between 20-30 years old were included in this analysis.

This study was approved by the Institutional Ethical Committee (CAAE: 82225617.0.0000.5411) and the written informed consent was obtained from all volunteers. For application and interpretation of this demonstrative tutorial, only the levator hiatal area measurement (cm^2) obtained by 3D transperineal ultrasound was considered. Imaging data sets were taken following these steps: rest, maximal voluntary PFM contraction, rest and maximal Valsalva maneuver. The levator hiatal area measurements of these 15 participants were generated from the descriptive

summaries based on the variation range of the calculation of the mean and extremes (minimum and maximum) of the values of the hiatal area (cm^2) of each position obtained. To demonstrate the application and interpretation tutorial based on real values, these descriptive summaries were used for simulation considering all performances, thus resulting in the database with measurements of five hypothetical participants. The application of this bank respected both the average and the amplitude of the data and simulated the behavior and distribution of the real values of the levator hiatal area.

Data analysis

An interpretative analysis of the demonstrative tutorial related to the results of the obtained indexes was performed and were presented in descriptive mode.

Results

PFM-US Diamater's Protocol

The PFM-US Diamater's Protocol was developed and presented in schematic drawing in order to evaluate PFM performance in their different activities, as shown in figure 1. Inside the balloons, it is possible to visualize the sequence of PFM activities that were performed and the arrows connecting the balloons indicating the presented formula. In addition, the lines of the connecting arrows contain mathematical formulas for indexes calculations, which can be obtained in absolute values measurements (cm or cm^2) or percentage values (%) for proportional differences between measurements. In this way, our protocols present the possibility to calculate the rest variation, relaxation, contractility, distensibility indexes, activity variation index and mobility index. The legend of the PFM-US Diamater's Protocol includes all the abbreviations and their

respective descriptions (Figure 1). PFM-US Diamater's Protocol can be used in clinical or research practices using ultrasound, being adapted according to the assessor needs.

Protocols based on PFM-US Diamater's Protocol

Additionally, four protocols were developed as examples from the PFM-US Diamater's Protocol (see them in Supplies Material figures), considering different activities combinations between PFM rest, contraction and distention. In this way, abbreviations and numbers have been replaced according to each proposed protocol.

Note that when the protocols have the same activities in a roll, the activity's numbers were sequential. When the activities were opposites, the numbers were not sequential and they followed the sequence of the respective activity.

PFM-US Diamater's Protocol application and interpretation demonstrative tutorial

Table 1 shows the results related to the application and interpretation of the demonstrative tutorial on our hypothetical sample. For this demonstration, levator hiatal area measurements were used.

The application of PFM-US Diamater's Protocol was demonstrated in accordance with Protocol 1, and the indexes were calculated in absolute (cm^2) and percentage (%) values. When compared the results, the calculations in absolute value did not show significant variability in opposite of the interpretation in percentage values where it was observed difference in all performances of the PFM among the participants (Table 1).

Discussion

In the present study, the calculation of the levator hiatal area in absolute indexes (cm^2)

did not show variability in this hypothetical sample, unlike the percentage index. Thus, the interpretation based on absolute indexes suggest that the participants presented the similar performances capability. On the other hand, considering percentage indexes analysis, we infer that PFM performances capability were different.

These findings suggest that depending on the chosen analysis method, the assessor will have different interpretations, however, both can be used in clinical practice or research in accordance of the proposal aim(7). However, we would like to emphasize that both measurements are necessary to be taken into account during the assessment of PFM performance, since a deficient PFM relaxation can occur between sequential activities. In this context, the index of some activity can be over or underestimated. It is noteworthy that depending on the activity performed and the formula applied, the results can generate positive or negative values. The negative values are related to the decrease in hiatal area and the positive values are related to the increase in hiatal area. After the application of this protocol in this hypothetical sample, it was observed that the results may be different depending on the applied formula using cm^2 or %.

The design of this study does not prove whether there will be differences in results with the use of this protocol in relation to protocols that already exist in the literature or even if this protocol is better for evaluating the performance of PFM. Thus, future studies with large simulation are recommended, in an attempt to investigate the indexes of PFM performance in different conditions.

Conclusions

PFM-US Diamater's Protocol was successfully developed for assessing PFM performance by ultrasound. The tutorial on how to apply and interpret different PFM

performances indexes were also demonstrated through one of the four assessment protocols.

Abbreviations:

US: ultrasonographic; PFM: pelvic floor muscles; cm: centimeter; cm^2: square centimeter; %: percentage; A_1: activity 1; A_2: activity 2; MI: mobility index; D_1: distension 1; CI_1; contractility index 1; R_b: Basal rest; C_1: contraction 1; DI_1: distensibility index 1: R_1: rest 1.

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Availability of data and materials

Please contact the corresponding author for data requests.

Authors´ contributions

FAP, AMPB and MVCR.: Project development and manuscript writing; FAP, AMPB and NM Project development, data management, data analysis, manuscript writing; FAP, AMPB, HRCN: Project development, statistical data analysis and manuscript

writing, editing and revisions. CISF: Project development and manuscript writing; CBP. HCMB and Diamater Study Group: Project development and manuscript writing. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study was approved by the Institutional Ethical Committee (CAAE: 82225617.0.0000.5411) and the written informed consent was obtained from all volunteers.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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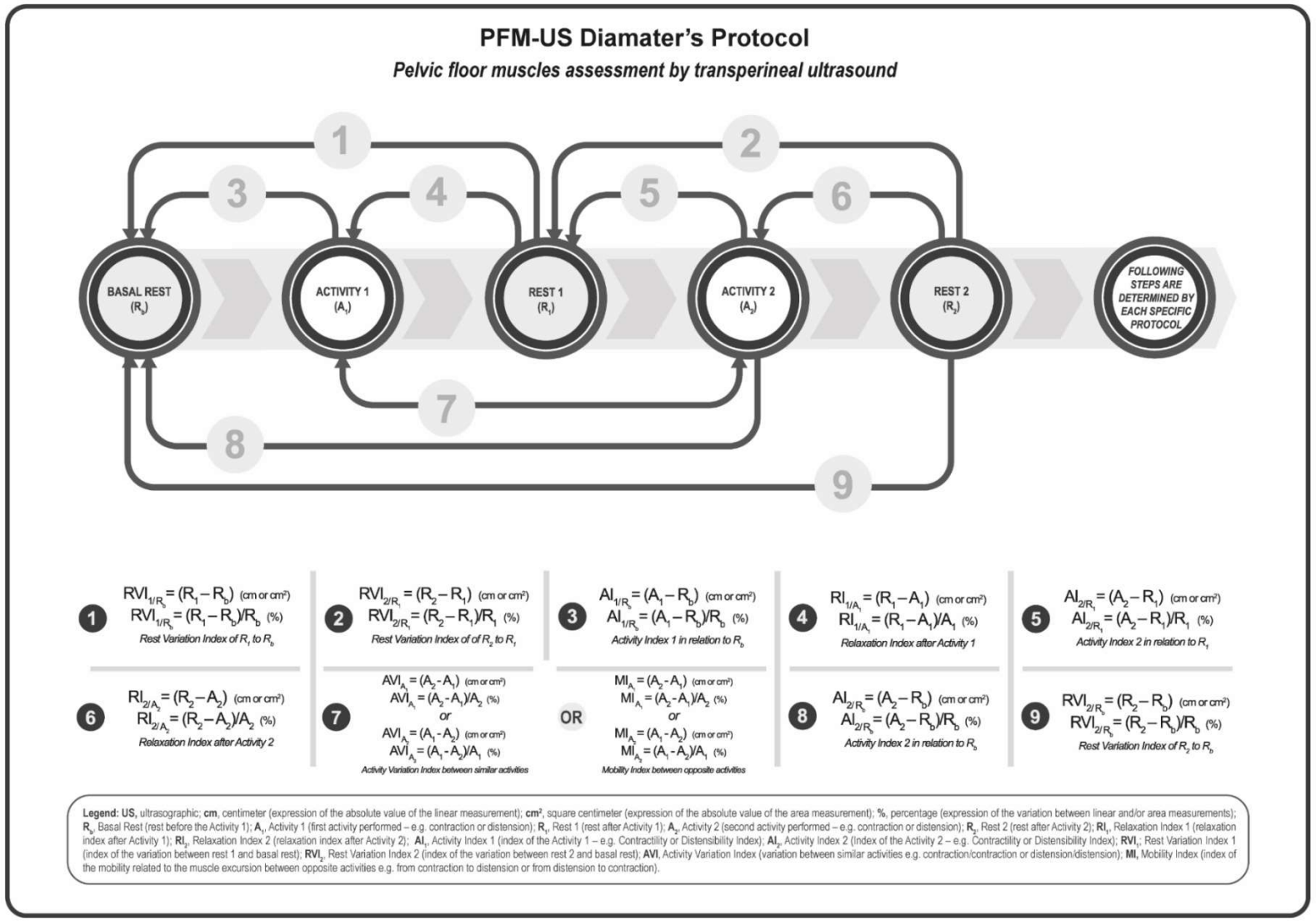

Figure 1 - Pelvic floor muscles assessment by transperineal ultrasound: PFM-US Diamater's Protocol**.**

Table 1: PFM-US Diamater's Protocol application and interpretation demonstrative tutorial in the hypothetical sample.

Variables of pelvic floor muscles performance		**Participants**					**min**	**max**	**range**
Levator Hiatal area measurements (cm^2)		**1**	**2**	**3**	**4**	**5**			
Basal Rest (R_b)		7,00	8,00	9,00	10,00	11,00			
Contraction 1 (C_1)		5,00	6,00	7,00	8,00	9,00			
Rest 1 (R_1)		7,01	8,01	9,01	10,01	11,01			
Distension 1 (D_1)		10,00	11,00	12,00	13,00	14,00			
Rest 2 (R_2)		8,00	9,00	10,00	11,00	12,00			
Indexes (cm^2 and %)	**Formula**								
Contractility Index 1 (CI_1) in relation to R_b	$CI_{1/Rb}=(C_1–R_b)$ (cm^2)	-2,00	-2,00	-2,00	-2,00	-2,00	-2,0	-2,0	0,00
	$CI_{1/Rb}=(C_1–R_b)/R_b$ (%)	-28,57	-25,00	-22,22	-20,00	-18,18	-28,57	-18,18	10,39
Relaxation Index after C_1	$RI_{1/C1}=(R_1–C_1)$ (cm^2)	2,01	2,01	2,01	2,01	2,01	2,01	2,01	0,00
	$RI_{1/C1}=(R_1–C_1)/C_1$ (%)	40,20	33,50	28,71	25,13	22,33	22,33	40,20	17,87
Distensibility Index 1 (DI_1) in relation to R_1	$DI_{1/R1}=(D_1–R_1)$ (cm^2)	2,99	2,99	2,99	2,99	2,99	2,99	2,99	0,00
	$DI_{1/R1}=(D_1–R_1)/R_1$ (%)	42,65	37,33	33,19	29,87	27,16	27,16	42,65	15,50
Distensibility Index 1 (DI_1) in relation to R_b	$DI_{1/Rb}=(D_1–R_b)$ (cm^2)	3,00	3,00	3,00	3,00	3,00	3,00	3,00	0,00
	$DI_{1/Rb}=(D_1–R_b)/R_b$ (%)	42,86	37,50	33,33	30,00	27,27	27,27	42,86	15,58
Relaxation Index 2 (RI_2) after D_1	$RI_2/_{D1}=(R_2–D_1)$ (cm^2)	-2,00	-2,00	-2,00	-2,00	-2,00	-2,00	-2,00	0,00
	$RI_{2/D1}=(R_2–D_1)/D_1$ (%)	-20,00	-18,18	-16,67	-15,38	-14,29	-20,00	-14,29	5,71
Rest Variation Index 1 (RV_1) of R_1 to R_b	$RVI_{1/Rb}=(R_1–R_b)$ (cm^2)	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,00
	$RVI_{1/Rb}=(R_1–R_b)/R_b$ (%)	0,14	0,12	0,11	0,10	0,09	0,09	0,14	0,05
Rest Variation Index 2 (RVI_2) of R_2 to R_1	$RVI_{2/R1}=(R_2–R_1)$ (cm^2)	0,99	0,99	0,99	0,99	0,99	0,99	0,99	0,00
	$RVI_{2/R1}=(R_2–R_1)/R_1$ (%)	14,12	12,36	10,99	9,89	8,99	8,99	14,12	5,13
Rest Variation Index 2 (RVI_2) of R_2 to R_b	$RVI_{2/Rb}=(R_2–R_b)$ (cm^2)	1,00	1,00	1,00	1,00	1,00	1,00	1,00	0,00
	$RVI_2/R_b=(R_2–R_b)/R_b$ (%)	14,29	12,50	11,11	10,00	9,09	9,09	14,29	5,19
Mobility Index (MI) from D_1 to C_1	$MID_1/C_1=(D_1- C_1)$ (cm^2)	5,00	5,00	5,00	5,00	5,00	5,00	5,00	0,00
	$MID_1/C_1=(D_1- C_1)/D_1$ (%)	50,00	45,45	41,67	38,46	35,71	35,71	50,00	14,29
Mobility Index (MI) from C_1 to D_1	$MIC_1/D_1=(C_1- D_1)$ (cm^2)	-5,00	-5,00	-5,00	-5,00	-5,00	-5,00	-5,00	0,00
	$MIC_1/D_1=(C_1- D_1)/C_1$ (%)	-100,00	-83,33	-71,43	-62,50	-55,56	-100,00	-55,56	44,44

PFM, pelvic floor muscles**; US**, ultrasonographic; **min**, minimum; **max**, maximum; **cm^2**, square centimeter; **%**, percentage.

Supplies Material: Protocols based on PFM-US Diamater's Protocol

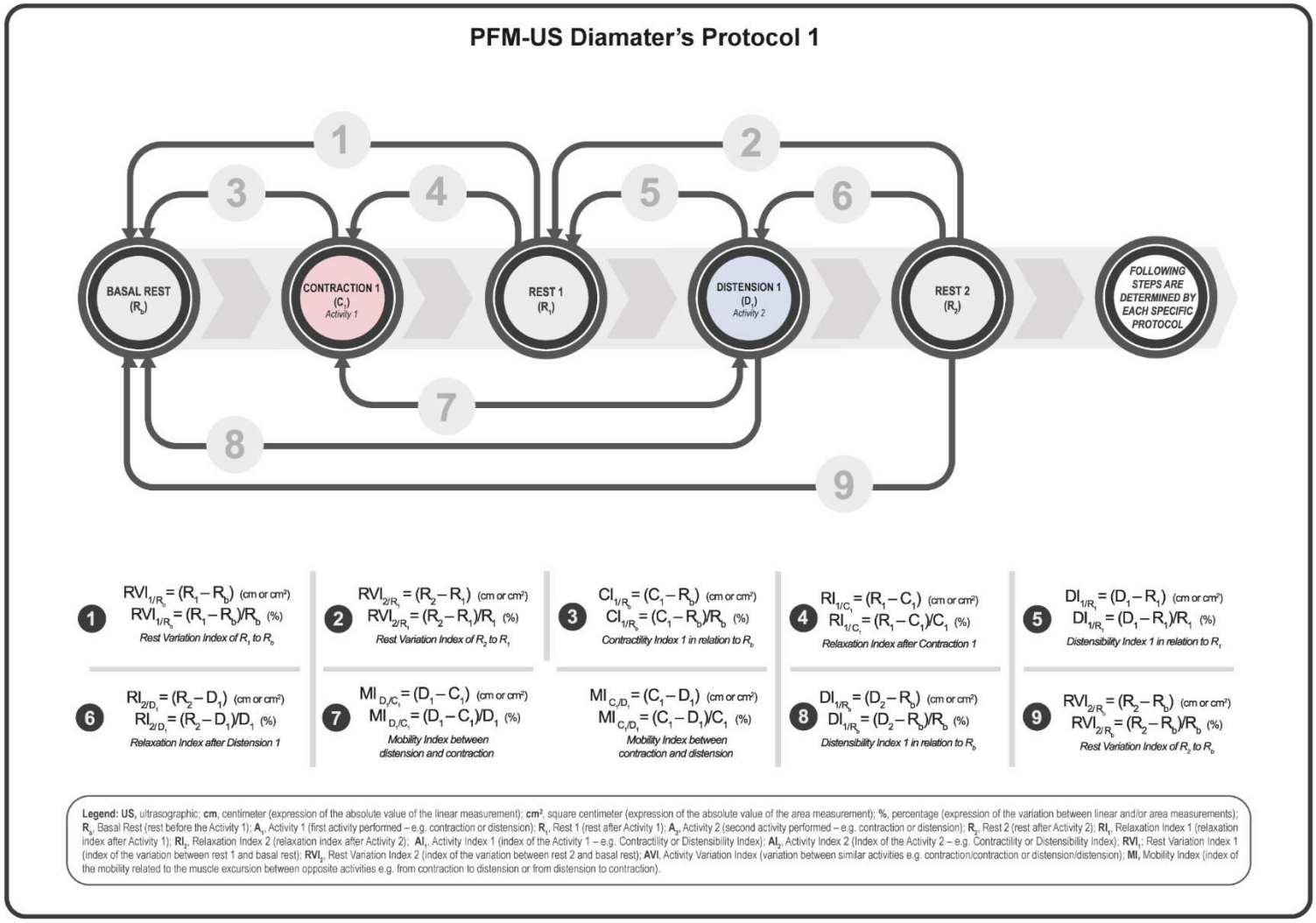

Figure 2 - Pelvic floor muscles assessment by transperineal ultrasound: PFM-US Diamater's Protocol 1.

