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"Júlio de Mesquita Filho"

Faculdade de Odontologia de Araraquara

LILIANE DE CARVALHO ROSAS GOMES

Osteoartrite da ATM em pacientes submetidos à cirurgia ortognática. Avaliação tridimensional quantitativa das alterações condilares e influência do reposicionamento dos discos articulares

Araraquara

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Orientador: Prof. Dr. João Roberto Gonçalves (FOAr-UNESP)

Co-orientadora: Profa. Dra. Lúcia Helena Soares Cevidanes (UMICH-EUA)

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COMISSÃO JULGADORA

TESE PARA OBTENÇÃO DO GRAU DE DOUTOR

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5° Examinador: Prof. Dr. Luiz Gonzaga Gandini Júnior

Araraquara, 10 de Março de 2017

Dados Curriculares

Liliane de Carvalho Rosas Gomes

Nascimento:
26/04/1982 - Salvador/BA

Filiação:
Luiz Carlos Rosas
Eliane Pinheiro de Carvalho

2000-2004:
Curso de Graduação em Odontologia. Universidade Estadual de Feira de Santana - UEFS

2004-2005:
Aperfeiçoamento em Ortodontia e Ortopedia Facial. Associação Brasileira de Odontologia - ABO/FSA

2006-2008:
Especialização em Ortodontia. União Metropolitana de Educação e Cultura - UNIME/BA

2010-2012:
Curso de Pós-Graduação em Ciências Odontológicas, Área de Concentração em Ortodontia, nível Mestrado. Faculdade de Odontologia de Araraquara - FOAr/UNESP

2013-2017:

Curso de Pós-Graduação em Ciências Odontológicas, Área de Concentração em Ortodontia, nível Doutorado, Faculdade de Odontologia de Araraquara - FOAr/UNESP com período sanduíche na Universidade de Michigan, Ann Arbor, MI, EUA (03/2014 a 04/2015)

Associações:

Associação Brasileira de Ortodontia e Ortopedia Facial - ABOR/BA

Associação dos Ex-Alunos de Ortodontia de Araraquara - AOA

Sociedade Brasileira de Pesquisa Odontológica - SBPqO

International Association for Dental Research - IADR

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Gomes LCR. Osteoartrite da ATM em pacientes submetidos à cirurgia ortognática. Avaliação tridimensional quantitativa das alterações condilares e influência do reposicionamento dos discos articulares [Tese de doutorado]. Araraquara: Faculdade de Odontologia da UNESP; 2017.

Resumo

Objetivos: O presente trabalho apresentou como objetivo geral estudar a osteoartrite da articulação têmporo-mandibular (ATM) em pacientes submetidos à cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular através de novas técnicas computacionais desenvolvidas para otimização do uso de imagens tridimensionais. Como objetivos específicos, buscou-se: avaliar quantitativamente o grau de deslocamento e remodelação condilar após cirurgia, considerando diferenças entre três grupos (Grupo 1, côndilos de pacientes que sofreram cirurgia de reposicionamento de disco articular simultaneamente à cirurgia ortognática; Grupo 2, côndilos de pacientes que apresentavam deslocamento de disco articular mas não foram submetidos à cirurgia de reposicionamento de disco; Grupo 3, côndilos de pacientes com ATM saudável); investigar a estabilidade do procedimento cirúrgico em longo prazo; identificar possíveis diferenças entre os gêneros quanto à remodelação condilar no período de acompanhamento pós-cirúrgico;

estudar potencial associação entre fatores clínicos e cirúrgicos com alterações remodelativas no côndilo mandibular de pacientes que sofreram cirurgia ortognática associada à cirurgia de reposicionamento do disco articular.

Materiais e Métodos: Três artigos científicos foram elaborados e utilizados para a avaliação dos propósitos apresentados.

Resultados: Em média, após cirurgia ortognática observou-se deslocamento condilar para posterior e medial, além de rotações nos três planos do espaço. Côndilos do Grupo 1 evidenciaram deslocamento para baixo, enquanto que os demais sofreram deslocamento para cima ($p \leq 0.001$). O procedimento cirúrgico mostrou-se estável em longo prazo principalmente nos Grupos 1 e 3. Pacientes do Grupo 2 evidenciaram maior grau de recidiva, além do maior percentual de pacientes que sofreram o problema. Quanto à remodelação condilar durante o período de acompanhamento pós-cirúrgico, o Grupo 1 apresentou aposição óssea no polo anterior do côndilo mandibular, diferença estatisticamente significante quando comparada aos demais grupos em estudo ($p \leq 0.001$). Não foram encontradas diferenças estatísticas significantes quanto à alteração em volume condilar entre os Grupos 1 e 3. Maior redução em volume foi observada em pacientes do Grupo 2 ($p \leq 0.05$). Embora, em média, côndilos de pacientes do gênero feminino tenham sofrido maior redução em volume, não foram observadas diferenças estatísticas significativas entre os gêneros. Coeficientes de correlação fracos, no

entanto, estatisticamente significantes foram observados considerando a relação entre variáveis clínicas e cirúrgicas com remodelação condilar. Quanto maior a idade do paciente, maior susceptibilidade à redução de volume condilar após cirurgia ortognática ($p \leq 0.001$). As alterações de deslocamento condilar geradas após cirurgia de reposicionamento de disco simultaneamente à cirurgia ortognática não parecem estar associadas com maior reabsorção condilar no período de acompanhamento pós-cirúrgico. Tais alterações apresentaram, em média, sentidos opostos àquelas correlacionadas com maior risco de reabsorção condilar.

Conclusões: Os resultados apresentados sugerem que o reposicionamento do disco articular seja um importante aliado à cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular, proporcionando um efeito de proteção ao côndilo acometido pela osteoartrite da ATM.

PALAVRAS-CHAVE: Cirurgia ortognática. Osteoartrite. Côndilo mandibular. Tomografia computadorizada de feixe cônico.

Gomes LCR. TMJ osteoarthritis in patients submitted to orthognathic surgery. Quantitative three-dimensional evaluation of condylar changes and influence of articular disc repositioning [Tese de doutorado]. Araraquara: Faculdade de Odontologia da UNESP; 2017.

Abstract

Objectives: The general purpose of this study was to investigate temporomandibular joint (TMJ) osteoarthritis in patients that underwent counterclockwise maxillomandibular advancement surgery, by using new computational techniques developed for optimizing the use of three-dimentional images. The specific goals consisted on: quantitatively assessing post-surgical condylar displacemet and remodeling changes, considering differences among three groups (Group 1, condyles from patients submmitted to disc replacement surgery simultaneoustly with the orthognathic surgery; Group 2, condyles from patients that presented with disc displacement but did not undergo disc replacement surgery; Group 3, condyles from patients with healthy TMJ); investigate long-term stability of the surgical procedure; identify possible gender differences considering condylar remodeling in the follow-up period; identify association between clinical and surgical factors with remodeling changes in the mandibular

condyles of patients that underwernt disc replacement surgery simultaneously with the orthognathic surgery.

Materials and Methods: Three scientific papers were elaborated and used for assessing the purposes presented.

Results: On average, after orthognathic surgery it was observed posterior and medial condylar displacement, besides rotations in the three planes of the space. Downward condylar displacement was noticed in Group 1, whereas it moved upward in the other groups ($p \leq 0.001$). The overall surgical procedure appeared to be fairly stable, particularly for Groups 1 and 3. Group 2 showed the larger amount and percentage of patients experiencing relapse. Regarding condylar remodeling during the postoperative follow-up period, Group 1 showed significant amount of bone apposition on the anterior pole ($p \leq 0.001$). No statistically significant differences were found regarding condylar volume changes between Groups 1 and 3. Larger volume reduction was observed in Group 2 ($p \leq 0.05$). Although, on average, female condyles showed greater volume reduction, statistically significant gender differences were not observed. Weak but statistically significant correlation coefficients were observed between some clinical and surgical variables with condylar remodeling changes in the follow-up period. The older the patient, the greater the susceptibility to condylar volume reduction after orthognathic surgery ($p \leq 0.001$). Displacement condylar changes generated by counterclockwise maxillomandibular advancement and disc repositioning surgery did not

seem to be associated with greater condylar resorption in the follow-up period. Such changes showed, on average, opposite direction from those correlated with greater risk of condylar resorption.

Conclusions: Our results suggest that disc replacement surgery is an important ally for counterclockwise maxillomandibular advancement surgery, providing a protective effect to the mandibular condyle affected by TMJ osteoarthritis.

KEYWORDS: Orthognathic Surgery. Osteoarthritis. Mandibular Condyle. Cone-Beam Computed Tomography.

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1 Introdução

A osteoartrite da articulação têmporo-mandibular (ATM) é uma condição patológica local que ocorre quando o equilíbrio dinâmico entre o colapso e o reparo dos tecidos articulares é comprometido (Cevidanes et al.[12], 2010; Hunter, Hellio Le Graverand-Gastineau[29], 2009; Tanaka et al.[59], 2008). O curso da doença surpreende especialistas quanto à sintomatologia e a progressão variável dos padrões morfológicos observados em suas várias fases. Pode evoluir com a reparação completa e adaptação morfológica, caracterizando uma remodelação funcional (Arnett et al.[4], 1996; Bland[10], 1983). No entanto, pode apresentar curso adverso com agressiva degeneração óssea, deformidade de estruturas relacionadas e comprometimento da função (Arnett et al.[4], 1996; Tanaka et al.[59], 2008). Este cenário pouco previsível dificulta o desenvolvimento de marcadores de doença clinicamente válidos e, consequentemente, contribui para terapêuticas limitadas e desprovidas de consenso no meio científico (Haskin et al.[24], 1995; Herr et al.[25], 2011; Hunter, Hellio Le Graverand-Gastineau[29], 2009; Wadhwa, Kapila[61], 2008).

Sua prevalência, etiologia e o mecanismo envolvido na patogênese da doença ainda não estão bem estabelecidos (Hwang et al.[31], 2004; Zarb, Carlsson[67], 1999). Relata-se que pacientes do sexo

feminino, com padrão vertical de crescimento crânio facial e retrusão mandibular, são mais frequentemente acometidos (Bertram et al.[7], 2012; Flores-Mir et al.[17], 2006; Gidarakou et al.[19], 2003; Gill et al.[20], 2008; Hwang et al.[30], 2006; Hwang et al.[31], 2004; Nebbe et al.[45], 1999). Além disso, existem fortes indícios de etiologia multifatorial com importante participação de fatores hormonais (Abubaker et al.[1], 1993; Galal et al.[18], 2008; Michael et al.[42], 2005) e alterações na expressão gênica (Lee et al.[37], 2006; Ribeiro-Dasilva et al.[51], 2009).

Embora a destruição óssea não se mostre claramente relacionada à sintomatologia (Ohlmann et al.[47], 2006; Palconet et al.[48], 2012; Wiese et al.[62], 2008), pacientes afetados por artrite das articulações temporomandibulares atravessam períodos de grande sofrimento que podem levar a quadros complexos de cronificação da dor e sensibilização central (Ballegaard et al.[6], 2008; Woolf [65], 2011). Os fatores que geram estas alterações morfológicas, assim como os sintomas clínicos ainda são desconhecidos. Entretanto, a deformação definitiva das articulações poderá ocorrer com ou sem relação com a sintomatologia (Lee et al.[38], 2012).

As ATMs têm especial capacidade adaptativa em relação às demais articulações em função de seu revestimento fibrocartilaginoso. No entanto, torna-se particularmente vulnerável a danos morfológicos decorrentes de processos inflamatórios ou carga mecânica que ultrapasse o limiar adaptativo (Arnett et al.[4], 1996; Lee et al.[38], 2012; Milam[43]; 2005).

Essas alterações morfológicas articulares afetam diretamente os maxilares, as relações dentais, vias aéreas e a musculatura relacionada (Bertram et al.[7], 2012; Bryndahl et al.[11], 2006; Emshoff et al.[16], 2011; Flores-Mir et al.[17], 2006; Gidarakou et al.[19], 2003; Hwang et al.[30], 2006; Legrell, Isberg[39], 1999; Nebbe et al.[45], 1999), podendo contribuir negativamente com a qualidade de vida do indivíduo.

Desarmonias esqueléticas acentuadas em adultos frequentemente requerem abordagem multidisciplinar. Visando estabelecer um padrão estético-funcional adequado e proporcionar o equilíbrio anatômico da face, a cirurgia ortognática pode estar indicada (Hodge et al.[26], 2012; Robinson, Holm[52], 2010). Osteotomias sagitais bilaterais de mandíbula isoladas ou associadas a cirurgias maxilares estão entre os procedimentos mais utilizados neste tratamento (Mobarak et al.[44], 2001; Schreuder et al.[54], 2007; Tucker[60], 2002).

A necessidade de cirurgia ortognática é especialmente prevalente em casos de severa retrusão mandibular, ou quando o padrão de crescimento craniofacial vertical é predominante e acentuado (Proffit et al.[50], 1992). Ou seja, quando ocorre rotação horária da mandíbula, promovendo um aumento excessivo da altura facial anterior inferior em detrimento da altura facial posterior (Bjork[9], 1969).

Em geral, o crescimento vertical está associado à retrusão mandibular, e é agravado por fatores epigenéticos ambientais relacionados com o padrão de respiração predominantemente bucal,

espaço naso e buco faringeanos diminuídos, presença frequente de processos alérgicos e hipertrofia de cornetos nasais inferiores, adenoides e amigdalas (Holmberg, Linder-Aronson[27], 1979; Joseph et al.[33], 1998; O'Ryan et al.[46], 1982).

Apesar da cirurgia ortognática de avanço mandibular associada à rotação anti-horária do plano oclusal oferecer resultados estéticos e funcionais extremamente satisfatórios (Gonçalves et al.[21], 2006; Wolford et al.[63], 1994), os pacientes submetidos a tal procedimento sofrem um aumento imediato da carga mecânica sobre suas articulações têmporo-mandibulares (Kertens et al.[34], 1990) mediada pelo estiramento dos músculos supra-hioideos e tecido conjuntivo adjacente (Sesenna, Raffaini[55], 1985). Dessa forma, compõem um grupo especialmente suscetível ao desenvolvimento de osteoartrite das ATMs ou ao agravamento de processos pré-existentes (Gonçalves et al.[22], 2008; Hwang et al., [31], 2004; Kertens et al.[34], 1990) que podem gerar certo grau de recidiva do procedimento cirúrgico (Arnett et al.[4], 1996; Bailey et al.[5], 2004; De Clercq et al.[15], 1994; Gill et al.[20], 2008; Gonçalves et al.[22], 2008; Hoppenreijs et al.[28], 1999; Hwang et al.[31], 2004; Kobayashi et al.[35], 2012; Sesenna, Raffaini[55], 1985).

O papel da posição e integridade do disco articular também tem sido enfatizado como indicador de risco à reabsorção condilar. Seu devido controle, através de reposicionamento cirúrgico é, segundo alguns autores, condição essencial nos casos de reabsorção condilar (Gonçalves

et al.[22], 2008; Mehra, Wolford[41], 2001; Wolford et al.[64], 2002). Por outro lado, estudos afirmam que a reabsorção do côndilo após cirurgia ortognática pode ocorrer independentemente do posicionamento do disco articular, sendo o torque condilar elencado como principal fator etiológico (Arnett et al.[4], 1996; Stavropoulos, Dolwick[57], 2003). Portanto, a cirurgia de reposicionamento de disco não seria necessária à estabilização da ATM (Arnett et al.[4], 1996; Stavropoulos, Dolwick[57], 2003).

A tomografia computadorizada de feixe cônico (TCFC) tem assumido um papel de destaque no diagnóstico das reabsorções condilares (Ahmad et al.[2], 2009). Através da análise conjunta dos diferentes cortes tomográficos torna-se possível a identificação de alterações na anatomia dos côndilos mandibulares acometidos por osteoartrite. Entretanto, para que seja viável a realização de estudos longitudinais comparativos que possam fornecer dados precisos quanto à progressão da doença, faz-se necessário o desenvolvimento de novos métodos de análise tridimensional, visando a padronização das mensurações obtidas ao longo do período de avaliação (Paniagua et al.[49], 2011).

Para enfrentar os grandes desafios quanto à observação e monitoramento de formas e estruturas biológicas, estudiosos têm sido envolvidos no desenvolvimento de ferramentas matemáticas e algoritmos complexos aplicados a softwares computacionais (Christensen et al.[14], 1996; Rueckert et al.[53], 1999; Yushkevich et al.[66], 2006).

A utilização de *modelos deformáveis* vem sendo bastante aplicada na análise computadorizada de imagens médicas, tais como tomografias computadorizadas e ressonâncias magnéticas, por possibilitarem a segmentação, visualização e quantificação de uma variedade de estruturas anatômicas. Estes modelos representam a interação de princípios da geometria, física e teoria da aproximação. Os fundamentos da geometria conferem a possibilidade da representação gráfica da forma do objeto em análise; a física impõe restrições sobre como a forma pode variar ao longo do espaço e do tempo; e teoria da aproximação ideal fornece as bases formais do mecanismo de ajuste dos modelos aos dados medidos (McInerney, Terzopoulos[40], 1996).

Atualmente, os métodos tridimensionais mais utilizados na análise quantitativa de alterações anatômicas incluem a obtenção do volume; utilização de escores e classificações previamente definidas; mensurações baseadas em pontos; e medidas de superfície pareadas através do algoritmo ICP (Interactive Closest Point) (Paniagua et al. [49], 2011).

As medidas de volume apresentam excelente aplicação para o estudo de determinados processos patológicos (Goo et al.[23], 2005; Joe et al.[32], 2007; Siegel et al.[56], 2007). Entretanto, deixam de oferecer informações relevantes na avaliação da osteoartrite por refletirem apenas alterações globais em tamanho, não apresentando ferramentas

adequadas para detecção de alterações estruturais em pontos específicos (Paniagua et al.[49], 2011).

A utilização dos escores desenvolvidos por Koyama et al.[36] (2007) para detecção da osteoartrite das ATMs tem sido relatada na literatura como de difícil padronização quanto à definição e classificação da doença (Palconet et al.[48], 2012; Paniagua et al.[49], 2011).

As mensurações baseadas em pontos apresentam erros relacionados à sua própria identificação na realização das análises. Autores afirmam que estes pontos são abstratos considerando que as informações quanto a espaço, curvas, ou superfícies entre eles são perdidas (Andresen et al.[3], 2000; Paniagua et al.[49], 2011).

O algoritmo ICP (Interactive Closest Point) é a abordagem utilizada pela maioria dos softwares comerciais e acadêmicos na avaliação de alterações observadas ao longo do tempo. O ICP mede as menores distâncias entre superfícies pareadas (Andresen et al.[3], 2000; Besl, McKay[8], 1992; Chen, Medioni[13], 1991; Zhang[68], 1994). No entanto, frequentemente, estas distâncias são obtidas a partir de regiões anatomicamente não correspondentes. Isto acontece especialmente quando do estudo em estruturas anatômicas altamente curvas como a mandíbula. Por esta razão, o ICP não quantifica adequadamente as adaptações fisiológicas, tais como a remodelação óssea condilar (Paniagua et al.[49], 2011).

A correspondência de formas tridimensionais tem despertado o interesse da comunidade médica devido à sua precisão em localizar e quantificar as alterações morfológicas entre estruturas saudáveis e patológicas. O método foi inicialmente desenvolvido para estudos morfométricos nas regiões cerebrais (Styner et al.[58], 2006), contudo, Cevidanes et al.[12] (2010), utilizaram-no para quantificar a morfologia condilar de pacientes portadores de reabsorções condilares. Este método inovador no diagnóstico da osteoartrite minimiza a importância da experiência do examinador, reduzindo erros intra e inter-examinadores; padroniza os achados, permitindo novas descobertas; e ainda contribui no desenvolvimento de novos marcadores por imagem para fatores de risco (Cevidanes et al.[12], 2010).

O presente estudo visa avaliar quantitativamente o grau de deslocamento e remodelação condilar após cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular associada ou não à cirurgia de reposicionamento do disco articular, utilizando metodologia inovadora, a qual propõe superposições por equivalência de voxels e mensurações através da correspondência de formas tridimensionais (SPHARM-PDM). A tecnologia apresentada possibilita o desenvolvimento de estudos longitudinais capazes de mapear os estágios de progressão das reabsorções condilares após cirurgia ortognática, contribuindo de forma significativa para a compreensão da etiopatogenia da osteoartrite das ATMs.

2 Proposição

2.1 Objetivo Geral

Estudar a osteoartrite da ATM em pacientes submetidos à cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular através de novas técnicas computacionais desenvolvidas para otimização do uso de imagens tridimensionais.

2.2 Objetivos específicos

1. Avaliar quantitativamente o deslocamento condilar imediatamente após cirurgia ortognática associada ou não à cirurgia de reposicionamento de disco articular;

2. Investigar a estabilidade do avanço e rotação anti-horária maxilo-mandibular em longo prazo;

3. Analisar quantitativamente a remodelação condilar durante o período de acompanhamento pós-cirúrgico;

4. Investigar diferenças entre os gêneros masculino e feminino quanto à remodelação condilar no período de acompanhamento pós-cirúrgico;

5. Investigar diferenças quanto ao deslocamento e remodelação condilar, assim como quanto à estabilidade do procedimento cirúrgico entre grupos de pacientes submetidos ou não à cirurgia de reposicionamento do disco articular simultaneamente à cirurgia ortognática;

6. Identificar associação entre fatores clínicos como idade, padrão esquelético facial e tempo de acompanhamento pós-cirúrgico com alterações remodelativas no côndilo mandibular de pacientes que sofreram cirurgia ortognática associada à cirurgia de reposicionamento do disco articular;

7. Identificar se fatores cirúrgicos como magnitude do avanço e rotação anti-horária maxilo-mandibular, assim como deslocamento ou torque condilar durante a fixação dos fragmentos cirúrgicos podem predizer alterações remodelativas no côndilo mandibular durante o período de acompanhamento pós-cirúrgico em pacientes que sofreram cirurgia ortognática associada à cirurgia de reposicionamento do disco articular.

3 Publicações

Esta tese de Doutorado foi redigida em publicações correspondentes a artigos científicos para periódicos internacionais.

Publicação 1 Three-dimensional quantitative assessment of surgical stability and condylar displacement changes following counterclockwise maxillomandibular advancement surgery: Effect of simultaneous articular disc repositioning

L. R. Gomes, L. H. Cevidanes, M. R. Gomes, A. C. Ruellas, D. P. O. Ryan, B. Paniagua, L. M. Wolford, J. R. Gonçalves

Publicação 2 3D condylar remodeling changes after counterclockwise maxillomandibular advancement surgery: Effect of simultaneous articular disc repositioning surgery

L. R. Gomes, L. H. Cevidanes, M. R. Gomes, A. C. Ruellas, D. P. O. Ryan, B. Paniagua, L. M. Wolford, J. R. Gonçalves

Publicação 3 Counterclockwise maxillomandibular advancement surgery and disc repositioning. Can clinical and surgical factors predict condylar remodeling in the long-term follow-up?

L. R. Gomes, L. H. Cevidanes, M. R. Gomes, A. C. Ruellas, D. P. O. Ryan, B. Paniagua, L. M. Wolford, J. R. Gonçalves

Considerações Éticas: O presente estudo foi previamente aprovado pela Comissão Nacional de Ética em Pesquisa (CONEP) (Anexo A) e Comitê de Ética em Pesquisa (CEP) da Faculdade de Odontologia de Araraquara (CAAE: 01125412.2.0000.5416) (Anexo B).

3.1 Publicação 1

Three-dimensional quantitative assessment of surgical stability and condylar displacement changes following counterclockwise maxillomandibular advancement surgery: Effect of simultaneous articular disc repositioning*

L. R. Gomes, L. H. Cevidanes, M. R. Gomes, A. C. Ruellas, D. P. O. Ryan, B. Paniagua, L. M. Wolford, J. R. Gonçalves

ABSTRACT

Introduction: The aim of this study was to quantitatively assess three-dimensional (3D) condylar displacement changes during counterclockwise maxillomandibular advancement surgery (CMMA) with or without articular disc repositioning, focusing on surgical stability in the follow-up period. **Methods:** 79 patients treated with CMMA had cone-beam computed tomography scans taken pre-surgery, immediately after surgery and, on average, 15 months post-surgery. 142 condyles were divided into 3 groups: G1 (n= 105), condyles from patients diagnosed with symptomatic pre-surgical TMJ articular disc displacement who

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underwent articular disc repositioning using the Mitek® anchor technique concomitantly with CMMA; G2 (n= 23), condyles from patients with clinical verification of pre-surgical bilateral articular disc displacement with minimal to no pre-surgical symptoms who underwent CMMA and no temporomandibular joint (TMJ) intervention; G3 (n= 14), condyles from patients with healthy TMJs who underwent CMMA and no TMJ intervention. Pre- and postsurgical 3D-models were superimposed using voxel-based registration on the cranial base. 3D-Cephalometrics and Shape correspondence were applied to assess surgical and post-surgical displacement changes. **Results:** It was observed that the condyles moved mostly backward, medially and experienced lateral yaw, medial roll and upward pitch in the three groups. Patients submitted to disc replacement surgery (G1) showed downward condylar displacement, whereas it moved upward in G2 and G3. Such differences were highly statistically significant ($p \leq 0.001$). Although condylar displacement changes occurred in the three groups, the overall surgical procedure appeared to be fairly stable, particularly for G1 and G3. G2 showed the larger amount of relapse and percentage of patients experiencing such changes. Statistically significant differences were observed relative to the stability of mandibular anteroposterior position during the follow-up period ($p \leq 0.05$). **Conclusions:** CMMA has shown to be a stable procedure for patients with healthy TMJs and for the ones submitted to simultaneous articular disc repositioning surgery.