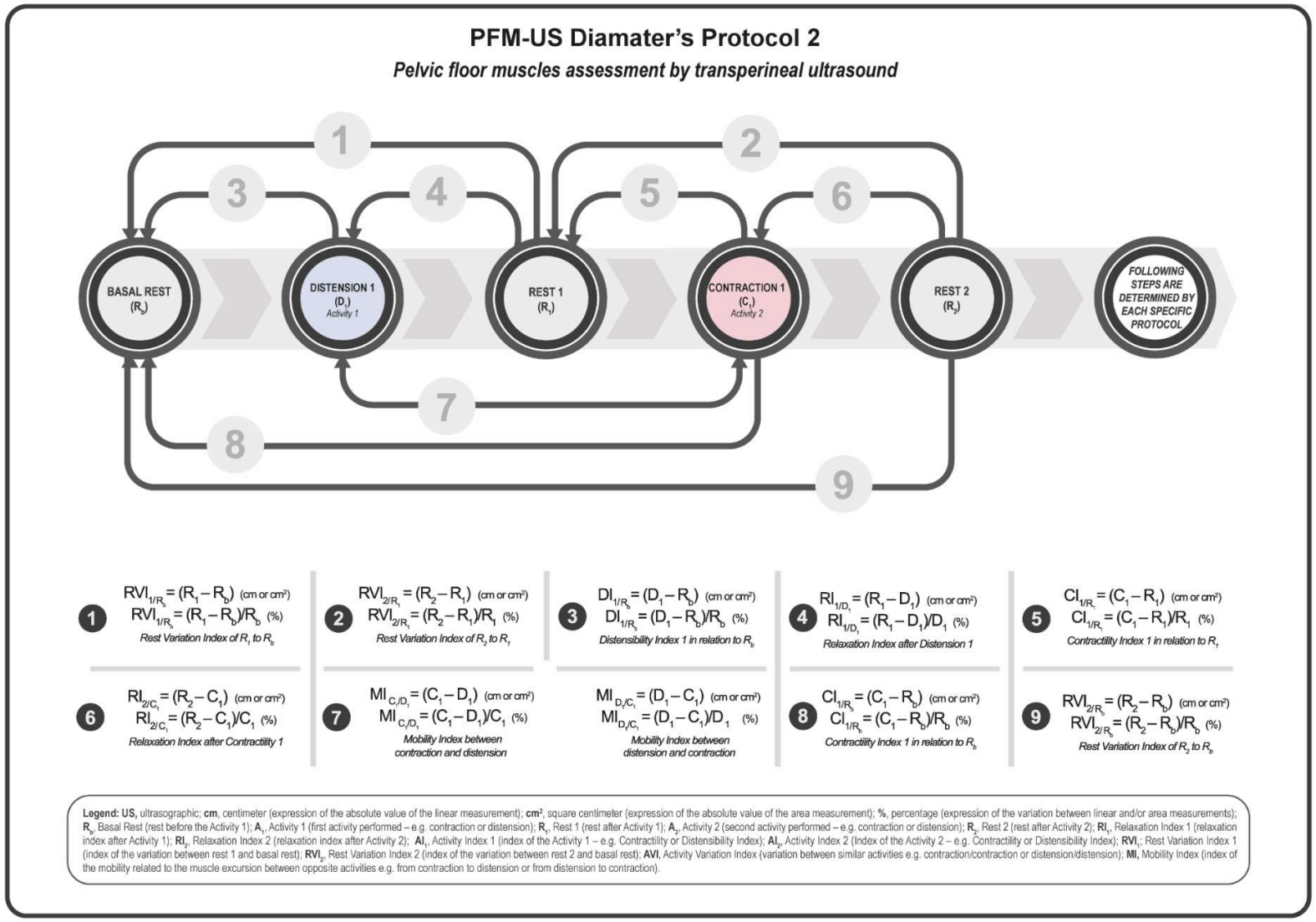

Figure 3 - Pelvic floor muscles assessment by transperineal ultrasound: PFM-US Diamater's Protocol 2.

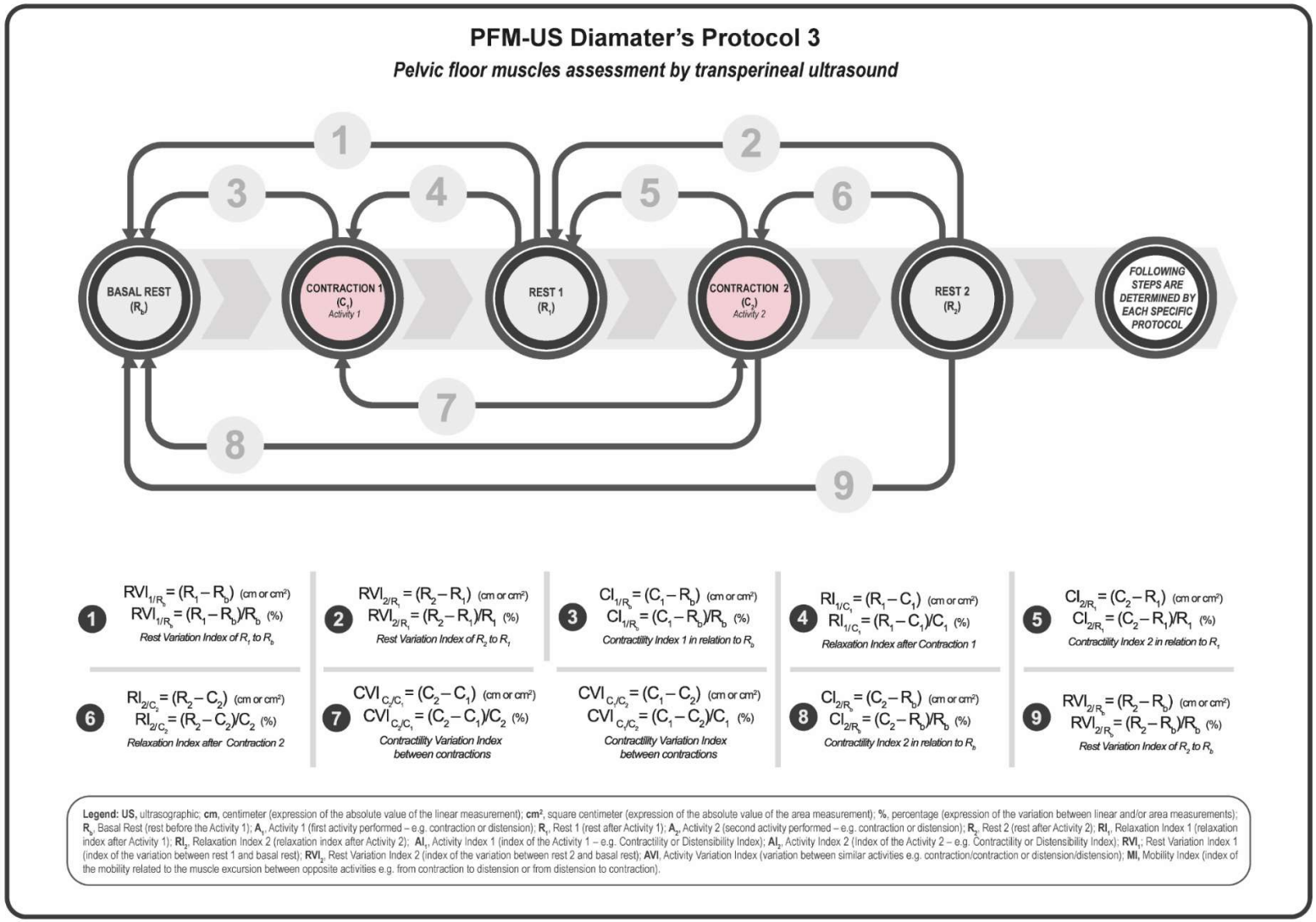

Figure 4 - Pelvic floor muscles assessment by transperineal ultrasound: PFM-US Diamater's Protocol 3.

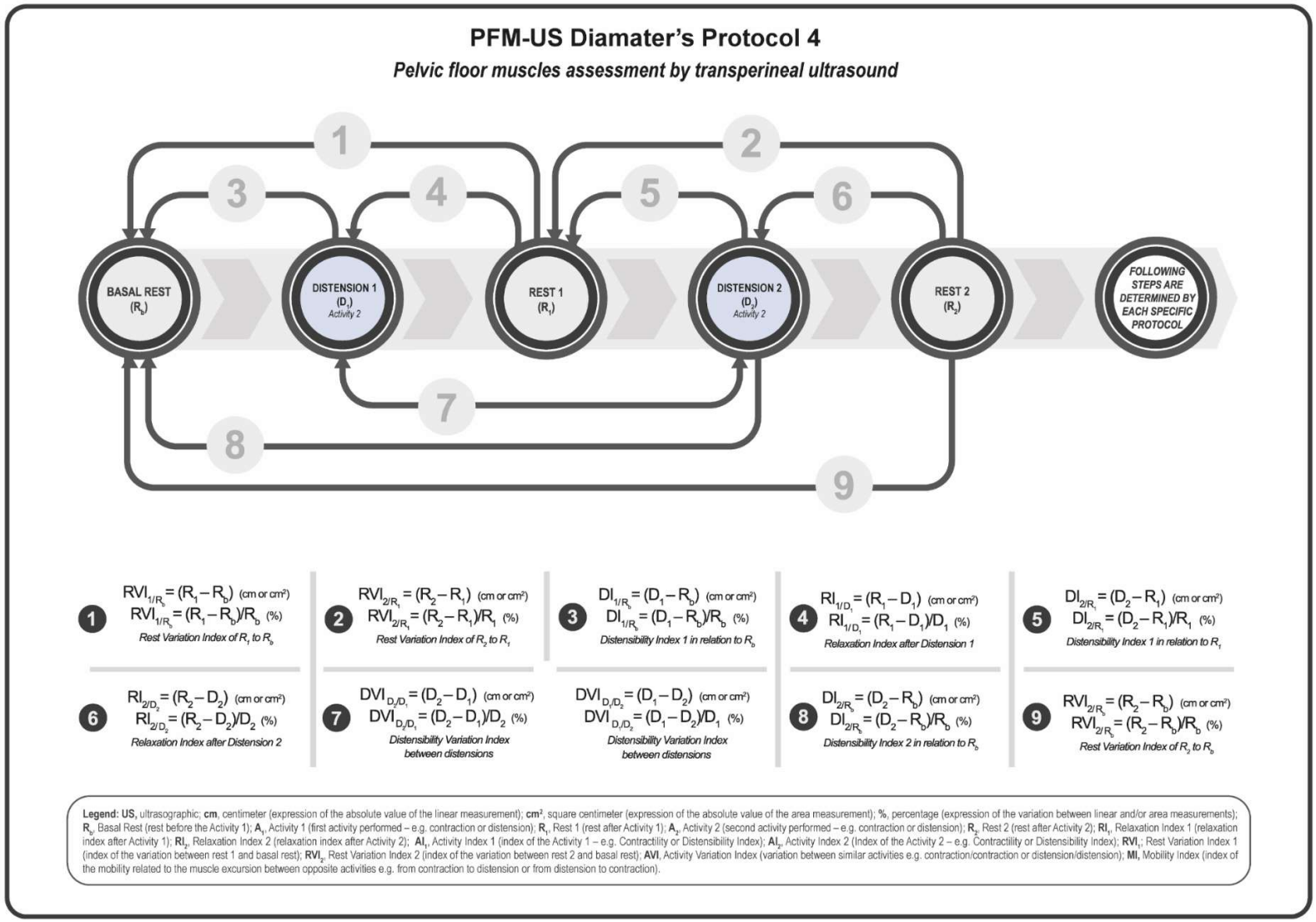

Figure 5 - Pelvic floor muscles assessment by transperineal ultrasound: PFM-US Diamater's Protocol 4.

Artigo 3

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Title Page

Distinct interpretations of pelvic floor muscle performance assessed through the PFM-US Diamater´s Protocol in pregnant women with and without pregnancy-specific urinary incontinence.

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Abstract

Objective: To interpret the pelvic floor muscle (PFM) performance of pregnant women with or without Pregnant Specific Urinary Incontinence (PS-UI), applying different analysis by the PFM-US Diamater´s Protocol.

Design: A cross-sectional study

Setting: Perinatal Research Center (PRC), São Paulo State University (UNESP), Botucatu Medical School, Brazil, by the Diamater Study Group.

Population: Data collection performed from November 2019 to February 2020. Including 49 pregnant women with PS-UI or non-PS-UI

Methods: Pregnant women > 18 years, primigravid, were invited to participate from 24 weeks of gestation and the informed consent to participate was obtained. Demographic data were collected. The PFM three-dimensional TPUS (3D-TPUS) images were acquired following the PFM-US Diamater's Protocol 1. Analyses were performed with SPSS Statistics 22.0 software.

Main outcome measures: The performance of PFM in relation to Levator Hiatal area (LHarea) measurements in absolute values and percentages evaluated by 3D-TPUS in women with PS-UI and without PS-UI.

Results: The LHarea measurements in absolute values (cm^2) in all PFM variables were greater in the PS-UI group. The variation index in absolute values (cm^2) presented lower variation index from rest 2 (post-distension) to rest 1(post-contraction) and from rest 2 to basal rest as well as a more negative relaxation index after distension in PS-UI group. Performing the same calculations in percentage (%), additional significant results for the comparisons between groups were showed. The mobility indexes and the distensibility index in relation to basal rest were also significantly lower in PS-UI. The comparison intragroup and between groups in absolute value (cm^2) were also demonstrated.

Conclusions: Pregnant women with PS-UI presented different PFM performance evaluated by 3D-TPUS compared to non-PS-UI. The interpretation of these differences is distinct depending of the formulas applied. Pregnant women with PS-UI present greater LHarea in all assessed activities as well as worse performance for PFM relaxation, contraction and distensibility.

Keywords: urinary incontinence, gestation, rest, pelvic floor muscle, ultrasound, function.

Tweetable abstract: Pregnant women with PS-UI performed differently in PFM activities when interpreted by the PFM-US Diamater's Protocol. Deserves further research and application.

Introduction

The involuntary urinary incontinence (UI)(1) hat started during pregnancy was termed pregnancy-specific UI (PS-UI)(2). Women who experience PS-UI have been shown to be more likely to develop UI later in life(2,3). PS-UI has been studied because this condition can reduce the quality of life in 54,3% of all pregnant women and interfere in several aspects of the maternal-fetal binomial(1,4).The prevalence of UI increases substantially during pregnancy(5), with prevalence rates varying between 20-67%(6,7).