INTRODUCTION AND LITERATURE REVIEW

Skeletal relapse after orthognathic surgical procedures has always been a major concern. However, since rigid fixation techniques became frequently used, the amount of sagittal relapse due to bone movement at the osteotomy sites has been significantly reduced. Therefore, clinical concerns have been raised regarding the influence of condylar displacement and/or morphological changes on postoperative relapse.[1, 2]

Counterclockwise maxillomandibular advancement surgery (CMMA) has been described as a stable procedure for patients with healthy temporomandibular joints (TMJs).[3] However, controversial opinions surrounds the appropriate treatment plan for patients with pre-existing TMJ internal derangement who need orthognathic surgery for correcting jaw deformities and malocclusions.[3, 4]

Although some investigators believe that orthognathic surgery alone reduces or eliminates TMJ dysfunction and symptoms, [5-7] others have reported that performing orthognathic surgery in the presence of TMJ disorder may cause further harmful effects to the TMJ.[8, 9] It may happen because mandibular advancement causes the discs to remain displaced as the condyles seek a superoposterior position in the fossa as a result of muscular activity, which increases mechanical loading over the TMJs.[3, 4]

Some studies have shown that the simultaneous surgical correction of coexisting dentofacial deformities and TMJ pathology by repositioning and stabilizing the

articular disc using Mitek® anchor (Mitek® Surgical Products, Westwood, MA) technique provides high-quality treatment outcomes for most patients concerning functional, esthetic and psychological aspects.[3, 10, 11]

On the other hand, specific condylar displacement changes during articular disc repositioning surgery might be investigated as a potential factor inducing condylar remodeling in the long-term follow-up, given condylar loading alteration.[12] Actually, the current literature regarding treatment effectiveness and options for preventing degenerative condylar changes after bimaxillary surgical advancement is not clear yet. This issue has been extensively studied and continues to be a subject of discussion.[11]

Cone beam computed tomography (CBCT) has been used for assessing condylar changes and surgical relapse. However, the great majority of previous studies have measured and interpreted longitudinal changes by using two-dimensional (2D) tools, which are susceptible to errors in determining corresponding landmark positions when bone remodeling occurs. Accurate quantitative three-dimensional (3D) image techniques are now available, providing clinicians with a new imaging modality to evaluate postoperative skeletal relapse as well as positional and dimensional condylar changes.[2, 11, 13-17]

The aim of this study was to quantitatively assess 3D condylar displacement changes during CMMA with or without articular disc repositioning, focusing on surgical stability in the follow-up period.

MATERIALS AND METHODS

The sample was composed of CBCT scans from 79 patients that underwent counterclockwise maxillomandibular advancement surgery (CMMA). Patients were consecutively operated on by the same surgeon (LMW) from October 2008 to January 2011. Inclusion criteria for this study included: 1) all osteotomies performed and stabilized in the same manner with rigid internal fixation; 2) female patients at least 15 years old and male patients at least 17 years old; 3) patients with no TMJ abnormalities and patients with TMJ disc displacement assessed by clinical examination and magnetic resonance imaging [MRI] interpreted by 2 experienced and calibrated doctors [LMW and JRG]; 4) CBCT scans acquired at 3 time-points: before surgery (T1), immediately after surgery (T2) and minimum 6 months follow-up (T3). The exclusion criteria were 1) craniofacial syndromes; 2) systemic degenerative conditions such as rheumatoid arthritis; 3) previous TMJ surgery (articular disc replacement and/or arthroplasty); 4) previous arthroscopy, arthrocentesis, or viscosupplementation; and 5) incomplete records or unwillingness to participate in the study.

A total of 158 condyles were analyzed. 16 condyles were excluded due to previous arthroplasty. The final sample was composed of 142 condyles divided into 3 groups: G1 (n= 105), condyles from patients diagnosed with symptomatic pre-surgical TMJ articular disc displacement who underwent articular disc repositioning using the Mitek® anchor technique concomitantly with CMMA; G2 (n= 23), condyles from patients with clinical verification of pre-surgical bilateral TMJ articular disc displacement with minimal to no pre-surgical symptoms who

underwent double-jaw surgery and no TMJ intervention; G3 (n= 14), condyles from patients with healthy TMJs (no TMJ- related signs or symptoms) who underwent CMMA and no TMJ intervention. All patients signed an informed consent form for hospital admission, surgical procedures, and release of information for research purposes. This study was approved by the university institutional review board and is in compliance with the Helsinki Declaration.

Surgical technique

If indicated, articular disc repositioning surgery was performed using the Mitek® anchor (Mitek® Products, Inc, Westwood, MA) technique.[10] This is an open joint procedure that was performed simultaneously with the orthognathic surgery procedures. Only salvageable discs were indicated for this surgery. A modified endaural incision was used to access the TMJ. The superior joint space was entered by incising the capsular ligaments, and the inferior joint space was entered with an incision just above the lateral pole of the condyle. The hyperplasic bilaminar tissue was wedge resected. The disc was mobilized and passively positioned over the condyle, with the lateral pterygoid muscle attachment preserved. The Mitek® anchor with two 0-Ethibond sutures (Ethicon, Inc, Somerville, NJ) attached was inserted in the postero-lateral surface of the condylar head, approximately 8 mm below the condylar top. The Ethibond sutures were then attached to the posterior aspect of the posterior band of the disc for stabilization. The joint was then irrigated and incision closed.[10]

Following completion of the TMJ surgery, the orthognathic surgery was performed. Counterclockwise rotation and advancement of the maxillomandibular complex was routinely performed on this patient population. That included bilateral mandibular ramus osteotomies and multiple maxillary (Le Fort 1) osteotomies. Bilateral mandibular ramus sagittal split osteotomies were performed, mandible placed into its final position with an intermediate splint and intermaxillary fixation, and application of internal rigid fixation using bone plates and screws. Maxillary osteotomies were then performed, internasal procedures completed if indicated, palatal splint inserted, intermaxillary fixation placed, and rigid fixation applied using 4 bone plates fixated with 2.0-mm diameter screws. Intermaxillary fixation was removed and this completed the surgical procedures.

Image acquisition and 3D analysis

The scanning protocol required the subjects to be seated upright with the Frankfurt plane (trago-infraorbital rim line) parallel to the ground. The mandible was positioned in centric relation, lips relaxed, and the patients were instructed to remain still and not to swallow. CBCT images were obtained in the same machine (i-Cat® CBCT, 120 kV, 5 mA, Imaging Sciences, Hatfield, PA) using a 17 x 23 cm extended field of view protocol, during an 17.8 second scan, with 0.3 mm isotropic voxel size. Pre-surgical (T1) records were taken 1 day (range 1–2 days) before the surgery; immediate postsurgical (T2) records were taken 5 days (range 3–9 days) after surgery; and the longest follow-up (T3) records were taken on average 15.4 months after surgery (range 6–52 months).

CBCT images were resampled to 0.5mm isotropic voxel size for proceeding the segmentation of anatomic structures of interest (CMF Registration, 3D slicer software, www.slicer.org). 3D models of the cranial base, maxilla and mandible were constructed by outlining the cortical boundaries using semi-automatic discrimination procedures that allowed manual editing, i.e., the operator was able to check out slice-by-slice all the three planes of space (ITK-SNAP software, www.itksnap.org).

The ITK-SNAP software was also used for separating and cropping the cranial base model (Fig 1). This model, called mask, indicated the registration program (CMF Registration, 3D slicer software, www.slicer.org) the specific place where we wanted the different time-point models to be superimposed. The cranial base was used as a stable structure of reference for registration because it does not changes over time or with surgical treatment. Thus, all post-surgical models were registered to the cranial base of their respective pre-surgical volumes (Fig 2). The registration method consists of a fully automated voxel-wise rigid registration that compares and matches the intensities of the voxel grey scales at the cranial base between different time-points and relocates the image with 6 degrees of freedom.[14]

3D cephalometric analysis was conducted to determine facial skeletal pattern before surgery (T1), to assess surgical changes (T1-T2), and postsurgical stability (T2-T3) (Q3DC, 3D slicer software, www.slicer.org). Firstly, landmarks were positioned in specific places in the cranium as described in Table I. Then, the software automatically calculated SNA and SNB angles to express the

anteroposterior position of the maxilla and mandible, respectively, relative to the cranial base (Fig 3). SN.GoMe angle was also calculated to show mandibular plane inclination (Fig 4).

In order to analyze specific mandibular condylar displacement changes, superposed models were simultaneously cropped (Easy Clip, 3D slicer software, www.slicer.org). All left condyles were mirrored in the sagittal plane to form right condyles to facilitate outcome analysis (Fig 5). Then, the condylar models were compared by subtraction to compute surgical (T1-T2) and post-surgical changes (T2-T3) by using shape correspondence analysis (SPHARM-PDM, 3D slicer software, www.slicer.org).

SPHARM-PDM generated a mesh with 4002 correspondent points, via spherical mapping and spherical parameterization of each input volumes. Another 3D Slicer tool was then used to calculate 3D point-wise linear distances between each time-point (Model to model distance, 3D slicer software, www.slicer.org)

Semi-transparent overlays were used to visually compare condylar displacement changes. The computed 4002 vector differences were also displayed on the condyle surface, scaled according to the magnitude of the difference and pointing in the direction of the change (vector maps).

Shape correspondence made it possible to mark the interest regions in one condyle alone (e.g., T1), and propagate such regions for the other surgical time-points (e.g., T2 and T3), obtaining x,y,z coordinates for each point (Pick ’n Paint,

3D slicer software, www.slicer.org) (Fig 6). Then, math formulas were applied considering the different correspondent points in the condylar surface, which allowed measuring both translational (antero-posterior, vertical and lateral) and rotational (pitch, roll and yaw) displacements (Fig 7). Each condylar translational displacement was measured in millimeters and rotational changes in degrees. Positive or negative signs indicated displacement direction (Table II).

To determine the reliability of the 3D cephalometric analysis, two examiners were calibrated by repeating the measurements until the method was considered adequate. The measurements were assessed on the CBCT volumetric datasets of 10 randomly selected subjects. In order to test intra-observer reproducibility, each examiner performed the measurements at two different times, respecting a minimum of 1 week between the assessments. For inter-observer reproducibility, measurements done by each examiner were compared. Both tests were conducted using the intraclass correlation coefficient (ICC).

Kolmogorov–Smirnov and Shapiro–Wilk tests were used to check for the normality of data distribution in each group. Descriptive statistics reported pre-surgical (T1), surgical (T1-T2) and post-surgical changes (T2-T3) in each one of the three groups. For normally distributed data, the differences among the groups were tested by using a one way analysis of variance (ANOVA) followed by Hochberg's GT2 post-hoc, appropriate for unequal sample sizes. Considering non-parametric data, Kruskal-Wallis was used to compare overall significance of the differences among the three groups whereas Mann-Whitney compared two

groups at a time (SPSS 16.0, Chicago, IL, USA). A significance level of $p \leq .05$ was applied.

RESULTS

The 3D cephalometric analysis showed high intra- and inter-observer reproducibility for all diagnostic variables (ICC ≥ 0.90) (Table III). Demographic characteristics of the sample are listed in Table IV. The three groups presented with similar mean age, follow-up period and craniofacial pattern ($p \geq 0.05$). Patients showed on average high mandibular plane angle and a bi-maxillary retrusion. There was a prevalence of female patients in G1 and G2 (72% and 61%, respectively). Male patients were slightly more prevalent in G3 (57%).

The amount of counterclockwise rotation and maxillary advancement was similar in the three groups. However, patients in G1 and G2 experienced greater mandibular advancement when compared to G3, a difference that was statistically significant (Tables V and VI).

Considering condylar translational displacement changes during surgery (T1-T2), it was observed that the condyle moved backward and medially in the three groups. Patients submitted to disc repositioning surgery (G1) showed downward condylar displacement, whereas it moved upward in G2 and G3. Such differences were highly statistically significant ($p \leq 0.001$).

Regarding condylar rotational changes, lateral yaw, medial roll and upward pitch were observed in the three groups. However, G1 showed greater amount of upward pitch when compared to G2 ($p \leq 0.05$) and G3 ($p \leq 0.01$). The amount of medial roll was also significantly larger in G1 relative to G3 ($p \leq 0.01$) (Tables VII and VIII).

Percentage of condylar displacement changes in each group is detailed in Fig 8. Fig 9 shows semi-transparencies and signed-distances color-coded maps illustrating the displacement. The distances observed in the maps were determined by subtracting each one of the 4002 corresponding surface points between T1 and T2 models. Fig 10 also illustrated condylar displacement by showing vectors maps.

It was not observed statistically significant differences among G1 and G3 considering post-surgical stability (T2-T3) (Tables IX and X; Fig 11). Mean relapse in CCW rotation, maxillary and mandibular advancement were quite small (≤ 0.9º) in such groups. On the other hand, G2 showed the larger percentage of patients experiencing relapse greater than 1.0º in SNGoMe, SNA and SNB angles during the follow-up period. Statistically significant differences were observed between G1 and G2 ($p \leq 0.05$) and G3 and G2 ($p \leq 0.05$) relative to the stability of mandibular anteroposterior position (SNB angle).