Physiological changes during pregnancy, such as increasing pressure of the growing uterus and fetal weight on the pelvic floor muscle (PFM) throughout pregnancy, together with pregnancy-related hormonal changes such as increased progesterone, decreased relaxin, and decreased collagen levels, may lead to reduced strength and supportive and sphincteric function of the PFM. Pregnancy may be associated with the reduction of the PFM strength, which can lead to stress urinary incontinence (SUI)(8). The PFM plays an integral role in pelvic organ support both at rest and during activity. A coordinate and effective PFM is related to close the urethral sphincter when contracting(9) and an adequate PFM distensibility may favor labor delivery and will probably reduce the incidence of levator ani muscles injuries(10,11).

Based on these facts, the assessment of PFM performance has been recommended by the International Continence Society (ICS)(1) and International Urogynecological Association (IUGA)(12), which can be performed by several methods, including three-dimensional transperineal ultrasound (3D-TPUS)(13). This method is considered as a valuable and objective method in the urogynecological evaluation, allowing the assessment of pelvic floor anatomy and its functions and dysfunctions. The ultrasonography approach has become an important tool for prevention, therapeutic care and understanding of the importance of the PFM function

in different periods of a woman's life(14). Additionally, the most important thing is that PFM assessment must include the evaluation of PFM function at rest as well as during dynamic activities, like contraction and distension in a dynamic and sequential way.

Therefore, the aim of this study was to interpret the PFM performance of pregnant women with or without PS-UI, applying different analysis by the PFM-US Diamater´s Protocol.

Methods

Data sources

A cross-sectional study was conducted at the Perinatal Research Center (PRC), São Paulo State University (UNESP), Botucatu Medical School, Brazil, by the Diamater Study Group. The STROBE statement was used as a guide to report this study. The data collection was performed from 24 weeks of gestation from November 2019 to February 2020. In total, 49 pregnant women were included in this analysis and distributed into two groups: PS-UI (n=23) and non-PS-UI (n=26). This study was approved by the Institutional Ethical Committee of Botucatu Medical School, São Paulo State University (UNESP), Botucatu, São Paulo State, Brazil (CAAE: 82225617.0.0000.5411). The women were invited to participate during the waiting room for routine from 24 weeks of gestation at PRC and the informed consent to participate document from all participants included was obtained by following the ethical guidelines (Resolution 466/2012) of the Brazilian Health Council.

Study population

The inclusion criteria were pregnant women over 18 years old, primigravid, continent or incontinent with specific onset in the current pregnancy. Women with pre-pregnancy UI, known type 1, type 2 diabetes or gestational diabetes mellitus and those who

refused to participate were not included in this study. The participants that during the pelvic floor assessment were not able to perform a correct PFM contraction or a maximal Valsalva maneuver as well as the ones in which ultrasound images presented technical failure was excluded. A questionnaire was also applied to collect the following data: ethnicity, smoking in pregnancy, physical activity in pregnancy, education level, age in pregnancy, weeks of gestation, body mass index (BMI) pre-pregnancy and in pregnancy (BMI= weight[kg]/ height^2[m]) and also maternal weight gain (kg).

Measures

A physical examination was conducted by a physical therapist (Pinheiro, FA) with 8 years of experience on PFM training and examination. In the first physical examination step all participants were instructed about how to perform the following sequence: rest, PFM contraction and PFM distension by Valsalva maneuver. The technique of PFM contraction was explained by this verbal prompt: “Please squeeze your pelvic muscle, as though you were trying to hold in gas and as hard as you can, maintaining it as long as possible"(15). A PFM contraction was considered correct when the examiner observed the best cranial shift of the levator ani muscle (LAM) and when felt inward pressure or upward traction on the finger inserted in the vagina(16). For the PFM distension task, the participants were instructed to do a forced expiration and to push as during delivery for at least 6 seconds(17). A correct distension was confirmed by a caudodorsal displacement of the LAM(17).

After the confirmation that the participants were able to understand and perform all functions correctly, an experienced investigator (Sartorão Filho, CI) acquired the PFM three-dimensional TPUS (3D-TPUS) images. A GE Voluson I system with a RAB 2-6RS (2-6 MHz) curved array 3D transducer (GE Healthcare, Zipf, Austria) was used. The probe was covered with a condom and placed on the perineum in the sagittal

plane. The field of view angle was set to its maximum of 70° in the sagittal plane and 85° in the coronal plane(18). Imaging data sets were taken following the PFM-US Diamater's Protocol 1 (Figure 1). This protocol was designed based on the importance of including, in addition to the basal rest measurement, the rest measurements post each performed dynamic activity.

This dynamic concept allows an expanded and detailed analysis of PFM performance, since distinct interpretations can be performed between rests, between activities (contraction and distension) and rest as well as between opposed activities (contraction and distension). To evaluate the PFM performance at rest and during different activities, using a 3D-TPUS assessment, 5 different images in the following sequence and colors were collected: 1) a gray image at basal rest (R_b), with no PFM movement, that was acquired to be used as a standard basal measurement; 2) a blue image at maximal voluntary PFM contraction (C1); 3) a gray image at rest post-contraction (R_1), with no PFM movement, that was acquired to be used as an intermediate rest between the activities (contraction and distension); 4) a sepia image at maximal distension (D1) obtained during Valsalva maneuver; 5) a gray image at rest post-distension (R_2), with no PFM movement that was acquired to be used as a final rest after the distension activity.

At the end, the images were saved anonymously following the US procedures recommended by Dietz(19). The 3D-TPUS images were analyzed offline in a random order by anonymous code numbers generated by the software, by one investigator blinded to group allocation and background data. Analysis of the Levator Hiatal (LH) area was carried out using the 4D View program, version 14, Ext. 3 (GE Healthcare). The LHarea was determined in the axial plane of minimal hiatal dimensions(20) and was analyzed at rest and during the dynamic activities. Furthermore, mathematical formulas were applied to calculate the indexes of LHarea variation in absolute (cm^2)

and percentage (%) values. The details of these mathematical formulas are presented in figure 1.

Statistical analysis

Baseline characteristics were compared between non-PS-UI and PS-UI groups using a Chi-square and Fisher's exact tests for categorical variables and Mann–Whitney U for continuous variables. Comparison between groups in relation to LHarea measurements was analyzed by Student's t test. The LHarea index variations (both in absolute and percentage values) were compared between groups using the Mann–Whitney U non-parametric test. ANOVA models for repeated measures were adjusted to explain the LHarea measurements over the three resting moments for the non-PS-UI and PS-UI groups. The Student´s t test was applied to explain the LHarea measurements over the three resting moments between groups. Differences were considered statistically significant if $P < 0.05$. Analyses were performed with SPSS Statistics 22.0 software.

Results

In total, 49 pregnant women consented to participate in this study from November 2019 to February 2020 and were allocated in a non-PS-UI (n=26) group and in a PS-UI (n=23) group (Figure 3).

Table 1 summarizes the demographic information of the study population, being all baseline characteristics similar between groups.

The comparison of LHarea measurements in absolute values (cm^2) between groups, showed that PFM variables (basal rest, contraction, rest post-contraction, distension, rest post-distension) were significantly greater on the PS-UI group ($P < 0.001$, $P <$ 0001, $P < 0.001$, $P = 0.012$ respectively) (Table 2).

Table 3 presented the comparison of LHarea variation indexes in absolute values (cm^2) between groups. In this analysis, it was found that the PS-UI group presented lower variation index from rest 2 to rest 1 (*P* = 0.006) and from rest 2 to basal rest (*P* = 0.000), as well as a more negative relaxation index after distension (*P* = 0.004), when compared to the non-PS-UI group.

On the other hand, performing the same calculations with LHarea measurements in percentage (%), we found additional significant results for the comparisons between groups. The PS-UI group presented lower variation index from rest 2 to rest 1 (*P* = 0.002), more negative variation index of relaxation after distension (*P* = 0.015), lower mobility index from distension to contraction (*P* = 0.043) and from contraction to distension (*P* = 0.043), lower distensibility index in relation to basal rest (*P* = 0.003) and lower variation index from rest 2 to basal rest (*P* = 0.000), when compared to the non-PS-UI group (Table 4).

Table 5 presented the comparison of the LHarea intragroup, in absolute value (cm^2), at the three rest-time points (basal rest, rest 1- post-contraction and rest 2- post-distension). The non-PS-UI presented smaller LHarea measurement in basal rest and rest 1 compared to rest 2 (*P < 0.001*) and the PS-UI group presented basal rest measurement greater than rest 1 (*P = 0.002*).

Lastly, the comparison of the LHarea in absolute value (cm^2) between groups and for the three rest-time points demonstrated that in the non-PS-UI group, all LHarea rests measurements (basal rest, rest 1 and rest 2) were significant lower in relation to the PS-UI group (*P = 0.000, P = 0.000, P = 0.012 respectively)* (Table 6).

Discussion

The results obtained through this study indicate that pregnant women with PS-UI present greater LHarea in all assessed performance (rests, contraction and distension)

as well as worse performance for PFM relaxation, contraction and distensibility. Additionally, the significant differences in results between groups were more evident when percentage values were used for the mathematical formulas, demonstrating a more comprehensive analysis of PFM performance in different activities.

The difference found in PFM performance between pregnant women with PS-UI and non-PS-UI has already been reported in other previous studies(21,22). These results are already expected and are not surprising, since we have already well reported in the literature the important role of the PFM in maintaining female urinary continence(23–26), especially during the gestational period and postpartum(27,28). In the gestational period, in particular, PFM are more susceptible to functional decline due to the increasing pressure of the growing uterus and fetal weight on PFM throughout pregnancy, added to the pregnancy-related hormonal changes. These pregnancy physiological adaptations may lead to PFM strength reduction, impacting on their supportive and sphincteric functions(21). Thus, pregnancy, by itself, contributes to the development of PFM dysfunctions, including PS-UI, which tends to worsen with gestational age and multiparity(29–31), reaching an incidence of 39.76% among pregnant women in the third trimester(32).

Given the above, the PFM performance during the pregnancy-puerperal cycle is important to be assessed in order to implement adequate preventive and/or corrective measures. Through the PFM dynamic functional assessment model used in this study, it was possible to analyze the isolated measures in absolute values and/or percentages; as well as allowed to calculate the PFM indexes at rest (baseline or pre-activity), during activity (contraction or straining) and mobility (elasticity).

However, differences in the interpretation of results were observed when using absolute and percentages values. For example, when observing the PFM distensibility indexes in relation to baseline rest by means of percentage values, pregnant women

with PS-UI presented a significant reduction in PFM distensibility when compared to continent pregnant women. Through the absolute value analysis, this significant difference between groups was not observed. However, especially during the evaluation of pregnant women, PFM distensibility is an important variable in the preparation of PFM for vaginal delivery, since a non-relaxing levator ani muscle at rest and during Valsalva maneuver seems to get the active second stage of labor longer(10,33,34), increasing, consequently, the odds of perineal trauma(35) and levator ani muscle injuries(36).

Similarly, pregnant women with pregnancy-specific UI presented lower PFM mobility from distension to contraction and from contraction to distension, when the results were analyzed through percentage. These findings suggest failure in the dynamic functionality of PFM, which may be related to the clinical condition of PS-UI, as previously described in other studies(21,22). Thus, identifying such differences in PFM functionality between groups is relevant for more assertive measures during the clinical follow-up of pregnant women; as well as to contribute to the direction of future clinical research.

These differences in interpretation according to the calculations used are likely to occur because the functional assessment of PFM through ultrasound is based on the displacement of its anatomical structures(11). Thus, even a mild contractile effort or a mild straining can lead to a greater anatomical change due to the displacement resulting from a lower baseline. In other words, a more laxity and opened LH allows a greater reduction in its measurement when compared to a smaller levator hiatus. However, it does not mean that a stretched PFM will be capable of performing a greater narrowing of LH. In this context, calculating the activity index based on the proportion of change (percentage values) may be more appropriate to assess who had the greater PFM performance.

To conclude, based on the clinical and research experience of our Research Group and also on the observation of other studies' forms of analysis of PFM ultrasound, we wondered whether including the intermediate relaxations between dynamic activities would be different between pregnant women with and without PS-UI. The measures of intermediate rest tend to have a direct impact on the measure of PFM dynamic activity (either contraction and/or distension), since the activity index is based on the modification of a rest measure in relation to the measure of the activity. Usually, activity indexes are calculated in relation to the basal resting value, even when several dynamic activities are performed sequentially. However, this way of analysis can generate bias, especially when there is no complete PFM relaxation between activity 1 and activity 2. In this case, the activity index 2 may be underestimated if it is calculated with reference to the baseline rest. Thus, the choice of resting measure that will be used (either basal rest, or rest immediately before or after the performed activities) can interfere in the results.

In the present study, there were no apparent differences between groups when evaluating the index in absolute values of a given activity considering the baseline rest or the pre-activity rest. However, it is recommended that the researcher/clinician pay attention to these issues and assess which rest (baseline or pre-activity) will be considered for the analysis of a certain activity index (either contraction or distensibility), in order to not generate misleading results.

The mobility index between activities (from distension to contraction and from contraction to distension) and the distensibility index in relation to basal rest when evaluated in percentage there were notable differences between groups.

Main findings

This data set provides a unique insight into the PFM performance related issues with

distinct interpretations in PS-UI. In this cross-sectional study including 49 pregnant women, 46,9% reported PS-UI. We found that the absolute values of LHarea dimensions in basal rest, contraction, rest post-contraction, distension, rest post-distension, were greater in PS-UI when compared with non-PS-UI. The interpretation by variation indexes in absolute values, presented differences between groups in 3 of the 10 performances analyzed, being them, rest variation index from rest post-distension to rest post-contraction, relaxation index after distension and rest variation index from rest post-distension to basal rest. The interpretation of the results considering the variation indexes in percentage, we found differences in 6 of the same 10 performances analyzed, being them rest variation index from rest post-distension to rest post-contraction, relaxation index after distension, mobility index from distension to contraction, mobility index from contraction to distension, distensibility index in relation to basal rest and rest variation index from rest post-distension to basal rest.

Strengths and Limitations

The limitations of our study include the fact that, as a first study, no sample calculation was performed, and also the 3D-TPUS images were collected in just one sequence of activities of PFM, which could have been continued, in order to evaluate and compare with the protocol applied behavior of PFM more completely over time. Despite the limitations of the study, some strengths should be acknowledged. This study is the first report assessment that allowed us to evaluate the differences in the PFM performance when assessing the functional PFM variation indexes in absolute and percentage values. These findings may contribute and enhance future studies related to the analysis of PFM functionality. Additionally, the examiner who analyzed the ultrasonographic data sets was blinded to the participant's group allocation and the results were reviewed by a second investigator. Although we did not perform the

sample calculation, we applied the test to verify the power of this sample. As for the test power associated with the comparisons made, it is estimated that most comparisons between moments in relation to HA in general and stratified by PS-UI are between 0.73 and 0.99. Most comparisons between the PS-UI and non-PS-UI groups in relation to measures at rest are above 0.70 and most comparisons in relation to the indexes were above 0.60. Finally, the findings of this study should be considered as providing possible biomarkers of PS-UI.

Interpretation

This study used a dynamic PFM functional assessment model, which can be implemented both in scientific research and in clinical practice; as well as it can be adapted for use through several PFM evaluation methods and not only through transperineal ultrasonography.

Practical implications

The use of this evaluation model in clinical practice allows the identification of PFM performance failures during dynamic activities, which can compromise its functions and predispose to dysfunctions.

In the specific case of pregnant women, an adequate capacity for PFM contraction and relaxation will benefit the maintenance of urinary continence during pregnancy and, consequently, will reduce the incidence of UI in the postpartum period(37). Additionally, the adequate PFM distension capacity will contribute to the correct PFM relaxation during the second stage of labor, reducing its duration(10) and, consequently, reducing the incidence of perineal trauma; since longer duration of second stage of labor is associated with increased odds for both spontaneous perineal trauma (OR 1.45; 95% CI: 1.28-1.63) and obstetric anal sphincter injuries (OASIS) (OR 1.49; 95% CI: 1.13-

1.98)(35).