About 30% of the sample in G2 showed clockwise rotation greater than 1.5º during the follow-up period. 5% showed more than 3º SNGoMe relapse. 23% of the sample in G1 also experienced clockwise rotation greater than 1.5º, but less

than 1% of the sample in this group showed more than 3º SNGoMe relapse. G3 showed a very small percentage of patients experiencing relapse greater than 1º (Fig 12).

Considering maxillary advancement (SNA), it was noticed that about 23% of the sample in G1, 35% of G2 and 15% of G3 experienced relapse greater than 1.0º. About 40% of the sample in G2 and 16% of G1 showed more than 1.0º of relapse on mandibular advancement surgery (SNB). G3 only showed SNB relapse lower than 1º (Fig 12).

DISCUSSION

Cone beam computed tomography has undergone rapid evolution and become a reliable and increasingly important source of 3D information. The present study used CBCT scans to quantitatively assess 3D condylar displacement changes during CMMA with or without articular disc repositioning, focusing on evaluating the stability of such bimaxillary advancement surgery in the follow-up period.

A validated semi-automatic segmentation method was used to construct 3D surface models of the regions of interest for the study.[15] By using the entire cranial base as a reference, a fully automated superimposition using voxelwise rigid registration was conducted, providing high accuracy in analyzing both condylar displacement changes and the overall surgical stability.[14, 18]

Diverse methods have used CBCT scans for assessing orthognathic surgery outcomes, such as linear measurements obtained from axial, coronal, and sagittal slices, 2D measurements based on 3D rendering, volume differences, or color maps obtained from 3D closest point surface distances. The interactive closest point has been used for quantifying pre- and post-surgical changes, allowing visual assessment of colour maps.[11, 13, 14, 16] However, when rotations or large displacement changes occurs, measurements could be affected because such algorithm measures the smallest surface distances between 3D models, which do not necessarily imply anatomical correspondence.

The current study is the first to assess condylar spatial changes following counterclockwise maxillomandibular advancement and TMJ articular disc repositioning using shape correspondence analysis (SPHARM-PDM) in a large sample. Such method allows a unique and symmetric point-to-point correspondence across all measured surfaces. Vector colour-coded maps provided information on the directionality of the movement by showing the before-to-after displacements in detail. Specific math formulas were also applied to evaluate each translational and rotational condylar changes, considering the six degrees of freedom.

The 3D cephalometric landmarks used to assess surgical stability in this study were thoroughly identified applying validated tools that presented high intra- and inter-observer reproducibility. The automated 3D analysis, with superimposition of follow-up scans in the same coordinate system, contributed to avoid errors inherent to CBCT assessments using cross-sectional slice measurements.

Although counterclockwise maxillomandibular advancement surgery provides great functional and esthetic results,[19] post-surgical skeletal relapse is still a common phenomenon.[1] Authors have attributed this fact mainly to suboptimal intraoperative positioning of the proximal segments, which may be associated with progressive condylar resorption (PCR).[20-23]

Literature has shown that higher incidence of PCR occurs in hyperdivergent class II female patients that underwent large surgical advancements[12, 20, 24-27] for these patients usually present with pre-surgical signs or symptoms of temporomandibular disorders (TMD).[2]

The position and morphology of the disc has shown to be closely related to the stress suffered by the joint.[22] Gonçalves et al.[3] found that patients with preoperative disc displacement who underwent mandibular advancement surgery without previous disc repositioning could experience greater relapse and take significantly longer to recover. However, controversies still exist regarding the possibility of conducting open joint articular disc repositioning previously or simultaneously with the orthognathic surgery.[3, 4, 10] Gonçalves et al. [11] stated that an adequately diagnosed and carefully performed TMJ disc repositioning may offer patients with previous TMJ disorders similar outcomes of bone adaptive changes and remodeling as those observed in patients with no history of TMJ disorders at 1-year follow-up. On the other hand, such procedure poses the risk of aggravating the degenerative process if the fibrocartilage is inadvertently damaged.[11] Moreover, some authors assure that condylar resorption may happen

regardless the position of the disc, being condylar torque the main etiological factor.[20-23]

The importance of optimal intraoperative positioning of the proximal segments was recognized many years ago.[21, 28] It has been advocated that precise repositioning of the condyles during surgery would ensure stability of the surgical results and reduce the chance of post-surgical TMD.[29] On the other hand, Dicker et al. [30] did not support the idea that increased postoperative joint loading and sagittal rotation of the condyle are a serious cause of condylar resorption or relapse.

By using different methods, researchers have studied the condylar movements that occur in patients who have undergone orthognathic surgery.[11, 31, 32] A usual finding is that both condyles move posteriorly in patients who underwent sagittal split ramus osteotomy to advance the mandible.[11, 31, 32]

The present study evaluated such changes in three different groups to also address the influence of TMJ health and articular disc surgical repositioning (Mitek® anchor technique) relative to postsurgical stability. It was observed that most condyles translated backward and medially in the three groups immediately after surgery (T1-T2). However, statistically significant differences among the groups were observed regarding vertical displacement. Patients submitted to disc repositioning surgery (G1) showed downward condylar displacement, whereas it moved upward in G2 and G3. It was an expected outcome because it is necessary to open some space for the disc that is being positioned back and held

in place with the Mitek® anchor inserted at the upper lateral region of the condyle.[11]

Gonçalves et al. [11] observed that patients submitted to disc repositioning surgery showed downward condylar displacement, whereas it moved upward when only maxillomandibular advancement was conducted, which corroborate our findings. However, the authors found that the condyles translated backward in patients treated with maxillomandibular advancement only, whereas it moved forward in patients treated with simultaneous articular disc repositioning.

In the present study, anteroposterior (AP) condylar displacement in G1 ranged from -3,2mm to 3,5mm, which means that the condyles in this group moved both backward and forward, being the backward displacement more prevalent (about 70% of the sample in G1). Although, on average, the condyles translated backward, the real amount of condylar AP movement was small, i.e., below 2mm for about 90% of the sample (Fig 8).

Greater mandibular advancement and counterclockwise rotation were observed in G1, which would generate higher condylar loading by the stretching of the submandibular soft tissue and muscles.[23, 28] However, the percentage of condyles showing backward displacement was about 10% lower in this group when compared to G2 and G3. This fact may confirm that disc repositioning surgery exert some forward pressure, not as strong as the downward one, but able to somehow compensate part of the backward load.

Regarding condylar rotational changes immediately after surgery (T1-T2), lateral yaw, medial roll and upward pitch were observed in the three groups. However, G1 showed greater amount of upward pitch and medial roll. Gonçalves et al. [11] also found that medial roll and lateral yaw occurred regardless of TMJ disc repositioning, but these authors noted similar amounts and frequency between the groups.

In the present study, a monocortical 2.0-miniplate was used to stabilize the sagittal splits and minimize condylar torque. Two or three non-compression bicortical screws improved stabilization. However, large mandibular advancements inevitably promote some condylar positional changes during surgery regardless the technique used due to the parabolic shape of the mandible and design of the sagittal split.

Our findings for patients submitted to CMMA corroborate those of previous studies on sagittal split osteotomy for mandibular advancement, showing that condylar displacements and rotations after mandibular advancement result in posterosuperior displacement and medial condylar angulations, as assessed from CBCT images.[11, 13, 16]

Although condylar displacements occured, only a small percentage of the patients in the 3 groups experienced post-surgical relapse measured by SNGoMe, SNA and SNB angles greater than 1.5º. Kim et al. [31] reported that condylar positional changes in all planes occurred without any TMD signs or symptoms, given the individual capacity of physiologic adaptation. These authors

stated that such condylar changes did not seem to affect the long-term skeletal and occlusal stability, corroborating our findings. Other studies have also found that small condylar rotations do not appear to have a functional compromise.[29, 32-34] However, the extent of condylar change that is compatible with normal function post-surgically is still unknown.[13]

In the current study, mean relapse in CCW rotation, maxillary and mandibular advancement was, in general, quite small (≤ 1.0º). However, G2 showed the largest post-surgical mean changes measured by SNB and SNGoMe angles. The percentage of patients experiencing changes in SNGoMe, SNA and SNB angles during the follow-up period was also the highest ones. Statistically significant differences among the groups were observed for SNB variable.

Kobayashi et al. [12] noted a higher incidence of progressive postoperative condylar resorption in hyperdivergent retrognathic patients with preoperative erosion, condyle deformity, or both. Therefore, patients in G1 would be expected to show higher levels of skeletal relapse because they presented with symptomatic pre-surgical TMJ articular disc displacement. A large number of patients in this group showed condylar osteoarthritis, with important flattening of condylar surface, subchondral cysts, erosions and/or osteophytes, generating considerable deformation of the condylar structure. On the other hand, G2 was composed of condyles from patients with clinical verification of pre-surgical bilateral TMJ articular disc displacement with minimal to no pre-surgical symptoms.

It may be inferred that the articular disc repositioning surgery with the Mitek® anchor technique provided patients with preoperative condylar osteoarthritic changes, similar CMMA follow-up results from the ones obtained for patients presenting with healthy TMJs, corroborating Gonçalves et al. [11] findings.

Another important aspect to be addressed refers to the controversy that still surrounds the counterclockwise rotation of the maxillomandibular complex. Authors have stated that avoid changing the mandibular plane inclination contributed to postoperative surgical stability.[28, 35] Xi et al. [23] concluded that the chance of experiencing a clinically significant relapse is 4.8 times higher in patients whose proximal segments were rotated and fixated in a more anterior position than prior to surgery. Authors suggested that such a counterclockwise rotation of the proximal segments in combination with a posterior inclination of the condylar neck may increase the loading of the preoperatively unloaded anterior-superior surface of the condyle, making the condyle more prone to resorption with subsequent skeletal relapse.[26, 36]

Although our sample, particularly the group that underwent simultaneous disc repositioning surgery (G1), showed higher mandibular advancement (mean 6.0 mm) and counterclockwise rotation (mean 5.9º) of the maxillomandibular complex than what has been shown in previous reports,[2, 37] the mean surgical relapse was small. Therefore, counterclockwise maxillomandibular surgical advancement has proven to be a stable procedure in properly selected cases, when recognizing pre-existent TMJ pathology and managing it appropriately.[38-40]

Future 3D studies with larger sample of patients presenting with healthy condyles or with clinical verification of pre-surgical bilateral articular disc displacement and no TMJ intervention are needed in order to confirm the importance of performing disc replacement surgery with Mitek® anchor prior to CMMA.

CONCLUSIONS

- Although condylar displacements occurred, the overall surgical procedure appeared to be fairly stable, particularly for G1 and G3. G2 showed the larger amount and percentage of patients experiencing relapse. Statistically significant differences were observed relative to the stability of mandibular anteroposterior position during the follow-up period.

- Articular disc repositioning surgery with the Mitek® anchor technique provided patients with preoperative condylar osteoarthritic changes, similar CMMA follow-up results from the ones obtained for patients presenting with healthy TMJs.

- Counterclockwise maxillomandibular surgical advancement has proven to be a stable procedure in properly selected cases, when recognizing pre-existent TMJ pathology and managing it appropriately.