Research implications

Future studies should pay attention to the fact that different analysis may generate different results and conclusions if data are used in absolute (cm/cm2) or percentage (%) values. Additionally, intermediate restings should be considered to avoid underestimating the activity index assessed in consecutive tasks, especially when the intermediate relaxation (pre-activity relaxation) does not return to its baseline value. Consequently, a better understanding of the PFM functional alterations will be favored. However, it is worth noting that the choice of the best calculation method depends on what the researcher wants to demonstrate/analyze.

Future work

Future studies can use these different models to prove the existence of significant differences between the two forms of performance analysis and which one is better to answer the questions proposed in the different studies. It should be implemented in different populations to verify the difference, especially with regard to rest, when it comes to patients with pelvic floor disorders.

Conclusion

Pregnant women with PS-UI presented different PFM performance evaluated by 3D-TPUS compared to pregnant women non-PS-UI. The interpretation of these differences is distinct depending of the formulas applied. The results of variation index in percentage demonstrate differences in more variables when compared to variation index in absolute values. The results obtained through this study indicate that pregnant women with PS-UI present greater LHarea in all assessed activities as well as worse

performance for PFM relaxation, contraction and distensibility.

Disclosure of Interests

Authors have no conflicts of interest. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

Conception & planning: FAP, AMPB, NM, CISF, BJ;
Data collection: FAP, AMPB, CISF, ABMM, SKN, MJ, LT, CBP;
Formal analysis: FAP, AMPB, CISF, ABMM, SKN, MJ, BJ;
Writing original draft: FAP, AMPB; NM, MVCR;
Review & editing: FAP, AMPB, NM, MVCR, MJ, LT;
Supervision: AMPB, MVCR;
Resources: FAP, AMPB, ABMM, CBP, BJ, SKN, LT

Details of ethics approval

This study was approved by the Institutional Ethical Committee of Botucatu Medical School, São Paulo State University (UNESP), Botucatu, São Paulo State, Brazil (CAAE: 82225617.0.0000.5411).

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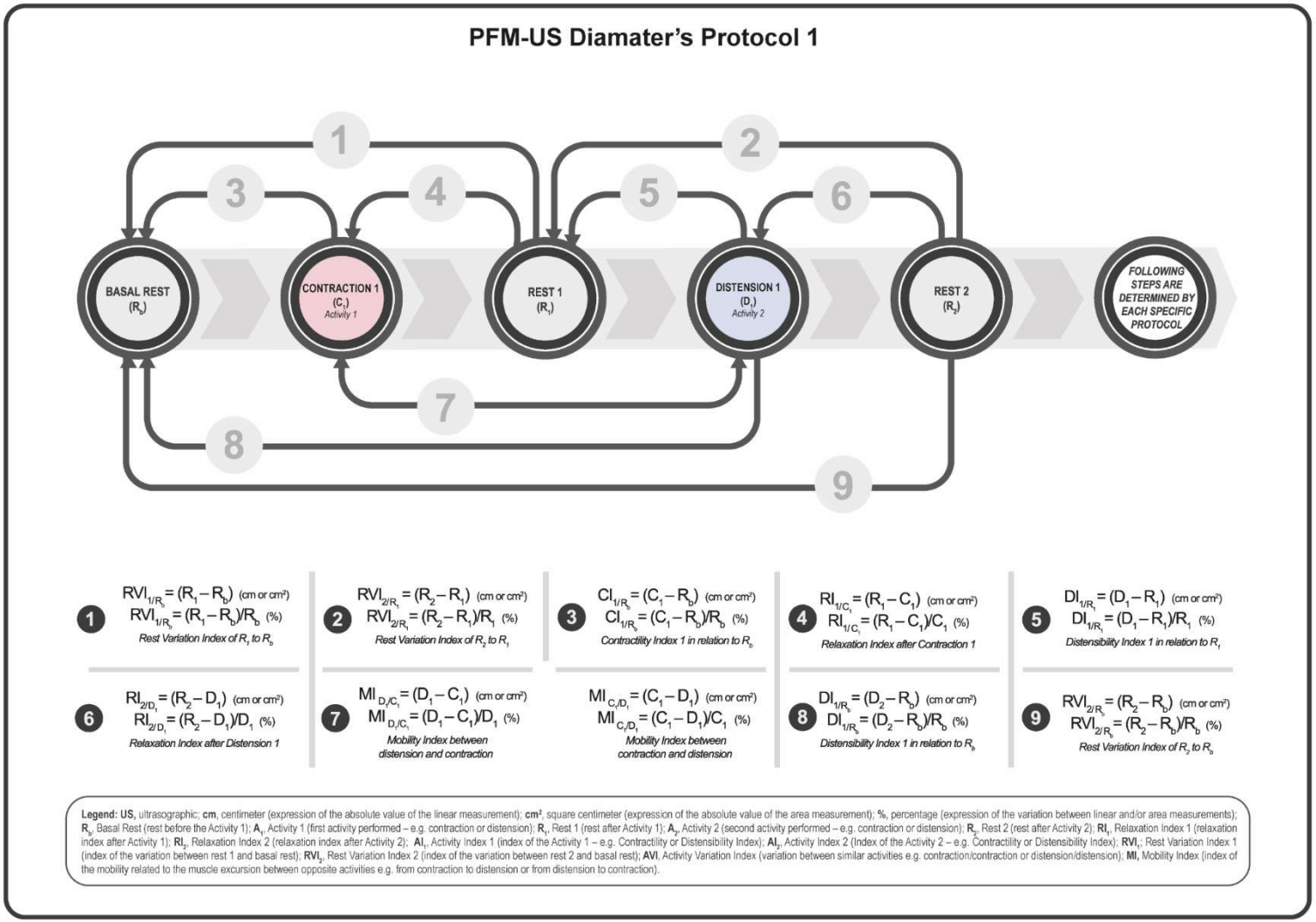

Figure 1 – Pelvic floor muscles assessment by transperineal ultrasound: PFM-US Diamater's Protocol 1 (publication in progress).

Figure 2 – Images collected in the following sequence and colors. (Source: Researchers)

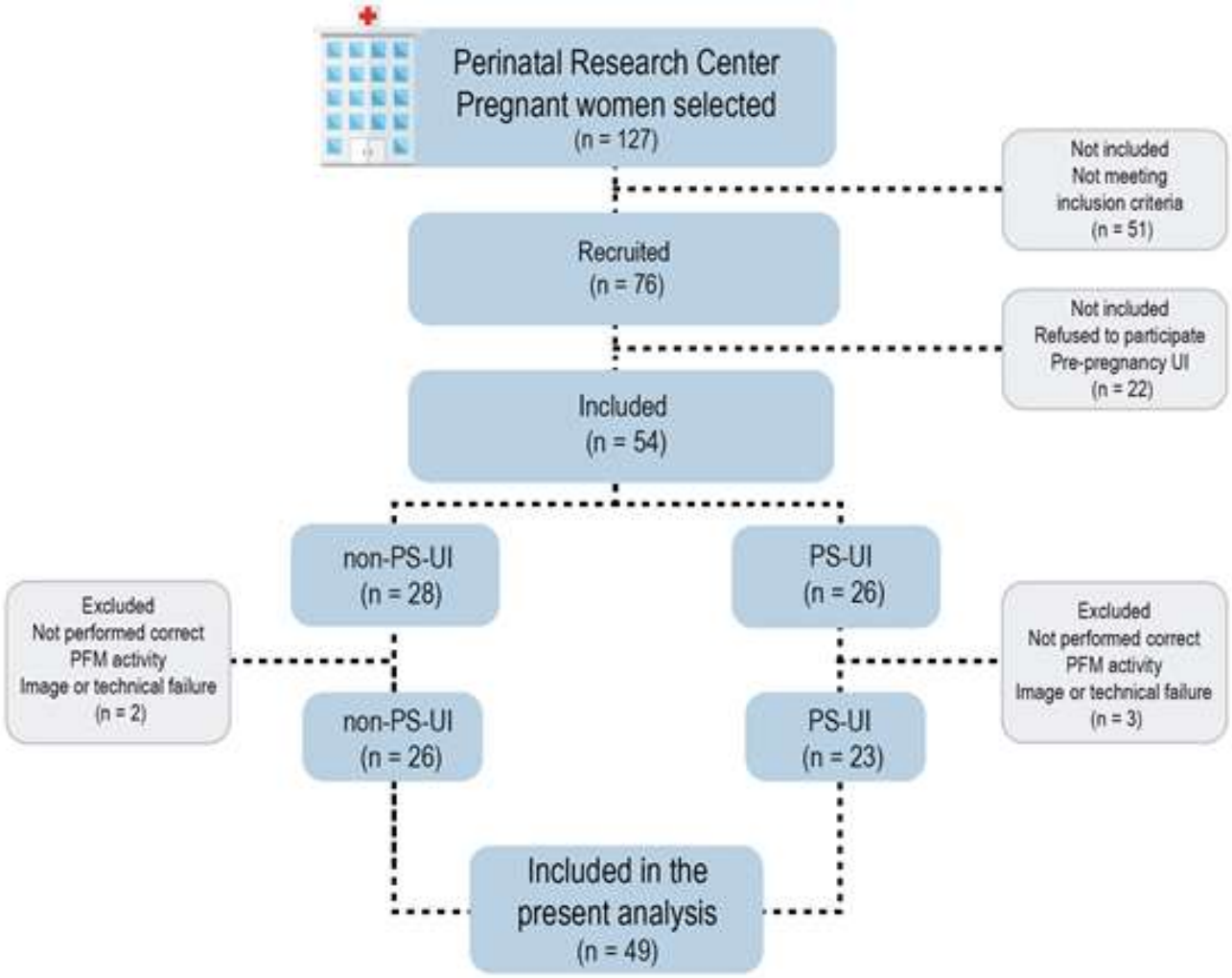

Table 1 – Demographic information of the study population.

Variables	**non-PS-UI (n=23)**					**PS-UI (n=26)**					
	N			%		N			%		***P***
Ethnicity											
Caucasian	19			73.1		17			73.9		1.000*
Other	7			20.9		6			26.1		
Smoking[1]	1			3.8		0			0		1.000*
Physical activity[1]	0			0		2			8.7		0.215*
Education level–min. High School	23			88.5		16			69.5		0.302*
	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max	
Age (years)[1]	27.5	26.5	4.6	21.0	38.0	27.9	28.0	5.9	20.0	39.0	0.827**
Weeks of Gestational	28.5	27.0	5.0	20.0	39.0	27.3	26.0	3.7	21.7	35.0	0.363**
BMI (kg/m^2) [0]	27.3	26.9	4.8	20.0	40.9	26.7	27.3	4.8	16.2	36.8	0.719**
BMI (kg/m^2) [1]	29.9	29.4	4.7	21.2	40.9	29.8	29.3	4.3	19.2	38.0	0.927**
Maternal weight gain (kg)	6.9	8.0	4.6	-1.0	17.0	6.7	7.5	6.8	-7.0	22.0	0.926**

Non-PS-UI, non-pregnancy specific-urinary incontinence; PS-UI, pregnancy specific-urinary incontinence; BMI, body mass index; 0, pre-pregnancy; 1, pregnancy, %, percentage; SD, standard deviation; min, minimum; max, maximum. *Based on Mann–Whitney U, **Chi- square and Fisher's exact. $P < 0.05$.

Table 2 – Comparison of levator hiatal (LH) area measurements in absolute values (cm^2) assessed during all PFM tasks between non- pregnancy specific-urinary incontinence (non-PS-UI) and pregnancy specific-urinary incontinence (PS-UI) groups.

Variables	non-PS-UI					PS-UI					
	mean	**median**	**SD**	**min**	**max**	**mean**	**median**	**SD**	**Min**	**max**	***P****
Basal Rest (R_b)	9.6419	9.6650	1.68443	6.17	13.76	13.4574	13.1200	1.91355	11.15	18.46	< 0.001
Contraction (C)	7.7650	7.9350	1.22001	5.43	9.31	10.6478	10.4400	.87392	9.40	12.70	< 0.001
Rest post-contraction (R_1)	9.3331	9.4500	1.33805	6.18	11.42	12.2813	12.2700	1.41812	10.10	15.73	< 0.001
Distension (D)	12.0623	11.9100	1.50868	9.83	16.70	15.1030	14.9500	2.26550	12.09	21.64	< 0.001
Rest post-distension (R_2)	11.6754	12.0200	2.01774	7.92	15.77	13.1352	13.1800	1.88652	10.80	18.88	0.012

PS-UI, pregnancy specific-urinary incontinence; Non-PS-UI, non-pregnancy specific-urinary incontinence; SD, standard deviation; min, minimum; max, maximum. *Based on Student's t- Test. $P < 0.05$.

Table 3 - Comparison of levator hiatal (LH) area variation indexes in absolute values (cm^2) between non- pregnancy specific-urinary incontinence (non-PS-UI) and pregnancy specific-urinary incontinence (PS-UI) groups.

Variables		**non-PS-UI**					**PS-UI**					
Hiatal Area	Formulas	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max	*p* *
Rest Variation Index 1 (RV_1) of R_1 to R_b	$RVI_{1/Rb}=(R_1–R_b)$ (cm^2)	-.309	-.390	.972	-2.340	1.430	-1.176	-.910	1.569	-5.880	1.080	0.054
Rest Variation Index 2 (RVI_2) of R_2 to R_1	$RVI_{2/R1}=(R_2–R_1)$ (cm^2)	2.342	1.945	2.175	-1.120	7.530	.854	.520	1.601	-.890	4.910	0.006
Contractility Index 1 (CI_1) in relation to R_b	$CI_{1/Rb}=(C_1–R_b)$ (cm^2)	-1.877	-1.710	1.459	-6.290	-.110	-2.810	-1.980	1.858	-8.140	-.540	0.070
Relaxation Index after C_1	$RI_{1/C1}=(R_1–C_1)$ (cm^2)	1.568	1.370	1.125	-.440	4.030	1.633	1.120	1.604	-1.590	5.410	0.968
Distensibility Index 1 (DI_1) in relation to R_1	$DI_{1/R1}=(D_1–R_1)$ (cm^2)	2.729	2.830	1.488	-.590	5.280	2.822	2.290	1.883	-.180	6.550	0.779
Relaxation Index 2 (RI_2) after D_1	$RI_2/_{D1}=(R_2–D_1)$ (cm^2)	-.387	-.585	1.765	-3.570	3.540	-1.968	-1.770	1.748	-7.390	.890	0.004
Mobility Index (MI) from D_1 to C_1	$MID_1/C_1=(D_1- C_1)$ (cm^2)	4.297	4.080	1.704	1.420	7.600	4.455	3.920	2.581	1.440	11.320	0.787
Mobility Index (MI) from C_1 to D_1	$MIC_1/D_1=(C_1- D_1)$ (cm^2)	-4.297	-4.080	1.704	-7.600	-1.420	-4.455	-3.920	2.581	-11.320	-1.440	0.787
Distensibility Index 1 (DI_1) in relation to R_b	$DI_{1/Rb}=(D_1–R_b)$ (cm^2)	2.420	2.210	1.547	-.420	5.710	1.646	1.380	1.775	-1.100	7.500	0.050
Rest Variation Index 2 (RVI_2) of R_2 to R_b	$RVI_{2/Rb}=(R_2–R_b)$ (cm^2)	2.033	1.810	2.072	-1.130	6.350	-.322	-.350	.819	-1.720	2.460	0.000

Non-PS-UI, non-pregnancy specific-urinary incontinence; PS-UI, pregnancy specific-urinary incontinence; sd, standard deviation; min, minimum; max, maximum; R_1, rest post-contraction; R_2, rest post- distension; R_b, basal rest; C_1, contraction 1; D_1, distension 1; cm^2, square centimeter. *Based on Mann-Whitney U. $P < 0.05$.

Table 4 – Comparison of levator hiatal (LH) area variation indexes in percentage (%) between non- pregnancy specific-urinary incontinence (non-PS-UI) and pregnancy specific-urinary incontinence (PS-UI) groups.

Variables		**non-PS-UI**					**PS-UI**					
Hiatal Area	Formulas	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max	p *
Rest Variation Index 1 (RV_1) of R_1 to R_b	$RVI_{1/Rb}=(R_1–R_b)/R_b$ (%)	-2.3696	-3.8350	9.73720	-17.77	16.86	-7.8874	-6.2000	10.15197	-34.61	9.65	0.144
Rest Variation Index 2 (RVI_2) of R_2 to R_1	$RVI_{2/R1}=(R_2–R_1)/R_1$ (%)	27.3492	19.3200	29.49892	-11.79	121.84	7.4174	3.7800	13.99915	-6.75	44.48	0.002
Contractility Index 1 (CI_1) in relation to R_b	$CI_{1/Rb}=(C_1–R_b)/R_b$ (%)	-18.3715	-17.3850	12.00975	-49.45	-1.29	-19.7165	-16.6900	10.33978	-44.10	-4.83	0.616
Relaxation Index after C_1	$RI_{1/C1}=(R_1–C_1)/C_1$ (%)	21.5077	17.7750	17.09085	-5.46	62.67	15.9326	10.5600	15.45487	-12.52	52.42	0.253
Distensibility Index 1 (DI_1) in relation to R_1	$DI_{1/R1}=(D_1–R_1)/R_1$ (%)	31.0727	30.3600	19.35374	-5.36	74.27	23.4935	16.6400	16.29095	-1.47	57.58	0.152
Relaxation Index 2 (RI_2) after D_1	$RI_{2/D1}=(R_2–D_1)/D_1$ (%)	-2.8369	-4.5000	15.50292	-30.53	34.17	-12.3665	-11.0300	10.02092	-38.89	6.99	0.015
Mobility Index (MI) from D_1 to C_1	$MID_1/C_1=(D_1- C_1)/D_1$(%)	34.9731	34.6150	11.51258	14.45	52.44	27.9891	26.0200	12.00939	11.05	52.31	0.043
Mobility Index (MI) from C_1 to D_1	$MIC_1/D_1=(C_1- D_1)/C_1$(%)	-58.6769	-52.9650	29.15153	-110.26	-16.88	-43.0665	-35.1700	26.80095	-109.69	-12.42	0.043
Distensibility Index 1 (DI_1) in relation to R_b	$DI_{1/Rb}=(D_1–R_b)/R_b$ (%)	27.6035	21.6900	21.12252	-3.76	84.76	12.9687	10.9100	14.91988	-7.95	65.22	0.003
Rest Variation Index 2 (RVI_2)of R_2 to R_b	$RVI_2/R_b=(R_2–R_b)/R_b$ (%)	23.3081	17.2650	25.37849	-11.88	86.28	-2.2213	-2.6600	6.13331	-11.19	19.95	0.000

Non-PS-UI, non-pregnancy specific-urinary incontinence; PS-UI, pregnancy specific-urinary incontinence; SD, standard deviation; min, minimum; max, maximum; R_1, rest post-contraction; R_2, rest post- distension; R_b, basal rest; C_1, contraction 1; D_1, distension 1; % percentage. *Based on Mann-Whitney U. $P < 0.05$.

Table 5 – Comparison intragroup of basal rest, rest 1 (post-contraction) and rest 2 (post-distension) of pelvic floor muscles in relation to the levator hiatal (LH) area in absolute values (cm^2) in non- pregnancy specific-urinary incontinence (non-PS-UI) and pregnancy specific-urinary incontinence (PS-UI) groups.

Variables	**Basal Rest (R_b)**					**Rest post-contraction (R_1)**					**Rest post-distension (R_2)**					
Hiatal Area	**median**	**mean**	**SD**	**min**	**max**	**median**	**mean**	**SD**	**min**	**Max**	**median**	**mean**	**SD**	**min**	**max**	**p**
non-PS-UI	9.64	9.67	1.68	6.17	13.76	9.33	9.45	1.34	6.18	11.42	11.68	12.02	2.02	7.92	15.77	< 0.001
PS-UI	13.46	13.12	1.91	11.15	18.46	12.28	12.27	1.42	10.10	15.73	13.14	13.18	1.89	10.80	18.88	0.002

Non-PS-UI, non-pregnancy specific-urinary incontinence; PS-UI, pregnancy specific-urinary incontinence; SD, standard deviation; min, minimum; max, maximum. *Based on Student's t- Test. $P > 0.05$.

Table 6 – Comparison of basal rest, rest 1 (post-contraction) and rest 2 (post-distension) of pelvic floor muscles in relation to the levator hiatal (LH) area in absolute values (cm^2) between non- pregnancy specific-urinary incontinence (non-PS-UI) and pregnancy specific-urinary incontinence (PS-UI) groups.

Variables	**non-PS-UI**					**PS-UI**					
	mean	**median**	**SD**	**min**	**max**	**mean**	**Median**	**SD**	**min**	**max**	***P****
Basal Rest (R_b)	9.64	9.67	1.68	6.17	13.76	13.46	13.12	1.91	11.15	18.46	0.000
Rest post-contraction (R_1)	9.33	9.45	1.34	6.18	11.42	12.28	12.27	1.42	10.10	15.73	0.000
Rest post-distension (R_2)	11.68	12.02	2.02	7.92	15.77	13.14	13.18	1.89	10.80	18.88	0.012

Non-PS-UI, non-pregnancy specific-urinary incontinence; PS-UI, pregnancy specific-urinary incontinence; SD, standard deviation; min, minimum; max, maximum. *Based on Student's t- Test. $P > 0.05$.

Seção 5

Perspectivas Acadêmicas e Científicas

Pensar nas perspectivas nesta fase final do doutorado, me fez rever todo o processo vivido até aqui e me estimulou ainda mais a cumprir esta etapa que é tão tensa e que exige dedicação, às vezes, até além da nossa capacidade. A formação no mestrado e doutorado, fortaleceram e ampliaram a perspectiva de iniciar a carreira docente e de pesquisadora.

Para a continuidade da busca do conhecimento e na colaboração para melhorar a assistência a mulher, a proposta é permanecer como colaboradora do *Diamater Study Group* e desenvolver o Pós-Doutorado na mesma linha de pesquisa desta trajetória e continuar colaborando na composição dos biomarcadores funcionais da miopatia diabética e da IU-EG como preditoras da IU pós-parto de gestantes com DMG e também estabelecer *cut off points* para classificação da contratilidade pela US-3D, baseada na correlação dos índices percentuais obtidos pela US-3D com a classificação funcional dos MAP obtidas pelo *PERFECT* em fraca, moderada, boa e forte.

Iniciar a carreira docente é objetivo a curto prazo e tenho participado de edital de seleção de concurso em instituições públicas e de reuniões com Coordenadores de Conselho de Curso de instituições privadas. Com o aprimoramento da técnica de avaliação da funcionalidade dos MAP feminino pela US-3D, estou me associando com outras colegas com expertise para organizarmos e oferecermos cursos de capacitação e aprimoramento na área.

Espero poder levar o conhecimento e principalmente beneficiar as mulheres, ao longo desta nova etapa da minha vida.

Seção 6

Diamater Study Group

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Ms. Sthefanie Kenickel Nunes
Ms. Bruna Bologna Catinelli
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Jose Vitor Freitas Melo (*in memoriam)*
Luiz Takano
Aline Medolago Carr
Gabriela Azevedo Garcia
Adriely Bittencourt Morgenstern Magyori
Carolina Neiva Frota de Carvalho
Luana Fávaro Iamundo
Henrique Caetano Mingoranci Bassin
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Carolina Pascon Marques
Michele Jacomin
Ana Julia Bimbatti Silva
Maiara Isabele Gonçalves Orlandi
Tatiana Daniele Dangió

Apoio à Pesquisa
Rita de Cássia Athanázio
Cinthia Scolastico Cecilio

Seção 7

Anexos

Anexo 1 - Especialização em Fisioterapia Pélvica - Uroginecologia Funcional

FACULDADE INSPIRAR.

Ser mais é nossa inspiração.

Faculdade Inspirar

Credenciada pela Portaria do Ministério da Educação nº 1.385, de 08 de dezembro de 2010, publicada no D.O.U. de 09/12/2010, página 28, seção 01.

CERTIFICADO

O Presidente, no uso de suas atribuições, confere o título de Especialista a

FABIANE AFFONSO PINHEIRO

por ter concluído o curso de **PÓS-GRADUAÇÃO LATO SENSU EM FISIOTERAPIA PÉLVICA – UROGINECOLOGIA FUNCIONAL** realizado entre 11 de março de 2016 e 11 de setembro de 2017, de acordo com a Resolução CNE/CES 01, de 08 de junho de 2007.

Curitiba, 10 de outubro de 2017

Prof. Dr. Esperidião Elias Aquim
Presidente

Fabiane Affonso Pinheiro
Titulada

Anexo 2 - Evento internacional - 2nd World Congress on Gynecology & Obstetrics

SCIENTIFIC FEDERATION
ABODE FOR RESEARCHERS

Certificate of Participation

Scientific Federation and Organizing Committee
WCGO-2019 wish to thank

Prof/Dr/Mr/Ms. **Fabiane Affonso Pinheiro**

Universidade Estadual Paulista (UNESP), Brazil

for his/her Participation as Moderator for
"2nd World Congress on Gynecology & Obstetrics"
held during September 19-20, 2019 at Miami, USA

Nicoletta Di Simone
Universita' Cattolica del S Cuore, Italy

SCIENTIFIC FEDERATION
ABODE FOR RESEARCHERS

Certificate of Recognition

Scientific Federation and Organizing Committee
WCGO-2019 wish to thank

Prof/Dr. **Fabiane Affonso Pinheiro**

Universidade Estadual Paulista (UNESP), Brazil

for his/her worthy Oral presentation
at "2nd World Congress on Gynecology & Obstetrics"
held during September 19-20, 2019 at Miami, USA

Nicoletta Di Simone
Universita' Cattolica del S Cuore, Italy

WCGO-2019 Organizing Committee Members

Theodoni Djenji — Dublin Giles — Howard Corp — Felice Gersh

Anexo 3 - Cursos complementares

fema
Fundação Educacional do Município de Assis

Diamater
Projeto Temático FAPESP

L.A.G.O.A.
LIGA ACADÊMICA DE GINECOLOGIA E OBSTETRÍCIA DE ASSIS

CERTIFICADO DE PARTICIPAÇÃO

CERTIFICO QUE Fabiane Affonso Pinheiro PARTICIPOU DO EVENTO

"INTERNATIONAL WORKSHOP: 3D ULTRASOUND OF FEMALE PELVIC FLOOR AND RECTUS ABDOMINIS MUSCLE"

NA QUALIDADE DE OUVINTE, TOTALIZANDO UMA CARGA HORÁRIA DE 8 HORAS, REALIZADO NA EUROCLÍNICA - RUA BENEDITO SPINARDI, 1440.

ASSIS-SP, 01 DE DEZEMBRO DE 2018.

PROF. MS. CARLOS IZAIAS SARTORÃO FILHO
ORIENTADOR DA LAGOA - FEMA MEDICINA

PROFA. DRA. ANGÉLICA MÉRCIA PASCON BARBOSA
PROFA. DRA. EM GINECOLOGIA, OBSTETRÍCIA E MASTOLOGIA PELA UNESP BOTUCATU

PROFA.BAERBEL JUNJUNGER,PhD
CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN - RESEARCH ASSISTANT AND PHYSIOTHERAPIST

CERTIFICADO

Cinesioterapia Pélvica Integrada

Certifico que

FABIANE AFFONSO PINHEIRO

participou do curso on-line
"**Exercícios para Incontinência urinária de esforço - Prática clínica baseada em evidência**".
Ministrado por Liris Leite Wuo e Colaboradores.

Carga horária: 12 horas |Período: 28 e 30 de Julho, 01, 04 e 06 de Agosto de 2020.

Liris Leite Wuo
Crefito 3/45624

Código do Certificado: 688642A1BA37CAE4807170 · Verifique autenticidade em: www.e-certificado.com

Curso de Upgrade em Incontinências Urinárias, Prolapsos e Hands on em Anatomia

Certificamos que

FABIANE AFFONSO PINHEIRO

participou do **"Curso de Upgrade em Incontinências Urinárias, Prolapsos e Hands on em Anatomia"**, promovido pela da FCM/UNICAMP e pela Associação Latino Americana do Piso Pélvico, realizado na Faculdade de Medicina da Universidade Estadual de Campinas, nos dias 26 e 27 de julho de 2018.

Paulo Palma
Professor Titular e Chefe da Urologia
FCM/Unicamp

Maura Regina Seleme
Dra. Especialista em Fisioterapia Pélvica
Diretora Internacional da Abafi HOLLAND

abafi · urologia · UNICAMP · astellas · Promedon

Sabrina Baracho
Fisioterapia na Saúde da Mulher

CERTIFICADO

Certifico que FABIANE AFFONSO PINHEIRO participou do Curso "Exercícios na Gestação: da prevenção ao tratamento de disfunções musculoesqueléticas"

Realizado em Belo Horizonte,
no período de 12 de Abril a 14 de Abril de 2019

Carga horária total de 25h/aula

Sabrina Baracho
Sabrina Baracho

Sabrina Baracho
Fisioterapia na Saúde da Mulher

CERTIFICADO

Certifico que FABIANE AFFONSO PINHEIRO participou do Curso de Atuação do Fisioterapeuta na Preparação do Assoalho Pélvico para o Parto e no Trabalho de Parto

Realizado em Belo Horizonte, no período de 15 de Março a 17 de Março de 2019

Carga horária total de 25h/aula

Sabrina Baracho
CREFITO 4/81614F
Ministrante

CERTIFICADO

instituto PATRÍCIA LORDÊLO ONLINE

Conferimos a **Fabiane Affonso Pinheiro** com o CPF de número **158.780.528-65** , o certificado de conclusão do curso **Formação em Fisioterapia na Função Miccional Feminina: da Evidência Científica à Prática Clínica ? Turma 2**, promovido por **Instituto Patrícia Lordêlo Online** no período de **10/09/2020** a **14/01/2021** com carga horária de **60 horas/aula**.

Salvador/BA, 24 de Janeiro de 2021

Código: 4Z42xcbZZ6yVy_W

Patrícia Lordêlo
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Anexo 4 - Artigos publicados em periódicos

PLOS ONE

RESEARCH ARTICLE

Alterations in the structural characteristics of rectus abdominis muscles caused by diabetes and pregnancy: A comparative study of the rat model and women

Giovana Vesentini[1,2]*, Angélica M. P. Barbosa[1,3], Débora C. Damasceno[2], Gabriela Marini[1,2,4], Fernanda Piculo[1,2], Selma M. M. Matheus[1,5], Raghavendra L. S. Hallur[1,2], Stefanie K. Nunes[1,2], Bruna B. Catinelli[1,2], Claudia G. Magalhães[1,2], Roberto Costa[1,2], Joelcio F. Abbade[1,2], José E. Corrente[1,4], Iracema M. P. Calderon[1,3], Marilza V. C. Rudge[1,2], The DIAMATER Study Group[¶]

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Altered maternal metabolism during mild gestational hyperglycemia as a predictor of adverse perinatal outcomes: A comprehensive analysis☆

Marilza Vieira Cunha Rudge[a,b,*], Angélica Mercia Pascon Barbosa[b,c], Luis Sobrevia[b,d,e,f], Rafael Bottaro Gelaleti[b], Raghavendra Lakshmana Shetty Hallur[b], João Paulo Castro Marcondes[b], Daisy Maria Fávero Salvadori[g], Caroline Baldini Prudêncio[b], Claudia Garcia Magalhães[a], Roberto Costa[a], Joelcio Francisco Abbade[a], José Eduardo Corrente[h], Iracema de Mattos Paranhos Calderon[a,b], The Perinatal Diabetes Research Group[i]

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ABSTRACT

Mild gestational hyperglycemia (MGH), as assessed using the normal oral glucose tolerance test (OGTT) and detection of an altered glycemic profile, is associated with adverse perinatal outcome. This study described the results of 40 years of research conducted at the Perinatal Diabetes Research Centre at São Paulo State University (UNESP), Brazil, on the maternal MGH environment and placental markers. This study also described the unidirectional relationship between MGH and excessive fetal growth, also applying moderator analysis. In addition to hyperglycemia, MGH is associated with an increased incidence of hypertension, metabolic syndrome, persistent insulin resistance after pregnancy, and high risk of developing type 2 diabetes mellitus (T2DM) after pregnancy. Structural changes and functional abnormalities resulting from MGH were observed in placenta. The fully adjusted model concluded that the predictor variable (MGH), which creates a complex environment for the fetus, has a direct effect on excessive birth weight and produces a z-score for ratio of birth weight to gestational age of > 2. Maternal age, pre-pregnancy BMI, number of previous pregnancies, numbers of prenatal visits, and 1 h OGTT are moderator variables that impact MGH and excessive fetal growth. These results show that maternal MGH has some characteristics associated with similar long-term T2DM development and similar adverse perinatal results to those of gestational diabetes mellitus (GDM) mothers, making it an intermediate maternal and placental marker between normoglycemic and GDM mothers.