ACKNOWLEDGMENT

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FIGURES

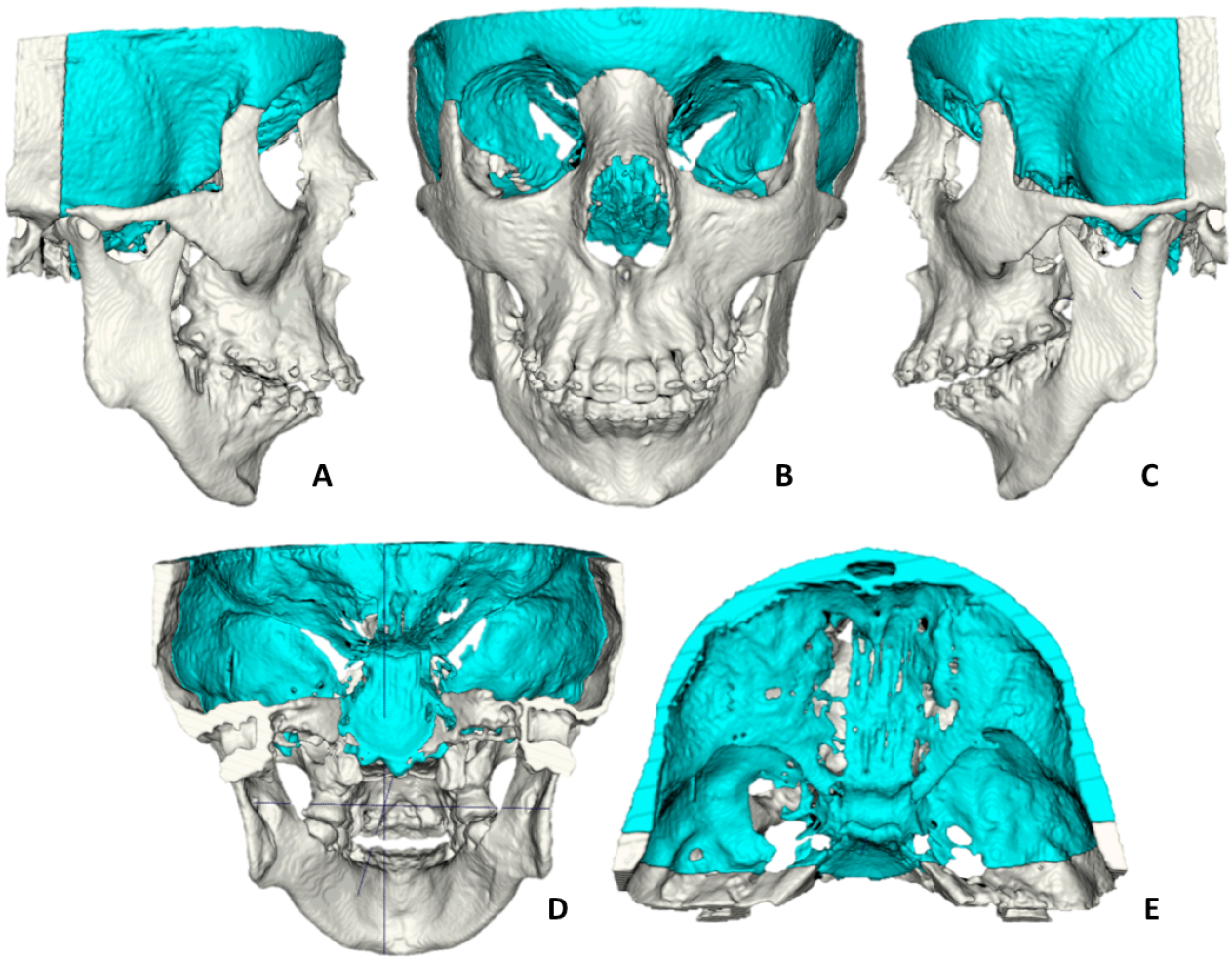

Fig 1. 3D model constructed from the segmentation process. Cranial base registration mask shown in blue. A, C lateral views; B, frontal view; D, posterior view; E, superior view

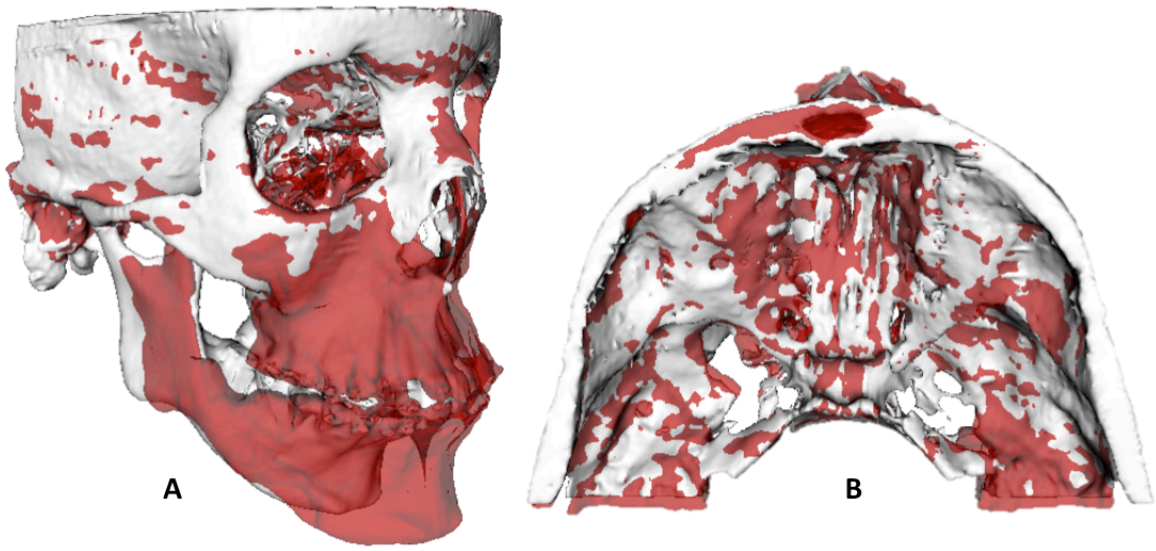

Fig 2. Pre- and post-surgical 3D models superimposed on the cranial base. A, lateral view; B, superior view. Note how the color are mixed at the cranial base

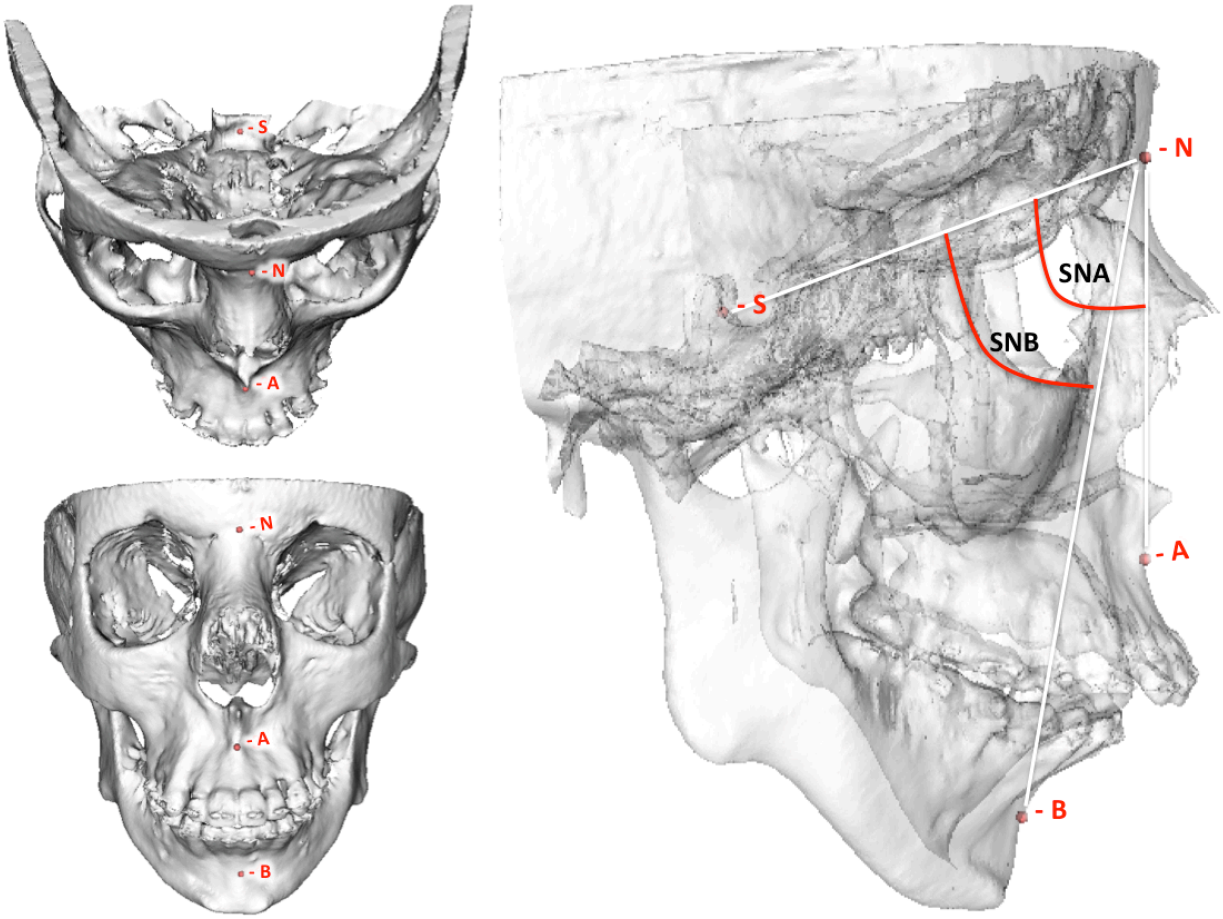

Fig 3. 3D Cephalometric analysis. SNA, angle obtained by the intersection of SN and NA lines. It reflects anteroposterior position of the maxilla relative to the cranial base; SNB, angle obtained by the intersection of SN and NB lines. It reflects anteroposterior position of the mandible relative to the cranial base

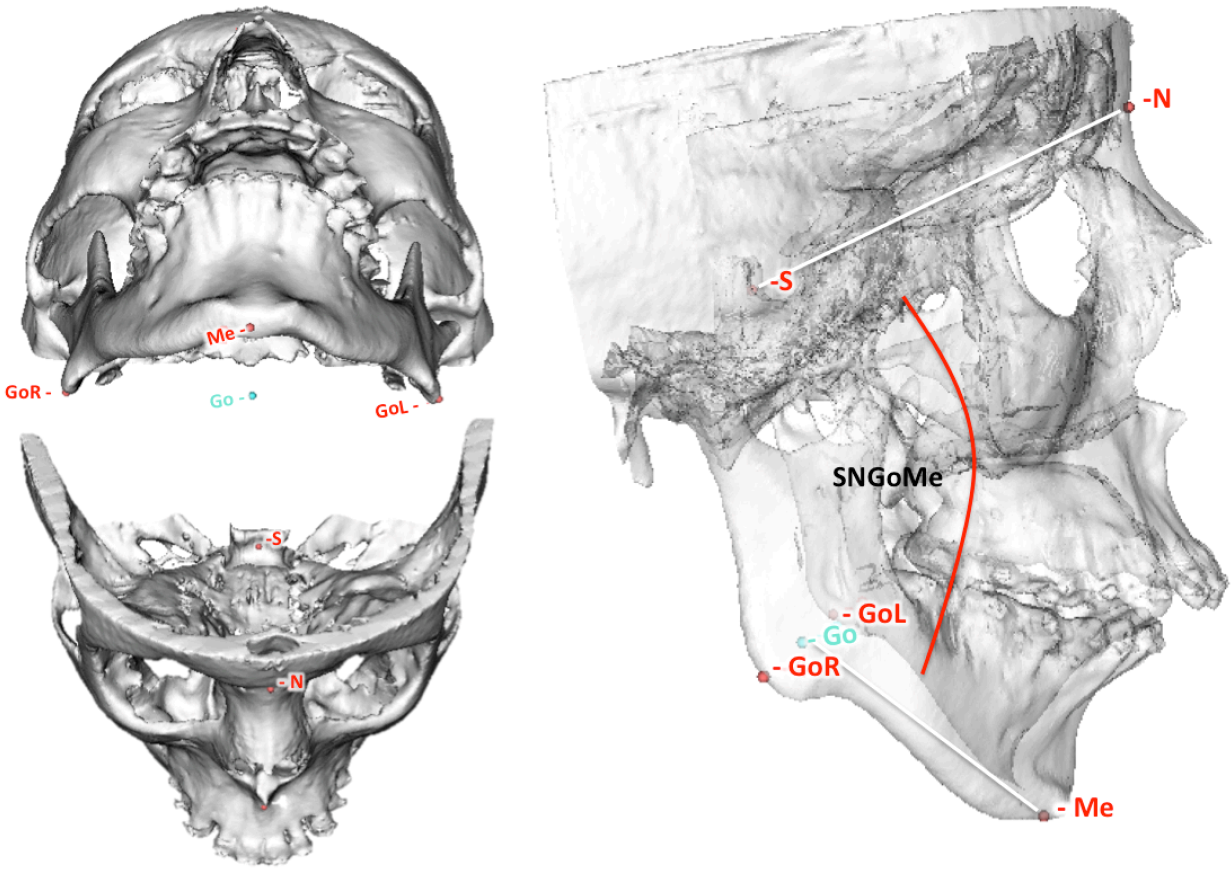

Fig 4. 3D Cephalometric analysis. SNGoMe, angle obtained by the intersection of SN and the mandibular plane defined by GoMe line. It reflects the mandibular plane inclination relative to the cranial base