☆ This article is part of a Special Issue entitled: Membrane Transporters and Receptors in Pregnancy Metabolic Complications edited by Luis Sobrevia.

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International Diabetes Federation

Deleterious effects of gestational diabetes mellitus on the characteristics of the rectus abdominis muscle associated with pregnancy-specific urinary incontinence

Giovana Vesentini [a,b], Angélica M.P. Barbosa [c], Juliana F. Floriano [a,b], Sérgio L. Felisbino [d], Sarah M.B. Costa [a,b], Fernanda Piculo [a,b], Gabriela Marini [a,b,e], Sthefanie K. Nunes [a,b], David R.A. Reyes [a,b], João P.C. Marcondes [a,b], Raghavendra L.S. Hallur [a,b], Ariane L. Rozza [d], Cláudia G. Magalhães [a,b], Roberto Costa [a,b], Joelcio F. Abbade [a,b], José E. Corrente [f], Iracema M.P. Calderon [a,b], Selma M.M. Matheus [g], Marilza V.C. Rudge [a,b,*], The Diamater Study Group [1]

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tions have been closely linked with the recruitment of the abdominal muscles [40,71–73].

There were some limitations to the present study. First, the size of the groups varied, given the difficulty in finding GDM women without PSUI. Second, the patients included in this study were not all primigravida, which may have influenced the results. Third, the RAM suffers from substantial strain (e.g., diastasis) during gestation. Diastasis recti abdominis is defined as a separation between the edges of the RAM at the linea alba [74] However, these limitations do not invalidate our results, as they also contribute to advancing knowledge in the field of urogynecology.

In conclusion, our results confirm that RAM is a plastic tissue that adapts its size and morphology in response to external and internal stimuli (here represented by GDM). GDM-related changes in muscular morphology may lead to the development of PSUI in pregnant women. Future studies are clearly needed to confirm RAM myopathy as a key factor of GDM-associated PSUI. In addition, this study may be a basis for the development of new therapies for pathologies with loss of muscle mass, diabetic myopathy, muscle atrophy, and consequently UI. Another relevant aspect of these findings is the identification of biomarkers that can be used as a diagnosis and prognosis allowing the implementation of early interventions and proper management of the patients, mitigating the deleterious impacts of GDM on the muscles.

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** **The Diamater Study Group:** Rudge MVc, Barbosa, AMP, Calderon IMP, Souza FP, Hijas A, Sobrevia L, Palma MS, Graeff CFO, Arni RK, Herculano RD, Salvadori DF, Mateus S, Dal Pai Silva M, Magalhães CG, Costa RA, Lima SAM, Emanueli C, Felisbino SL, Barbosa W, Atallah A, Girão MJB, Di Bella Z, Uchoa SM, Payão S, Berghman B, De Bie R, Junginger B, Alves FCB, Rossignoli PS, Abbade J, Prudencio CB, Orlandi MIG, Gonçalves MI, Nunes SK, Catinelli BB, Quiroz S, Sarmento BV, Pinheiro FA, Sartorio CI, Quiroz SBCV, Reyes DRA, Enriquez EMA, Oliveira RG, Floriano JF, Marcondes JPC, Sarmento, Costa SMB, Dangió TD, Pascon T, Hallur LSR, Melo JVF, Takano L, Reis FVDS, Caldeirão TD, Carr AM, Garcia GA, Rabadan GB, Bassin HCM, Suyama KS, Damasceno LN, Takemoto MLS, Menezes MD, Bussaneli DG, Nogueira, VKC, Lima PR, Lourenço IO, Marostica de Sá J, Megid RA, Caruso IP, Rasmussen LT, Prata GM, Piculo F, Vesentini G, Arantes MA, Ferraz GAR, Camargo LP, Kron MR, Corrente JE, Nunes HRC.

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PLOS ONE

REGISTERED REPORT PROTOCOL

Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol

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Abstract

Background

There is ample evidence that gestational diabetes mellitus has a direct influence on urinary incontinence and pelvic floor muscles. There are no standardized pelvic floor muscle exercise programs in the literature for the physiotherapy and differ in the type of exercise, intensity, type and duration of application, and the frequency and duration of treatment sessions. The aim of this systematic review will be to investigate that Pelvic Floor Muscle Training can prevent and/or decrease the pregnancy specific urinary incontinence in women with gestational diabetes mellitus or gestational hyperglycemia.

Methods

We will perform a systematic review according to the Cochrane methodology of Randomized Controlled Trials. An overall search strategy will be developed and adapted for Embase, MEDLINE, LILACS, and CENTRAL databases, with the date of consultation until

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ORIGINAL CLINICAL ARTICLE

WILEY

Impact of gestational diabetes on pelvic floor: A prospective cohort study with three-dimensional ultrasound during two-time points in pregnancy

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Abstract

Aim: To evaluate the pelvic floor (PF) biometry using three-dimensional ultrasound (US) at two-time points of gestational in pregnant women with gestational diabetes mellitus (GDM).

Methods: A prospective cohort study conducted at the Perinatal Diabetes Research Center including 44 pregnant women with GDM and 66 pregnant women without GDM at 24 to 28 weeks of gestation. Three-dimensional transperineal US was performed at 24 to 28 and 34 to 38 weeks of gestation in the lithotomy position at rest. The axial plane of the minimal Levator hiatal dimensions was used to determine Levator ani muscle and Hiatal area (HA) biometry at 24 to 28 and 34 to 38 weeks of gestation.

Results: Of the 110 pregnant women, 100 (90.9%) completed the follow-up at 34 to 38 weeks of gestation. The evaluation by US showed a negative biometric change between the two-time points, during pregnancy in women with GDM; in the HA (β coefficient: estimative of effect in biometric progression according to GDM diagnosis, using the non-GDM group as reference = −6.76; $P = .020$), anteroposterior diameter ($\beta = -5.07$; $P = .019$), and Levator ani thickness ($\beta = -12.34$; $P = .005$).

Conclusions: Pregnant women with GDM had a significantly lower than expected percentage of changes in biometry of Levator ani thickness and HA from 24 to 28 to 34 to 38 weeks of gestation when compared with the group of pregnant women without GDM. GDM alters the morphology of PF structures assessed by three-

Carlos I. Sartorão Filho, Fabiane A. Pinheiro, Caroline B. Prudencio, Sthefanie K. Nunes, Luiz Takano, Eusebio M.A. Enriquez, Maiara I. Orlandi, Baerbel Junginger, Marilza V. C. Rudge, and Angélica M.P. Barbosa contributed equally to this work.

Carlos I. Sartorão Filho and Fabiane A. Pinheiro are the first authors on this work.

Angélica M.P. Barbosa and Marilza V. C. Rudge are the last authors on this work.

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Impact of Gestational Diabetes Mellitus on Sexual Function: A Case–Control Study

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Abstract

Background: The prevalence of gestational diabetes mellitus (GDM) is increasing worldwide, and this condition may be compromising female sexual function. However, there are controversial findings regarding the impact of GDM diagnosis and proposed treatments on sexual function during pregnancy. Therefore, this study seeks to elucidate the impact of GDM on sexual function in pregnant women by making a comparison between GDM and non-GDM groups using pregnancy sexual response inventory (PSRI).
Materials and Methods: A case–control study involved 303 [168 women without GDM (control group) and 108 women diagnosed with GDM (case group)] Brazilian pregnant women at the Perinatal Diabetes Research Centre-Universidade Estadual Paulista, Brazil. PSRI was used to collect the data. The sexual function was scored in 10 domains as composite and specific scores by domains, categorized into quartiles ($0<25$ "very low," $25<50$ "low," $50<75$ "high," and 75–100 "very high"), for "before pregnancy" and "during pregnancy." The obtained data were subjected to statistical analysis using Student's *t*-, *F*-, and chi-square tests.
Results: GDM women (PSRI composite score <50) are at risk of decreased sexual function during pregnancy, while non-GDM women are not at risk (PSRI composite score >50). There were no significant differences in the sexual functions between the two groups before pregnancy ($p>0.0001$). After GDM diagnosis and proposed treatment, the differences were significant ($p<0.0001$), notably in the frequency, arousal, orgasm, satisfaction, and dyspareunia score.
Conclusions: This study showed that GDM diagnosis and proposed treatment resulted in decreased sexual functions during pregnancy.

Keywords: gestational diabetes mellitus, pregnancy, pregnancy sexual response inventory

Introduction

SEXUAL FUNCTION IN PREGNANT WOMEN has been attributed to several factors such as religious, sociocultural, relationships, physical, and psychological changes. Multiple studies have reported that pregnant women may experience impaired sexual function across all phases of the female sexual response cycle.[1,2]

Gestational diabetes mellitus (GDM), defined as impaired glucose tolerance during pregnancy, has long been suspected of causing sexual dysfunction in pregnant women[3] caused by the sudden transformation of a normal pregnancy to a high-risk pregnancy without maternal clinical symptoms.

GDM is associated with maternal and fetal risks related to diagnosis, including strict glycemic control, altered well-being and fetal growth, timely decision-making and route of delivery, and increased short- and long-term complications for mother and newborn.[4] To reduce this risk, women with GDM should change their habits and undergo rigorous medical follow-up. It is recommended to maintain adequate and controlled diet to ensure control of weight gain, active lifestyle, continuous monitoring of glucose level, and sometimes

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PLOS ONE

RESEARCH ARTICLE

Negative impact of gestational diabetes mellitus on progress of pelvic floor muscle electromyography activity: Cohort study

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Abstract

Background and objective

Pelvic floor muscles are involved in postural stability, in maintenance intra-abdominal pressure, and on mechanical support for pelvic organ. Gestational Diabetes Mellitus' (GDM) pregnancies complicated by fetal macrosomia, large placenta and polyhydramnios contribute for abrupt and intense increase in maternal intra-abdominal pressure. Our objective was analyze the impact of GDM on pelvic floor muscle (PFM) electromyography (EMG) activity progress from 24–30 to 36–38 weeks of gestation. We conducted a prospective cohort study. PFM EMG was performed in nulliparous or primiparous women with one previous elective cesarean delivery and with or not GDM diagnosed by the American Diabetes Association criteria. A careful explanation of the muscle anatomy and functionality of the PFM was given before EMG assessment. The outcome measures were PFM recruitment and progress from 24–30 to 36–38 weeks of gestation analyzed by the normalized root mean square (RMS) during rest-activity, fast and hold pelvic floor muscle contraction.

Results

Fifty-two pregnant women were assigned to 2 groups: the GDM (n = 26) and normoglycemic (NG) (n = 26). The demographic and obstetric data showed homogeneity between the groups. PFM activity progress was decreased in rest-activity ($P = 0.042$) and hold contraction ($P = 0.044$) at 36–38 weeks of gestation in the GDM group relative to that in the NG group.

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BMC Pregnancy and Childbirth

STUDY PROTOCOL Open Access

Study protocol to investigate biomolecular muscle profile as predictors of long-term urinary incontinence in women with gestational diabetes mellitus

Maritza V. C. Rudge[1*], Fátima P. Souza[2], Joelcio F. Abbade[1], Raghavendra L. S. Hallur[1], João Paulo C. Marcondes[1], Fernanda Piculo[1,3], Gabriela Marini[1,4], Giovana Vesentini[1], Lehana Thabane[5,6], Steven S. Witkin[7,8], Iracema M. P. Calderon[1], Angélica M. P. Barbosa[1,9], and The Diamater Study Group

Abstract

Background: Pelvic floor muscles (PFM) and rectus abdominis muscles (RAM) of pregnant diabetic rats exhibit atrophy, co-localization of fast and slow fibers and an increased collagen type I/III ratio. However, the role of similar PFM or RAM hyperglycemic-related myop… investigated. This study aims to assess the… incontinence (PS-UI) 12 months after the … RAM hyperglycemic myopathy will be exa…

Methods: The Diamater is an ongoing co… Diabetes Research Centre (PDRC), Botucat… Diagnosis of GDM and PS-UI will be made… in the study will occur at the time of C-se… months postpartum. Study groups will be… plus PS-UI; and (4) Non-GDM without PS-… myopathy at 12 months after C-section. Th… squeeze pressure, 3D pelvic floor ultrasou… be analyzed for ex-vivo contractility, morp… hyperglycemic myopathy. Additional varia… educational level, ethnicity, body mass in… therapy.

Discussion: To our knowledge, this will b… PFM physical and biomolecular muscle pr… for the assessment of cause-effect relation… may reveal previously undetermined cons…

Keywords: Gestational diabetes mellitus, … Urinary incontinence, Proteomics, Collagen

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risk of long-term UI in GDM mothers. An enhanced understanding of the impact of modifiable risk factors can lead to protocols to reduce the rates of UI and associated health care costs, improve the quality of life of affected women and contribute to the global eradication of UI after GDM exposure. It will also enable clinicians to deal more effectively with individual women after their pregnancy and facilitate the transition of the Brazilian Health System from a curative to a preventive strategy [65].

Conclusion

In conclusion, Diamater is an ongoing study recruiting GDM pregnant women at a prenatal care outpatient clinic to investigate the relationship between GDM plus PS-UI with the occurrence of symptomatic UI plus PFMD 1 year after C-section and assess whether this relation can be explained by hyperglycaemic myopathy. It offers the unique opportunity to establish well-powered biomarker research in a new triad composed of GDM + PS-UI+ hyperglycemic myopathy as a predictor of long-term UI and PFMD. This approach allows for future innovative treatment proposals.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12884-020-2749-x.

Additional file 1. Specific protocols for clinical assessment and laboratory analysis of PFM and RAM.

Abbreviations

ANOVA: One-way analysis of variance; CCL7: Chemokine C-C motif ligand 7; CRF: Case Report Forms; C-section: Cesarean section; DIAMATER: Diabetes and Maternity; ECM: Extracellular Matrix; EMG: Electromyography; EMGs: Surface electromyograms; GAGs: Glycosaminoglycans; GDM: Gestational Diabetes Mellitus; HPLC: High-Performance Liquid Chromatography; ICIQ-SF: International Consultation on Incontinence Questionnaire-Urinary Incontinence-Short Form; IRB: The Institutional Review Board; ISI: Incontinence Severity Index; OGTT: Oral Glucose Tolerance Test; OPLS: Orthogonal partial least squares; PCR: Polymerase chain reaction; PDRC: The Perinatal Diabetes Research Centre; PFM: Pelvic Floor Muscles; PLS: Partial least squares; PSUI: Pregnancy Specific Urinary Incontinence; PTH: Parathyroid Hormone; RAM: Rectus Abdominis Muscles; RNA: Ribonucleic acid; SENIAM: Surface Electromyography for the Non-Invasive Assessment of Muscles; T2DM: Type 2 Diabetes Mellitus; UI: Urinary Incontinence; UNESP: Universidade Estadual Paulista Júlio de Mesquita Filho

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The Diamater Study Group: Rudge MVC, Barbosa AMP, Calderon IMP, Souza FP, Abbade JF, Hallur LSR, Piculo F, Marini G, Vesentini G, Thabane L, Palma MS, Graeff CFO, Ami RK, Herculano RD, Salvadori DF, Mateus S, Dal Pai Silva M, Magalhães CG, Costa RA, Lima SAM, Feitosa SL, Barbosa W, Arafan A, Grilo MJB, Di Bella Z, Uchoa SM, Payão S, Hijas A, Bergfman B, De Be R, Sobrevia L, Junginger B, Alves FCB, Rossignoli PS, Prudencio CB, Orlandi MG, Gonçalves MI, Nunes SV, Gatinelli BB, Quiroz S, Sarmento BV, Pinheiro TA, Sartorão CI, Lucas RR, Reyes DRA, Quiroz SBCV, Enriquez EMA, Oliveira RD, Floriano JF, Marcondes JPC, Bannwart S, Dangió TD, Panzon T, Rossignoli P, Freitas JV, Takano L, Reis F, Calderido TD, Fernandes JN, Carr AM, Galeno MVC, Corrente JE, Nunes HRC, Candido AF, Sarmento, Costa SMB, Dangió TD, Pascon T, Melo JVF, Talano L, Reis FVDS, Calderão TD, Carr AM, Garcia GA, Rabadan GB, Bassin HOM, Suyama KS, Damacemo LN, Talermoto MLS, Menezes MD, Bussanel DG, Nogueira VAC, Lima PR, Lourenço ID, Marostica de Sá J, Megid RA, Caruso IP, Rasmussen LT, Prata GM, Piculo F, Vesentini G, Arantes MA, Ferraz GAR, Camargo LP, Kern MR, Corrente JE, Nunes HRC.

Authors' contributions

MVCR and AMPB conceived the study concept; developed the funding proposal; applied for funding, and initiated the writing of the protocol paper. JFA and LT were responsible for the critical review of the final draft. SSW and RLSH were responsible for clarifying manuscript content and word usage for an English language audience. MVCR is the principal investigator (PI) and the grant holder of the CNPq -Brasil (PQ-1C). AMPB, IMPC and FPS are Co-PI of the Project, and IMPC is grant holder of CNPq-Brasil (PQ-1D). MVCR, AMPB, IMPC, and FPS initiated the study design. MVCR, AMPB, RLSH, and JP wrote the protocol for research ethics committee and conceptual model. AMPB, IMPC, JFA, RLSH, and JEC develop the statistical analysis plan and will contribute to the interpretation of data. MVRC, SPP, JFA, RLSH, JPM, IP, GM, GV, LT, IMPC, SSW, and AMPB drafted and revised the manuscript after feedback from all authors. All authors contributed to the refinement of the present manuscript and approved the final version of the manuscript.

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Availability of data and materials

This is an ongoing study, and data sharing does not apply to this article. No data were generated or analyzed during the current study. Protocol related information can be obtained from the corresponding author (Maritza VC. Rudge) upon request.

Ethics approval and consent to participate

Institutional Research Bureau (IRB) of Botucatu Medical School-UNESP approved the study, on 2nd December 2017 (R17/036/NL60484.100.17). Written informed consent will be obtained from all subjects, and the procedures used in the study are in accordance with the guidelines of the Helsinki Declaration on human experimentation.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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PLOS ONE

RESEARCH ARTICLE

Prenatal exposure to gestational diabetes mellitus increases developmental defects in the enamel of offspring

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Competing interests: The authors have declared that no competing interests exist.

Abstract

Background and objective

Gestational diabetes mellitus (GDM) is associated with short- and long-term maternal and perinatal repercussions. Our objective was to evaluate the long-term consequences of intrauterine exposure to *hyperglycemia* on Developmental Defects of Enamel (DDE) in offspring.

Results

Overall, 50 children of women with GDM and 250 children of normoglycemic women participated, the latter serving as controls. Children were examined at the age between 3 and 12 years. In addition to physical examination, two independent observers examined and rated photographs to identify specific types of DDE in a blinded fashion. Among offspring of mothers with GDM, rates of DDE (all types combined) and hypoplasia (specific type) were significantly higher ($p<0.001$, $p = 0.04$), in comparison to offspring of normoglycemic mothers. Considering only the affected teeth (1060 in GDM category; 5499 in controls), rates of DDE (all types combined) were significantly higher for total teeth ($p <0.001$) and deciduous teeth ($p<0.001$), but not permanent teeth. In specific types of DDE involving deciduous teeth, rates of demarcate opacity were significantly higher ($p<0.001$; canine and 2nd mandibular molars) and hypoplasia ($p <0.001$; 2nd maxillary molars and 2nd mandibular molars). In permanent teeth, the rate of diffuse opacity in association with GDM was significantly higher ($p<0.001$; maxillary central incisors and 1st maxillary molars).

Conclusion

GDM was associated with the adverse effects of DDE on offspring. This study lays the foundation for future studies to determine the impact of GDM on long-term risk of DDE.

Anexo 5 – Comprovante de submissão de Artigo na revista PLOS ONE

PONE-D-21-03396
Dynamic Model for Pelvic Floor Muscles Assessment by Transperineal Ultrasound: A New Approach of the Diamater Study Group
Dr Angélica Mércia Pascon Barbosa

Dear Fabiane Pinheiro,

You are receiving this email because you have been listed as an author on a manuscript recently submitted to PLOS ONE, which is entitled "Dynamic Model for Pelvic Floor Muscles Assessment by Transperineal Ultrasound: A New Approach of the Diamater Study Group".

The corresponding author for the submission process is: Dr Angélica Mércia Pascon Barbosa
The full author list for the submission is: Fabiane A Pinheiro; Natalia Martinho; Carlos I Sartorão Filho; Sthefanie K Nunes; Luis Takano; Helio R.C Nunes; Caroline B Prudencio; Henrique C.M Bassin; Marilza V.C Rudge; Angélica Mércia Pascon Barbosa; The Diamater Study Group

You are not required to confirm your co-authorship of this submission, but if you would like to add an ORCID iD please click the link below to confirm co-authorship and link your ORCID iD.
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Anexo 6 - Resumos publicados em anais de congressos

FIGO WORLD CONGRESS OF GYNECOLOGY AND OBSTETRICS XXII · RIO

CERTIFICATE

FIGO International Federation of Gynecology and Obstetrics
the Global Voice for Women's Health

We hereby certify that the paper entitled

COMPARATION OF THE ELECTROMYOGRAPHIC RESPONSE BETWEEN THE SUPERFICIAL AND DEEP PELVIC FLOOR MUSCLES

by the authors **ANGÉLICA MÉRCIA PASCON BARBOSA; CAROLINE BALDINI PRUDENCIO; BARBARA VAZ SARMENTO; MAIARA ISABELE GONÇALVES ORLANDI; FABIANE AFFONSO PINHEIRO; STHEFANIE KENICKEL NUNES; CRISTIANE RODRIGUES PEDRONI; MARILZA VIEIRA CUNHA RUDGE**

Was presented as an **E-POSTER** during the International Federation of Gynecology and Obstetrics (FIGO) XXII FIGO World Congress 2018 at RioCentro, Brazil, from October 14 to 19, 2018.

CN Purandare
FIGO President

Luis Cabero
Chair of Organizing Committee FIGO 2018

Johan Vos
FIGO Chief Executive

EMS

ICS 2018 PHILADELPHIA

Certificate of Acceptance

Presented to

Rudge M V C1, Nunes S K1, Rudge C V C1, Quiroz S C B V1, Prudencio C B1, Pinheiro F A1, Heliodoro M L A1, Pascon T1, Sartorão Filho C I1, Calderon I M P1, Medolago A2, Barbosa A M P2

Had the following abstract accepted at the 48th International Continence Society Annual Meeting
28-31 August, Philadelphia, United States

Open Discussion ePoster, Abstract 558: A study of sexual function evaluated by the pregnancy sexual response inventory (PSRI) among women with gestational diabetes mellitus diagnosis.

SOGESP

CERTIFICADO

Certificamos que
PRUDENCIO, C.B.; PINHEIRO, F.A.; PEDRONI, C.R.; NUNES, S.K.; RUDGE, M.V.C.; BARBOSA, A.M.P.
participaram do **XXIII Congresso Paulista de Obstetrícia e Ginecologia 2018**
realizado do dia 23 a 25 de Agosto de 2018 no Transamerica Expo Center,
em São Paulo – SP com o trabalho
0026 – "ALTERAÇÕES NEUROMUSCULARES DO ASSOALHO PÉLVICO DURANTE A GESTAÇÃO COMPLICADA PELO DIABETES GESTACIONAL"
em forma de e-pôster.

Rossana Pulcinelli Vieira Francisco
Presidente do Congresso

Manoel João Batista Castello Girão
Diretor Científico

Roseli Mattar
Coordenadora Científica de Obstetrícia

Rogério Bonassi Machado
Coordenador Científico de Ginecologia

14/01/2021 ICS 2020 Abstract #271 Correlation Between Vaginal Digital Palpation and Pregnancy Specific Urinary Incontinence

ICS 2020 ONLINE

ICS 2020 › Programme › S20 › ePoster Station 3 › Abstract 271

Correlation Between Vaginal Digital Palpation and Pregnancy Specific Urinary Incontinence

Angélica M[1], Ana Júlia B[2], Sthefanie K[1], Fabiane A[1], Henrique C[1], Tatiana D[1], Maiara I[1], Carlos I[1], Marilza V[1], Caroline B[1]

RESEARCH TYPE
Clinical

ABSTRACT CATEGORY
Female Lower Urinary Tract Symptoms (LUTS) / Voiding Dysfunction

Comments

#271 Correlation Between Vaginal Digital Palpation and Pregnancy Specific Urin...

#	Abstract 271
	ePoster 4 Scientific Open Discussion ePoster Session 20
	ON-DEMAND

https://www.ics.org/2020/abstract/271 1/4

Certificado

Certificamos que o trabalho CORRELAÇÃO DA FUNÇÃO MUSCULAR DO ASSOALHO PÉLVICO COM A INCONTINÊNCIA URINÁRIA ESPECÍFICA DA GESTAÇÃO do(s) autor(es) SILVA, ANA JÚLIA BIMBATTI (); HIKARU NAGAMI, DANIELLE (UNESP); AFFONSO PINHEIRO, FABIANE (UNESP); BALDINI PRUDENCIO, CAROLINE (UNESP); PASCON BARBOSA, ANGÉLICA MÉRCIA (UNESP) integra os anais do VIII Congresso de Fisioterapia da UNESP de Marília, promovido pelo Conselho de Curso de Fisioterapia e pelo Departamento de Fisioterapia e Terapia Ocupacional da Faculdade de Filosofia e Ciências da UNESP, Câmpus de Marília, tendo sido realizado entre os dias 6 e 8 de novembro de 2019, na categoria Pôster.

Marília, 08 de novembro de 2019.

Doutor Marcos Eduardo Scheicher
Coordenador Geral do Evento

Professor Doutor Pedro Geraldo Aparecido Novelli
Presidente da CPEU
Vice-Diretor da Faculdade de Filosofia e Ciências

SOGESP

CERTIFICADO

Certificamos que
PINHEIRO, F.A.; SARTORÃO FILHO, C.I.; PRUDENCIO, C.B.; GAITERO, M.V.C.; BARBOSA, A.M.P.; RUDGE, M.V.C.
participaram do XXIII Congresso Paulista de Obstetrícia e Ginecologia 2018,
realizado do dia 23 a 25 de Agosto de 2018, no Transamerica Expo Center,
em São Paulo - SP, com o trabalho
O025 - "FUNCIONALIDADE DOS MÚSCULOS DO ASSOALHO PÉLVICO EM GESTANTES COM DIABETES MELLITUS GESTACIONAL AVALIADA PELA ULTRASSONOGRAFIA TRIDIMENSIONAL"
em forma de e-pôster.

Rossana Pulcineli Vieira Francisco
Presidente do Congresso

Manoel João Batista Castello Girão
Diretor Científico

Rosiane Mattar
Coordenadora Científica de Obstetrícia

Rogério Bonassi Machado
Coordenador Científico de Ginecologia

ICS 2018
PHILADELPHIA

Certificate of Participation

Presented to

Barbosa A M P1, Pinheiro F A1, Sartorão Filho C I1, Prudencio C B1, Kenickel S1, Orlandi M I G1, Pascon T1, Sarmento B V1, Melo J V F1, Oliveira L G D1, Sarmento B V1, Rudge M V C1

Had the following abstract accepted at the 48th International Continence Society Annual Meeting
28-31 August, Philadelphia, United States

Podium Short Oral, Abstract 42: Effect of gestational diabetes mellitus on pelvic floor muscle function: three-dimensional ultrasound

Laurence Stewart | Roger R. Dmochowski | Lori Birder

XXIII Congresso Paulista de Obstetrícia e Ginecologia | 23 a 25 de agosto de 2018 | Transamerica Expo Center • São Paulo, SP

SOGESP

CERTIFICADO

Certificamos que
PINHEIRO, F.A.; SARTORÃO FILHO, C.I.; PRUDENCIO, C.B.; GAITERO, M.V.C.; BARBOSA, A.M.P.; RUDGE, M.V.C.
participaram do XXIII Congresso Paulista de Obstetrícia e Ginecologia 2018,
realizado do dia 23 a 25 de Agosto de 2018, no Transamerica Expo Center,
em São Paulo - SP, com o trabalho
O025 - "FUNCIONALIDADE DOS MÚSCULOS DO ASSOALHO PÉLVICO EM GESTANTES COM DIABETES MELLITUS GESTACIONAL AVALIADA PELA ULTRASSONOGRAFIA TRIDIMENSIONAL"
em forma de e-pôster.

Rossana Pulcineli Vieira Francisco — *Presidente do Congresso*
Manoel João Batista Castello Girão — *Diretor Científico*
Rosiane Mattar — *Coordenadora Científica de Obstetrícia*
Rogério Bonassi Machado — *Coordenador Científico de Ginecologia*

XXIII Congresso Paulista de Obstetrícia e Ginecologia | 23 a 25 de agosto de 2018 Transamerica Expo Center • São Paulo, SP

SOGESP

CERTIFICADO

Certificamos que
QUIROZ, S.B.C.V.; PRUDENCIO, C.B.; HELIODORO, M.L.A.; COSTA, S.M.B.; PINHEIRO, F.A.; BARBOSA, A.M.P.
participaram do XXIII Congresso Paulista de Obstetrícia e Ginecologia 2018,
realizado do dia 23 a 25 de Agosto de 2018, no Transamerica Expo Center,
em São Paulo - SP, com o trabalho
O071 - "INCONTINENCIA URINÁRIA ESPECÍFICA DA GESTAÇÃO E DIABETES GESTACIONAL"
em forma de e-pôster.

Rossana Pulcineli Vieira Francisco — *Presidente do Congresso*
Manoel João Batista Castello Girão — *Diretor Científico*
Rosiane Mattar — *Coordenadora Científica de Obstetrícia*
Rogério Bonassi Machado — *Coordenador Científico de Ginecologia*

XXIII Congresso Paulista de Obstetrícia e Ginecologia | 23 a 25 de agosto de 2018 Transamerica Expo Center • São Paulo, SP

SOGESP

CERTIFICADO

Certificamos que
SARTORÃO FILHO, C.I.S.; PINHEIRO, F.A.; PRUDENCIO, C.B.; NUNES, S.K.; BARBOSA, A.M.P.; RUDGE, M.V.C.
participaram do XXIII Congresso Paulista de Obstetrícia e Ginecologia 2018,
realizado do dia 23 a 25 de Agosto de 2018, no Transamerica Expo Center,
em São Paulo - SP, com o trabalho
O034 - "PROGRESSÃO DA BIOMETRIA DA ÁREA HIATAL DO ASSOALHO PÉLVICO DE GESTANTES COM DIABETE MELLITUS GESTACIONAL AVALIADA PELA ULTRASSONOGRAFIA TRIDIMENSIONAL"
em forma de e-pôster.