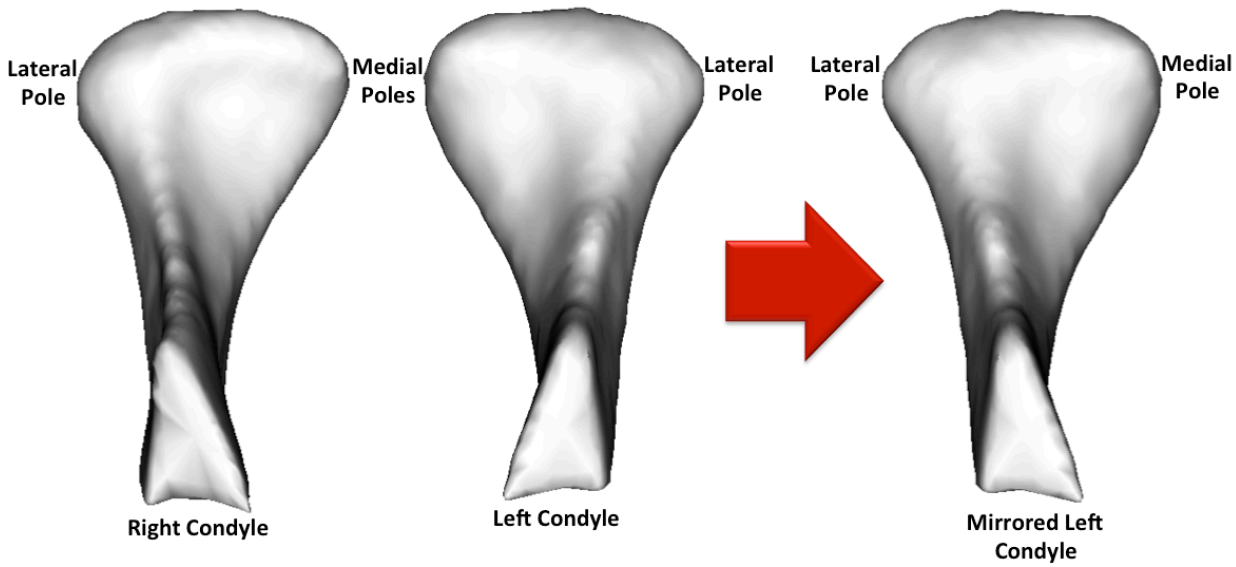

Fig 5. All left condyles were mirrored as right condyles

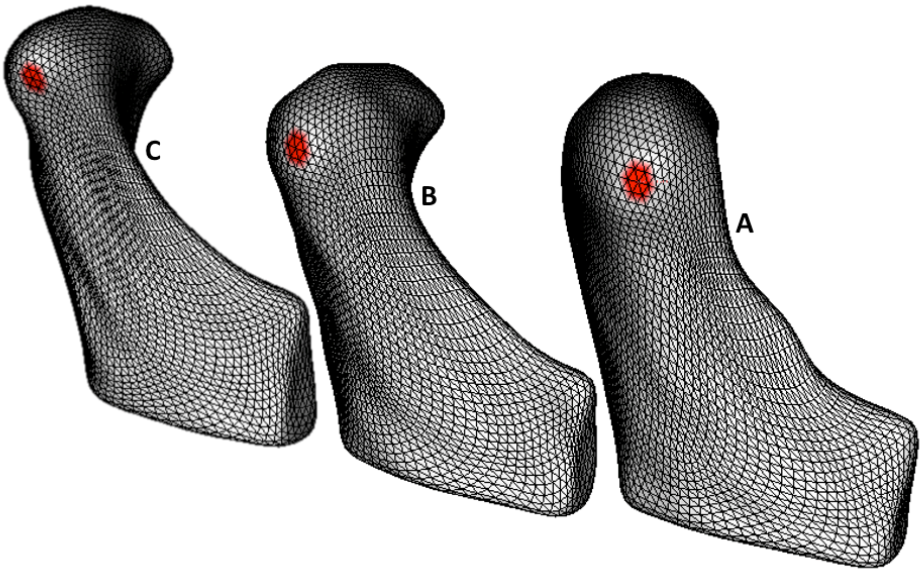

Fig 6. Example of lateral pole propagation considering correspondent surface mesh points. A, before surgery (T1). B, immediately after surgery (T2). C, Follow-up period (T3)

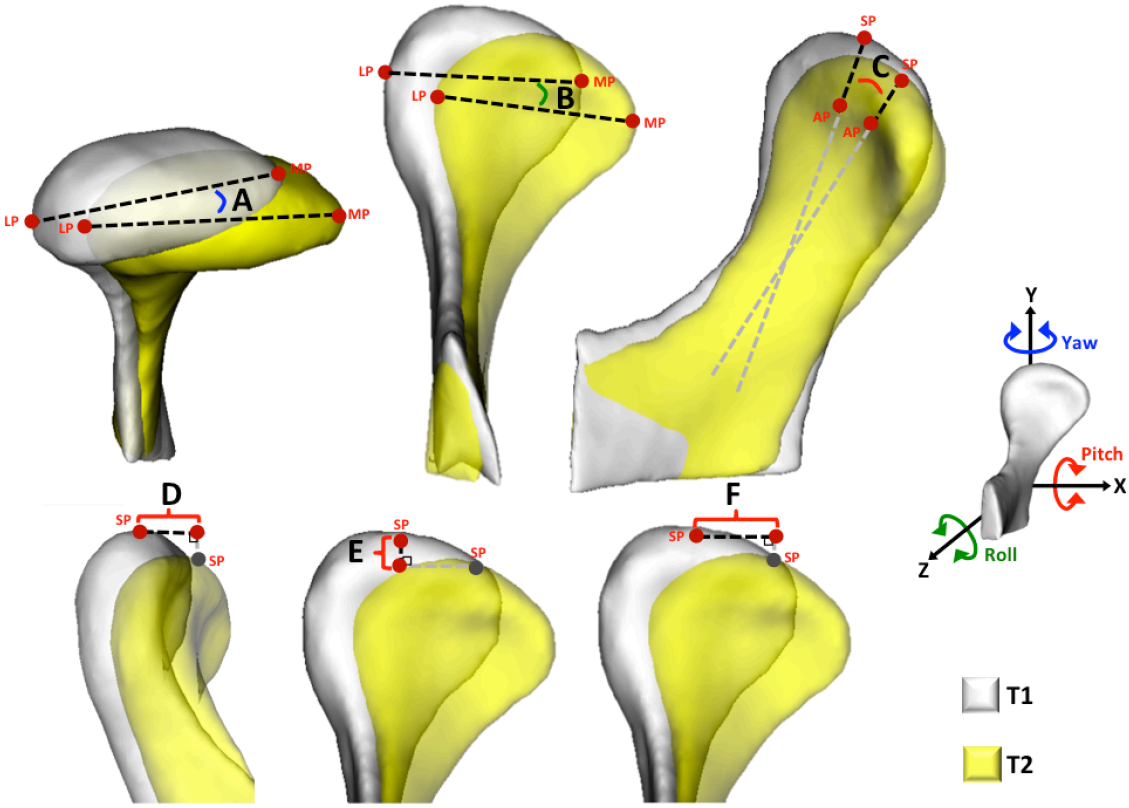

Fig 7. Rotational and translational measurements used to assess condylar changes. A, Yaw, rotation around the Y axis (axial view). B, Roll, rotation around the Z axis (coronal view). C, Pitch, rotation around the X axis (sagittal view). D, Antero-posterior displacement (sagittal view). E, Vertical displacement (coronal view). F, Lateral displacement (coronal view)

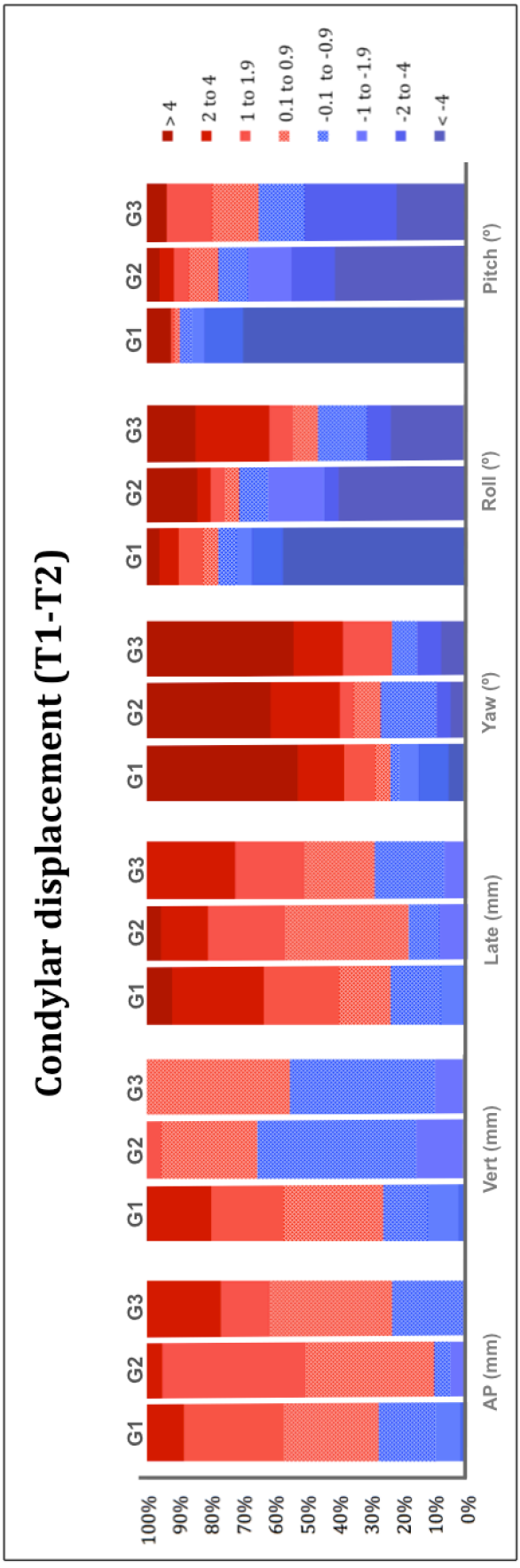

Fig 8. Percentage of patients according to direction and magnitude of condylar translational and rotational changes during surgery (T1-T2)

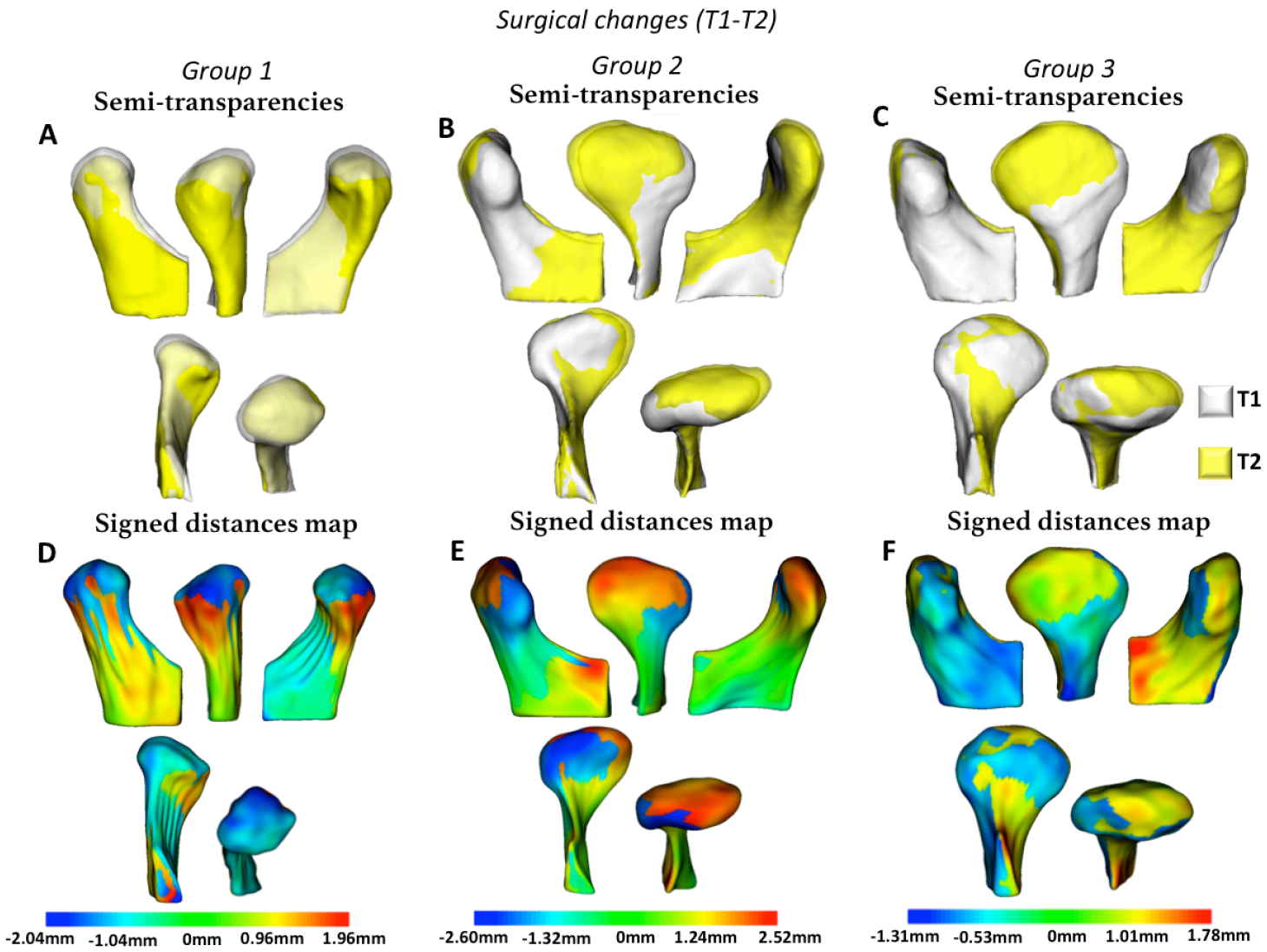

Fig 9. Right condyle models of patients randomly selected from groups 1, 2 and 3. A, B, C, Semi-transparency overlays showing condylar displacement during surgery (T1-T2). D, E, F, Respective color-coded signed distances maps of surgical changes (T1-T2)

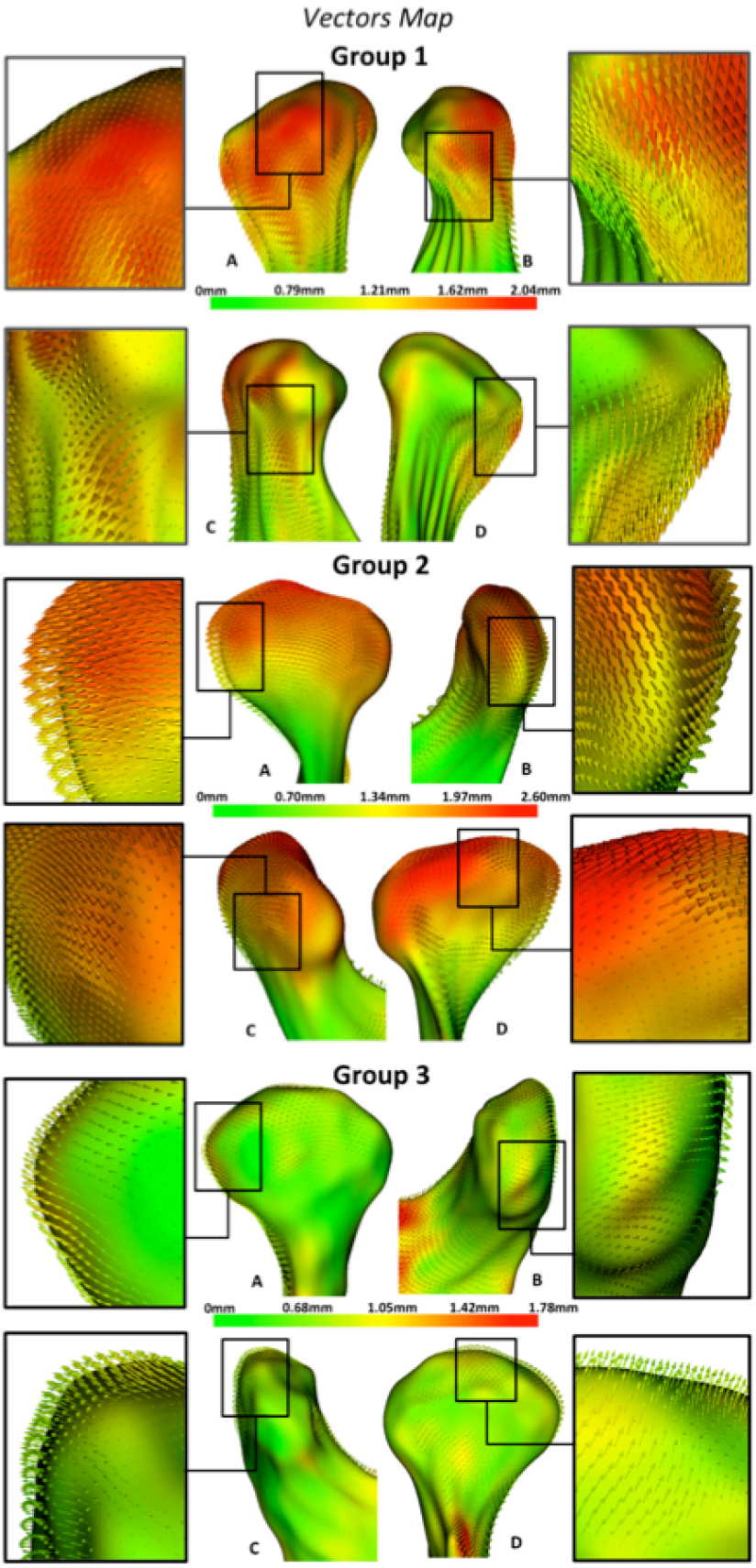

Fig 10. Vectors map showing changes from T1 to T2 in randomly selected patients from groups 1, 2 and 3. A, Posterior view. B, Medial view. C, Lateral view. D, Anterior view

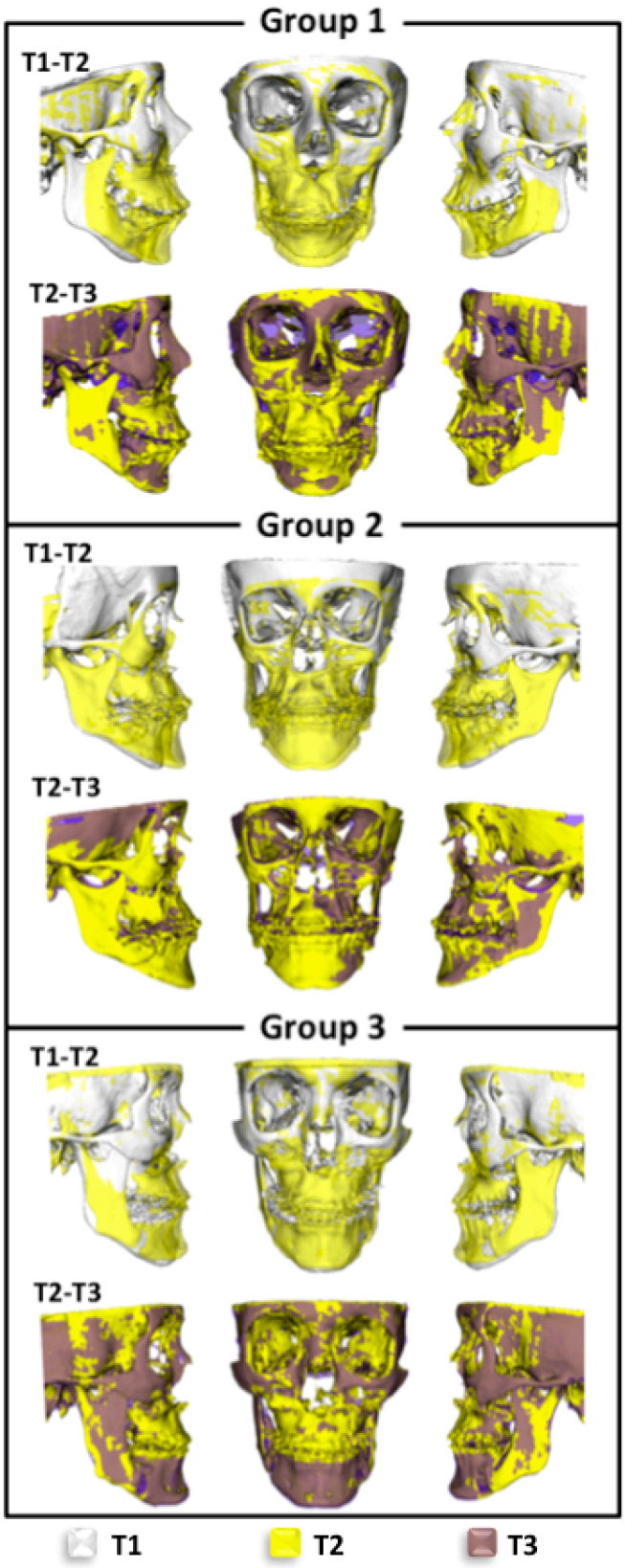

Fig 11. Semi-transparency overlays showing overall surgical (T1-T2) and post-surgical (T2-T3) changes from randomly selected patients. Group 1, 18 months follow-up; Group 2, 13 months follow-up; Group 3, 8 months follow-up

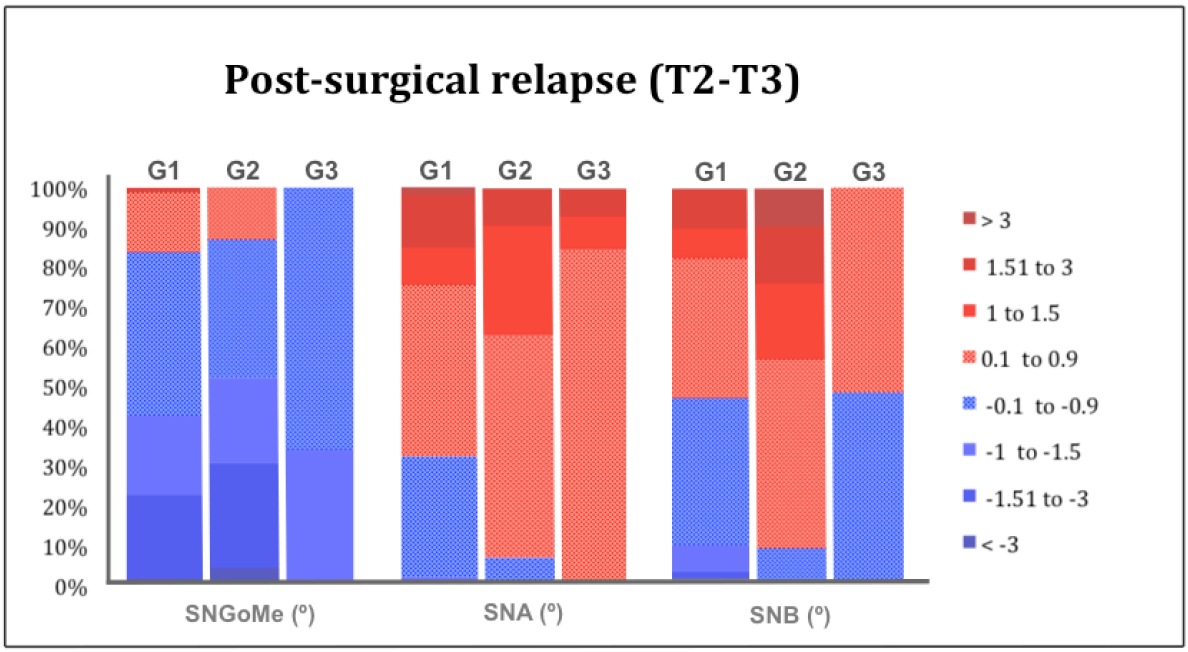

Fig 12. Percentage of patients according to post-surgical relapse (T2-T3). Positive values indicate counterclockwise rotation and negative values indicate clockwise rotation for SNGoMe measurements; Considering SNA and SNB angles, negative values indicate the maxilla/mandible moved anteriorly and positive values indicate it moved posteriorly

TABLES

Table I. Definition of landmarks used for 3D cephalometric analysis

Anatomical landmarks	Symbol	Definition
Nasion	N	Anterior point on the frontonasal suture in the midsagittal plane
Sella	S	Midpoint at the posterior wall of the Sella Turcica. Obtained by the projection of the geometric center of the Sella passing through the Nasion point
Subspinale	A	Deepest point on the anterior contour of the maxillary alveolar process in the midsagittal plane
Supramentale	B	Deepest point on the anterior contour of the mandibular alveolar process in the midsagittal plane
Menton	Me	Lowest point on the lower border of the mandibular symphysis in the midsagittal plane
Gonion	Go	Midpoint at the angle of the mandible. Obtained by the mean distance between the right (GoR) and left (GoL) sides

Table II. Direction of translational and rotational condylar displacement changes

Condylar displacement	Orthogonal view-planes	Negative values	Positive values
Translational changes			
AP*	Sagittal and Axial	Anterior translation	Posterior translation
Vert*	Sagittal and Coronal	Upward translation	Downward translation
Late*	Coronal and Axial	Lateral translation	Medial translation
Rotational changes			
Yaw	Axial	Posterior rotation of the medial pole and/or anterior rotation of the lateral pole (Medial Yaw)	Anterior rotation of the medial pole and/or posterior rotation of the lateral pole (Lateral Yaw)
Roll	Coronal	Medial rotation	Lateral rotation
Pitch	Sagittal	Counterclockwise rotation (Upward Pitch)	Clockwise rotation (Downward Pitch)

*AP, Antero-posterior displacement; Vert, Vertical displacement; Late, Lateral displacement

Table III. Intraclass correlation coefficient (ICC) values for intra- and inter-observer reproducibility of the 3D cephalometric analysis

	SNA	SNB	SN.GoMe
Intra-observer reliability			
Examiner 1, ICC	0.97	0.95	0.98
Examiner 2, ICC	0.99	0.98	0.97
Inter-observer reliability			
ICC	0.91	0.93	0.90

Table IV. Demographic data

			Before Surgery (T1)		
	Age (yr)	Follow-up (mo)	SNGoMe (°)	SNA (°)	SNB (°)
Group 1 (n= 105, 75 female and 30 male)					
Mean	27.3	16.8	40.7	79.1	74.6
SD	12.2	8.6	7.4	3.7	4.3
Min	16.0	6.0	25.1	69.5	59.4
Max	58.0	52.0	61.0	87.0	83.0
Percentile					
15th	16.0	9.6	32.9	75.2	71.1
85th	46.0	25.4	48.6	82.9	78.6
Group 2 (n= 23, 14 female and 9 male)					
Mean	29.7	14.7	39.6	79.9	76.6
SD	10.8	7.7	4.5	3.6	3.1
Min	15.0	7.0	29.1	72.7	69.6
Max	46.0	39.0	47.4	85.5	81.6
Percentile					
15th	17.3	11.0	36.3	76.8	73.5
85th	41.0	21.4	44.0	84.9	79.4
Group 3 (n= 14, 6 female and 8 male)					
Mean	33.3	14.7	41.7	80.0	78.0
SD	17.4	7.7	7.2	6.9	5.0
Min	15.0	8.0	28.8	67.7	71.7
Max	63.0	31.0	49.3	90.4	86.1
Percentile					
15th	18.8	8.0	34.6	75.8	72.1
85th	48.8	17.7	47.4	85.2	82.1