Rossana Pulcineli Vieira Francisco — *Presidente do Congresso*
Manoel João Batista Castello Girão — *Diretor Científico*
Rosiane Mattar — *Coordenadora Científica de Obstetrícia*
Rogério Bonassi Machado — *Coordenador Científico de Ginecologia*

ICS 2018
PHILADELPHIA

Certificate of Participation

Presented to

Barbosa A M P1, Prudencio C B2, Pinheiro F A2, Sartorão Filho C I2, Pedroni C R1, Kenickel S2, Orlandi M I G2, Gaitero M V C2, Prata G M2, Sarmento B V2, Quiroz S C B V2, Rudge M V C2

Had the following abstract accepted at the 48th International Continence Society Annual Meeting
28-31 August, Philadelphia, United States

Podium Short Oral, Abstract 321: Pelvic floor muscles rest-activity and hold contraction in diabetic pregnant women during pregnancy: cohort study

Laurence Stewart | Roger R. Dmochowski | Lori Birder

COMPARAÇÃO DA AVALIAÇÃO FUNCIONAL E ELETROMIOGRÁFICA DOS MÚSCULOS DO ASSOALHO PÉLVICO ENTRE GESTANTES COM E SEM INCONTINÊNCIA URINÁRIA ESPECÍFICA DA GESTAÇÃO

Ha sido presentado en formato Poster por

David Rafael Abreu Reyes
Larissa Neves Damasceno
Caroline Baldini Prudencio
Fabiane Affonso Pinheiro
Maria Victoria Candido Galtero
Marilza Vieira Cunha Rudge
Cristiane Rodrigues Pedroni
Sthefanie Kenickel Nunes
Matara Isabelle Gonçalves Orlandi
Angélica Márcia Pascon Barbosa

celebrado en
Cartagena, Colombia, del 4 al 7 de marzo de 2020

Dra. Simone Botelho
Presidenta del Comité Científico

Dr. Alejandro Tarazona
Presidente de ALAPP

Dr. Carlos Díaz Támara
Presidente del 2do Congreso Internacional ALAPP

ALADD 2020

SCIENTIFIC FEDERATION
ABODE FOR RESEARCHERS

Certificate of Recognition

Scientific Federation and Organizing Committee
WCGO-2019 wish to thank

Prof/Dr. ***Angélica M. P. Barbosa***

"Influence of gestational diabetes mellitus on defects in the enamel of offspring"

Co-authors
Tatiana Pascon, Caroline B. Prudencio, Stheffanie Kenickel, Fabiane A. Pinheiro, Vinicius Krüger Costa Nogueira, Diego G. Bussanelli, Marilza V. C. Rudge, Angélica M. P. Barbosa

for his/her worthy Oral presentation
at "2nd World Congress on Gynecology & Obstetrics"
held during September 19-20, 2019 at Miami, USA

Nicoletta Di Simone
Universita' Cattolica del S Cuore, Italy

WCGO-2019 Organizing Committee Members

Theodhosi Giorgji
Ex-president of Albanian Association of Obstetrics and Gynecology, Albania

Dabie Giles
University of Wisconsin USA

Howard Carp
Tel Aviv University Israel

Felice Gersh
Integrative Medical Group of Irvine, USA

Anexo 7 - Bancas examinadoras de Trabalhos de Conclusão de Curso

Universidade Estadual Paulista
Faculdade de Filosofia e Ciências
Campus de Marília
Secretaria dos Conselhos de Cursos de Graduação

Conselho de Curso de Fisioterapia

DECLARAÇÃO

D E C L A R O, para os devidos fins, que a Mestra **Fabiane Affonso Pinheiro** participou, na qualidade de **BANCA EXAMINADORA** do Trabalho de Conclusão de Curso (TCC) em Fisioterapia, da aluna **Bárbara Vaz Sarmento**, monografia intitulada: "**Comparação da resposta eletromiográfica entre os músculos superficiais e profundos do assoalho pélvico**", realizada no dia 27 de novembro de 2017, às 08:00h, na sala 04 do prédio de Fisioterapia e Terapia Ocupacional da Faculdade de Filosofia e Ciências da UNESP - Campus de Marília.

Participaram, também, da Banca Examinadora, a Doutora Angélica Mércia Pascon Barbosa e o Mestre Guilherme Thomaz de Aquino Nava.

Marília, 27 de dezembro de 2017.

Dra. Flávia Roberta Faganello Navega
Coordenadora do Conselho de Curso de Fisioterapia

UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Campus de Marília

Marília, 28 de janeiro de 2021.

DECLARAÇÃO

Declaro para os devidos fins que a **Profª Fabiane Affonso Pinheiro** participou em 2019 como membro da banca do Trabalho de Conclusão de Curso da aluna **Ester Pereira Dezan Martins Gonçalves**, intitulado "Evolução da assistência fisioterapêutica no trabalho de parto e desfechos obstétricos ocorridos em maternidade de risco habitual: estudo retrospectivo de 8 ano."

Participaram ainda como membros da banca: Profª Angélica Mércia Pascon Barbosa e Profª Patrícia de Souza Rossignoli

Marcos Eduardo Scheicher
Coordenado do curso de Fisioterapia

Faculdade de Filosofia e Ciências - Departamento de Fisioterapia e Terapia Ocupacional
Av. Hygino Muzzi Filho, 737 CEP 17525-900 Marília São Paulo Brasil
Tel 14 3402 1350 deffto@marilia.unesp.br

unesp UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Campus de Marília

Marília, 28 de janeiro de 2021.

DECLARAÇÃO

Declaro para os devidos fins que a **Profª Fabiane Affonso Pinheiro** participou em 2017 como membro da banca do Trabalho de Conclusão de Curso da aluna **Raissa Escandiuzi Avramidis,** intitulado "Efetividade do programa de hidroterapia na função muscular do assoalho pélvico de gestantes: estudo de caso."

Participaram ainda como membros da banca: Profª Angélica Mércia Pascon Barbosa e Caroline Baldini Prudêncio.

Marcos Eduardo Scheicher
Coordenado do curso de Fisioterapia

Faculdade de Filosofia e Ciências - Departamento de Fisioterapia e Terapia Ocupacional
Av. Hygino Muzzi Filho, 737 CEP 17525-900 Marília São Paulo Brasil
Tel: 14 3402 1350 defito@marilia.unesp.br

UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Campus de Marília

Marília, 07 de junho de 2021.

DECLARAÇÃO

Declaro para os devidos fins que o(a) Prof(a) Dr(a) Angélica Mércia Pascon Barbosa participou como orientador(a) da banca do Trabalho de Conclusão de Curso (TCC) de Vitória Vargas Figueiredo, intitulado **"Prevalência, severidade e impacto da incontinência urinária especifica da gestação em primigestas e secundigestas."** A defesa do TCC ocorreu via plataforma Google Meet.

Participaram também da banca o(a) Prof(a) Me(a) Fabiane Affonso Pinheiro e o(a) Prof(a) Me(a) Raissa Escandiusi Awiamidis.

Marcos Eduardo Scheicher
Coordenador do curso de Fisioterapia/ FFC-Unesp/Marília

Faculdade de Filosofia e Ciências - Departamento de Fisioterapia e Terapia Ocupacional
Av. Hygino Muzzi Filho, 737 CEP 17525-900 Marília São Paulo Brasil
Tel 14 3402 1353 defto@marilia.unesp.br

Anexo 8 - Seleção pública para função docente

fema
Fundação Educacional do Município de Assis

PORTARIA N. 40, 06 DE DEZEMBRO DE 2019

Divulga resultado final do Processo Seletivo.

O Presidente da Comissão Gestora de Seleção Pública da Fundação Educacional do Município de Assis (FEMA), no uso das atribuições que lhe confere as Normas para o Edital de Seleção Pública de Docentes, **RESOLVE**:

ARTIGO 1º Divulgar o resultado final do Processo Seletivo, objeto do edital 14/2019 (Ciências da Saúde – Fisioterapia e Terapia Ocupacional):

CLASSIFICAÇÃO	NOME	PROVA ESCRITA	PROVA DIDÁTICA	CURRICULO	RESULTADO FINAL
1º	MARIANA ROMANHOLI PALMA	8,80	7,87	6,00	7,55
2º	FABIANE AFFONSO PINHEIRO	8,50	7,62	5,10	7,07

ARTIGO 2º Essa portaria entrará em vigor na data de sua publicação, revogadas as disposições em contrário.

Arildo José de Almeida

Anexo 9 - Aprovação Comitê de Ética em Pesquisa

UNESP -FACULDADE DE MEDICINA DE BOTUCATU

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: Projeto Mãe: Estudo de coorte prospectivo: nova tríade gestacional (hiperglicemia, incontinência urinária e perfil clínico, molecular e ômico da miopatia hiperglicêmica) na predição de incontinência. Pesquisa translacional com biodevice para regeneração muscular em ratas com diabetes

Subprojeto 1: Relação dos achados eletromiográficos dos músculos do assoalho pélvico com os níveis de relaxina ao longo da gestação e após o parto de mulheres com hiperglicemia gestacional e incontinência urinária específica da gestação (Orientador: Mariliza Vieira Cunha Rudge/ Orientando: Caroline Baldini Prudencio/ Nível: Doutorado)

Subprojeto 2: Ultrassonografia Tridimensional do assoalho pélvico de mulheres com hiperglicemia gestacional 16-18 meses após a gestação (Orientador: Mariliza Vieira Cunha Rudge/ Orientando: Carlos Izaias Sartorão Filho/ Nível: Doutorado);

Subprojeto 3: Coorte prospectiva da tríade hiperglicemia gestacional, incontinência urinária específica da gestação e disfunção muscular do assoalho pélvico, avaliada pela ultrassonografia funcional, como preditora da incontinência urinária e disfunção muscular 6-18 meses após o parto (Orientador: Mariliza Vieira Cunha Rudge/ Orientando: Fabiane Affonso Pinheiro/ Nível: Doutorado)

Subprojeto 4: Níveis de micronutrientes e da expressão de seus receptores em mulheres com diabetes mellitus gestacional e incontinência urinária específica da gestação(Orientador: Mariliza Vieira Cunha Rudge/ Orientando: Sarah Maria Barreze Costa/ Nível: Doutorado).

Pesquisador: Mariliza Vieira Cunha Rudge

Área Temática:

Versão: 5

CAAE: 82225617.0.0000.5411

Instituição Proponente: Departamento de Ginecologia e Obstetrícia

Patrocinador Principal: FUNDACAO DE AMPARO A PESQUISA DO ESTADO DE SAO PAULO

DADOS DO PARECER

Número do Parecer: 3.747.338

Endereço: Chácara Butignoli , s/n
Bairro: Rubião Junior **CEP:** 18.618-970
UF: SP **Município:** BOTUCATU
Telefone: (14)3880-1609 **E-mail:** cep@fmb.unesp.br

Apresentação do Projeto:

Trata a presente solicitação de emenda ao projeto em questão referente ao envio de amostras para análise em dois destinos diferentes,com a finalidade de aprendizado da técnica e maior sensibilidade/especificidade da técnica adotada.

Objetivo da Pesquisa:

Avaliar a solicitação de emenda ao presente projeto para envio de amostras a dois destinos diferentes.

Avaliação dos Riscos e Benefícios:

Já avaliados.

Comentários e Considerações sobre a Pesquisa:

A pesquisadora solicita a emenda ao presente projeto para envio de amostras para dois destinos diferentes:

1) para Londres - UK: com a finalidade de envio de amostras já coletadas para o mesmo fim aprovado anteriormente por este CEP, sendo exclusivamente para aprendizado da técnica pela aluna de doutorado (Dra Juliana) com o grupo em questão. Os pesquisadores informam que não haverá alteração no projeto anteriormente aprovado.

2) Para Lincoln / Neblaska - EUA: com a finalidade de envio de amostras já coletadas para o mesmo fim aprovado anteriormente por este CEP, sendo para substituição da técnica anteriormente descrita (espectoscopia por RMN) pela técnica de 2 espectômetro de massa, justificando maior especificidade e sensibilidade destas técnicas. Os pesquisadores informam que não haverá alteração no projeto anteriormente aprovado.

Os pesquisadores informam que o envio de amostras para o exterior, será feito por transportadora especializada], devendo seguir legislação vigente brasileira.

Considerações sobre os Termos de apresentação obrigatória:

Já avaliados.

Recomendações:

Não há.

Conclusões ou Pendências e Lista de Inadequações:

Após análise em REUNIÃO EXTRAORDINÁRIA, o Colegiado deliberou APROVADA A EMENDA apresentada.

Considerações Finais a critério do CEP:

Conforme deliberação do Colegiado, em REUNIÃO EXTRAORDINÁRIA do Comitê de Ética em

Pesquisa FMB/UNESP, realizada em 19/11/2019, a EMENDA apresentada encontra-se APROVADA.

Atenciosamente,

Comitê de Ética em Pesquisa FMB/UNESP

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_1440649_E2.pdf	23/09/2019 15:11:41		Aceito
Outros	OficioLondres.doc	23/09/2019 15:10:28	Marliza Vieira Cunha Rudge	Aceito
Outros	OficioenvioEUA.doc	23/09/2019 15:09:10	Marliza Vieira Cunha Rudge	Aceito
Outros	Oficioexplicativo_envio.docx	23/09/2019 15:06:36	Marliza Vieira Cunha Rudge	Aceito
Outros	Carta_resposta_comite_c.pdf	11/04/2019 13:41:35	Marliza Vieira Cunha Rudge	Aceito
Folha de Rosto	FolhaDeRostoAssinada_Sub_Proje_4_Sarah.pdf	29/01/2019 11:51:24	Sarah Maria Barneze Costa	Aceito
Outros	TermoDeAnuenciaInstitucional_Sub_Proj_4_Sarah.pdf	29/01/2019 11:44:05	Sarah Maria Barneze Costa	Aceito
Projeto Detalhado / Brochura Investigador	Oficio_ao_comite_sub_proj_4_Sarah.pdf	29/01/2019 11:41:10	Sarah Maria Barneze Costa	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_tematico_com_subprojeto_4_de_Sarah_Barneze.pdf	29/01/2019 11:35:52	Sarah Maria Barneze Costa	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_doutorado_Sarah_Barneze_sub_projeto_4.pdf	29/01/2019 11:32:45	Sarah Maria Barneze Costa	Aceito
Outros	EAP_Marliza_Rudge.pdf	18/01/2018 17:27:08	Marliza Vieira Cunha Rudge	Aceito
Outros	Fluxograma_Tematico_CEP.pptx	26/11/2017 19:18:14	Marliza Vieira Cunha Rudge	Aceito
Outros	HRA.pdf	26/11/2017 19:09:17	Marliza Vieira Cunha Rudge	Aceito
Outros	termodeautorizacao_HRA.pdf	26/11/2017 19:01:53	Marliza Vieira Cunha Rudge	Aceito

Continuação do Parecer: 3.747.338

Outros	coparticipacao_assis_municipio.jpeg	26/11/2017 18:53:44	Marliza Vieira Cunha Rudge	Aceito
Outros	SUBPROJETO_3.doc	05/10/2017 23:41:43	Marliza Vieira Cunha Rudge	Aceito
Outros	SUBPROJETO_2.docx	05/10/2017 23:41:04	Marliza Vieira Cunha Rudge	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_mae.docx	05/10/2017 23:39:04	Marliza Vieira Cunha Rudge	Aceito
Outros	Projeto_mae_Subprojetos.docx	05/10/2017 23:37:51	Marliza Vieira Cunha Rudge	Aceito
Orçamento	orcamento_tematico.pdf	05/10/2017 23:36:42	Marliza Vieira Cunha Rudge	Aceito
Outros	SUBPROJETO_1.doc	05/10/2017 22:54:11	Marliza Vieira Cunha Rudge	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_tematico.docx	05/10/2017 22:48:47	Marliza Vieira Cunha Rudge	Aceito
Outros	Co_participacao_FFC.pdf	21/09/2017 17:02:46	Marliza Vieira Cunha Rudge	Aceito
Outros	Co_participacao_Famema.jpeg	21/09/2017 17:02:11	Marliza Vieira Cunha Rudge	Aceito
Outros	Co_participacao_Araraquara.pdf	21/09/2017 17:00:09	Marliza Vieira Cunha Rudge	Aceito
Outros	Co_participacao_Bauru.pdf	21/09/2017 16:59:26	Marliza Vieira Cunha Rudge	Aceito
Outros	Co_participacao_RioPreto.pdf	21/09/2017 16:58:52	Marliza Vieira Cunha Rudge	Aceito
Outros	Co_participacao_RioClaro.pdf	21/09/2017 16:57:56	Marliza Vieira Cunha Rudge	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

BOTUCATU, 05 de Dezembro de 2019

Assinado por:
Trajano Sardenberg
(Coordenador(a))

Endereço: Chácara Sudgnoli , s/n
Bairro: Rubião Junior **CEP:** 18.618-970
UF: SP **Município:** BOTUCATU
Telefone: (14)3880-1809 **E-mail:** cep@fmb.unesp.br