Abbreviations: SD, Standard deviation; Min, Minimum; Max, Maximum; SNGoMe, sella-nasion to mandibular plane angle; SNA, sella-nasion to A point angle; SNB, sella-nasion to B point angle

Table V. Descriptive statistics and Kruskal-Wallis test for comparing the amount of surgical displacement (T1-T2) changes

Surgical changes [a] (T1-T2)	Group 1 (n=105)					Group 2 (n=23)					Group 3 (n=14)					
	Mean	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*P value*
SNGoMe (°)	5.9	3.4	5.25	0.7	14.6	5.2	2.7	5.1	1.5	11.2	5.4	3.0	6.6	1.5	9.0	0.772
SNA (°)	-3.7	2.2	-3.6	-8.0	1.2	-4.2	2.4	-5.1	-7.9	-0.4	-3.2	2.2	-3.6	-6.0	1.3	0.545
SNB (°)	-6.0	2.3	-6.0	-12.6	-0.6	-5.4	1.9	-5.2	-8.3	-0.3	-3.9	2.0	-4.2	-6.7	-0.2	**0.002**

Abbreviations: SD, Standard Deviation; Med, Median; Min, Minimum; Max, Maximum; SNGoMe, sella-nasion to mandibular plane angle; SNA, sella-nasion to A point angle; SNB, sella-nasion to B point angle

[a] Positive values indicate counterclockwise rotation and negative values indicate clockwise rotation for SNGoMe measurements; Considering SNA and SNB angles, negative values indicate the maxilla/mandible moved anteriorly and positive values indicate it moved posteriorly

Significant if $P \leq 0.05$

Table VI. Mann-Whitney post-hoc comparisons of the amount of surgical displacement between groups

Surgical changes (T1-T2)	Group 1 - Group 2		Group 1 - Group 3		Group 2 - Group 3	
	Mean Difference	*P value*	*Mean Difference*	*P value*	*Mean Difference*	*P value*
SNGoMe (°)	0.7	0.454	0.5	0.888	-0.2	0.875
SNA (°)	0.5	0.388	-0.5	0.662	-1.0	0.222
SNB (°)	-0.6	0.166	-2.1	**0.001**	-1.5	**0.036**

Significant if $P \leq 0.05$

Table VII. Descriptive statistics and one-way ANOVA test for comparing the amount of condylar linear and rotational displacements during surgery (T1-T2)

Condylar displacement[a] (T1-T2)	Group 1 (n=105)					Group 2 (n=23)					Group 3 (n=14)					
	Mean	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*P value*
AP (mm)	0.6	1.2	0.6	-3.2	3.5	0.7	0.7	0.6	-1.0	2.4	0.9	1.1	0.7	-0.4	3.2	0.523
Vert (mm)	0.9	1.2	0.9	-2.3	5.0	-0.1	0.8	-0.3	-1.2	1.9	-0.3	0.9	-0.2	-2.0	0.8	**0.000**
Late (mm)	1.5	1.7	1.3	-2.5	7.3	1.0	1.4	0.7	-1.4	4.8	0.9	1.3	1.2	-1.1	2.6	0.243
Yaw (°)	4.0	5.5	3.6	-11.8	18.3	3.2	5.1	3.0	-10.6	12.1	3.8	5.1	2.9	-5.0	11.6	0.797
Roll (°)	-5.5	6.6	-5.3	-30.5	8.7	-2.4	5.4	-1.6	-13.5	6.1	-0.3	5.3	0.3	-12.3	8.9	**0.005**
Pitch (°)	-7.7	7.6	-7.8	-32.3	14.0	-3.3	5.5	-2.1	-18.6	7.9	-1.4	4.6	-1.6	-8.5	10.7	**0.001**

Abbreviations: SD, Standard Deviation; Med, Median; Min, Minimum; Max, Maximum; AP, Antero-posterior displacement; Vert, Vertical displacement; Late, Lateral displacement; Yaw, rotation around the Y axis; Roll, rotation around the Z axis; Pitch, rotation around the X axis

[a] See table II for direction of translational and rotational condylar displacement changes

Significant if $P \leq 0.05$

Table VIII. Hochberg's GT2 post-hoc comparisons of the amount of condylar linear and rotational displacements between groups

Condylar displacement (T1-T2)	Group 1 - Group 2		Group 1 - Group 3		Group 2 - Group 3	
	Mean Difference	*P value*	*Mean Difference*	*P value*	*Mean Difference*	*P value*
AP (mm)	-0.1	0.920	-0.3	0.640	-0.2	0.942
Vert (mm)	1	**0.000**	1.2	**0.001**	0.2	0.975
Late (mm)	0.5	0.448	0.6	0.542	0.1	1.000
Yaw (°)	0.8	0.877	0.2	0.998	-0.6	0.984
Roll (°)	-3.1	0.109	-5.2	**0.014**	-2.1	0.691
Pitch (°)	-4.4	**0.023**	-6.3	**0.006**	-1.9	0.793

Significant if $P \leq 0.05$

Table IX. Descriptive statistics and group comparisons relative to post-surgical stability (T2-T3)

Post-surgical changes [a] (T2-T3)	Group 1 (n=105)					Group 2 (n=23)					Group 3 (n=14)					
	Mean	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*P value*
SNGoMe (°)	-0.9	1.0	-0.8	-4.5	2.3	-1.0	1.0	-1.0	-3.0	0.8	-0.9	0.3	-0.8	-1.4	-0.4	0.872*
SNA (°)	0.9	0.7	0.9	-1.0	3.1	0.6	0.7	0.6	-0.5	2.0	0.7	0.5	0.5	0.2	1.6	0.566*
SNB (°)	0.2	1.0	0.2	-1.7	3.2	1.0	1.1	0.8	-0.7	3.2	0.1	0.4	0.0	-0.3	0.7	**0.031‡**

Abbreviations: SD, Standard Deviation; Med, Median; Min, Minimum; Max, Maximum; SNGoMe, sella-nasion to mandibular plane angle; SNA, sella-nasion to A point angle; SNB, sella-nasion to B point angle

[a] Positive values indicate counterclockwise rotation and negative values indicate clockwise rotation for SNGoMe measurements; Considering SNA and SNB angles, negative values indicate the maxilla/mandible moved anteriorly and positive values indicate it moved posteriorly

* ANOVA, ‡ Kruskal-Wallis

Significant if P ≤ 0.05

Table X. Post-hoc comparisons of post-surgical stability (T2-T3) between groups

Post-surgical changes (T2-T3)	Group 1 - Group 2		Group 1 - Group 3		Group 2 - Group 3	
	Mean Difference	*P value*	*Mean Difference*	*P value*	*Mean Difference*	*P value*
SNGoMe (°)	1.0	0.872	0.9	1.000	-0.1	0.957*
SNA (°)	0.3	0.981	0.2	0.713	-0.1	0.661*
SNB (°)	-0.8	**0.014**	-0.1	0.824	0.9	**0.012‡**

* Hochberg's GT2, ‡ Mann-Whitney

Significant if P ≤ 0.05

3.2 Publicação 2

3D condylar remodeling changes after counterclockwise maxillomandibular advancement surgery: Gender difference and effect of simultaneous articular disc repositioning*

L. R. Gomes, L. H. Cevidanes, M. R. Gomes, A. C. Ruellas, D. P. O. Ryan, B. Paniagua, L. M. Wolford, J. R. Gonçalves

ABSTRACT

Purpose: Assess three-dimensional condylar remodeling changes following counterclockwise maxillomandibular advancement surgery (CMMA) with or without articular disc repositioning, investigating possible gender differences. **Methods:** 87 condyles (60 female, 27 male) from 49 patients treated with CMMA had cone beam computed tomography (CBCT) scans taken pre-surgery, immediately after surgery and, on average, 14 months post-surgery. The sample was divided into two major groups: CMMA-Drep (n= 63), condyles from patients diagnosed with pre-surgical articular disc displacement who underwent articular disc repositioning using the Mitek® anchor technique concomitantly with the orthognathic surgery; and CMMA (n= 24), condyles from patients who underwent double-jaw surgery and no temporomandibular joint (TMJ) intervention. The CMMA group was subdivided into 2 groups: CMMA-1 (n= 16), condyles

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from patients with pre-surgical bilateral TMJ articular disc displacement with minimal to no pre-surgical symptoms; CMMA-2 (n= 8), condyles from patients with healthy TMJs. Three-dimensional (3D) condylar models were superimposed using an automatic voxel-based regional registration. Shape correspondence and volume measurements were applied to assess post-surgical condylar-remodeling changes. **Results:** Although female patients showed greater volume reduction in both major groups, statistically significant gender differences were not observed. Condyles into CMMA-Drep group showed significant amount of bone apposition on the anterior pole during the follow-up period ($P \leq 0.001$). CMMA-1 group experienced larger volume reduction when compared to CMMA-Drep and CMMA-2 groups ($P \leq 0.05$). No statistically significant differences were observed between CMMA-Drep and CMMA-2 on overall volume changes. **Conclusion:** TMJ disc repositioning surgery may offer some protective effect to condyles of patients presenting with previous TMJ disorders, providing similar post-surgical overall volume changes to those observed in patients with healthy TMJs.

INTRODUCTION

Temporomandibular joint (TMJ) osteoarthritis (OA) has been defined as a progressive degenerative joint disorder caused by a pathological imbalance between processes of breakdown and repair of the organic tissues.[1-3] The complex pathogenesis of the disease has remained unclear.[4] According to the magnitude and rate of progression, condylar morphologic changes may be defined as physiologic, when evolving into morphological and functional

adaptation,[5, 6] or pathologic, when generating aggressive bone destruction, deformity of related structures, and functional impairment.[3, 5, 7-9]

Clinical and pathological presentation of TMJ OA ranges from mild failure of the joint components with disc displacement and degeneration, to loss of articular fibrocartilage, synovitis, and subchondral bone alterations such as sclerosis, flattening, erosions, and bone overgrowth with osteophytes formation.[1, 10] Early diagnosis of such conditions is important to monitor bone destruction, either localized to the TMJ or systemic, before loading the joints with orthodontic/orthopedic forces or undertaking jaw surgery.[1, 11]

Degenerative condylar changes after counterclockwise maxillomandibular advancement surgery (CMMA) are undesirable outcomes that may occur when the altered mechanical load during or after the surgical procedure exceeds the adaptive capability of the TMJs, leading to subsequent skeletal and occlusal relapse.[5, 8, 9]

Hyperdivergent skeletal class II female patients have been frequently associated with greater susceptibility to TMJ internal derangements.[8, 12-17] Therefore, the stability of CMMA performed in such patients may be less predictable,[18, 19] particularly when the patient presents with some TMJ arthritic changes (disc displacements or osteoarthritis) previously to the orthognathic procedure.[20-23]

Among alternative treatment options for such patients, simultaneous articular disc repositioning has been advocated to avoid condylar resorption and improve

stability.[21, 22, 24, 25] However, controversy still surrounds the effectiveness of different strategies for preventing degenerative condylar changes after bimaxillary surgical advancement. Some authors are still skeptical about TMJ surgery because of the unpredictable and sometimes devastating outcomes in the past.[21, 26]

Cone beam computed tomography (CBCT) has assumed a prominent role in the diagnosis of temporomandibular joint (TMJ) dysfunction, particularly for assessment of morphologic changes in mandibular condyles presenting with osteoarthritis (OA).[27] CBCT has been shown to render high-resolution images providing a clear visualization of the hard tissues of the TMJ.[1, 10, 27]

The analysis of different tomographic slices, make it possible to identify specific changes in the anatomy of the mandibular condyles with OA. On top of that, the use of new technologies, such as CBCT-based surface models, allow for a comprehensive qualitative and quantitative evaluations of the overall TMJ morphologic alterations.[28]

Three-dimensional (3D) shape-correspondence analysis (SPHARM-PDM) has been described as a method to precisely locate and quantify morphologic changes between healthy and pathologic structures.[29] This innovative method for diagnosing TMJ osteoarthritis potentially minimizes the importance of the examiner's experience, reducing intra- and inter-rater related errors, standardizes findings, and contributes to more accurate comparisons of the results, which

were not possible with two-dimensional landmark linear or angular measurements.[1]

The present study used longitudinal quantitative measurements in 3D models to assess condylar remodeling changes following CMMA with or without articular disc repositioning, investigating possible gender differences.

MATERIALS AND METHODS

CBCT scans from 49 hyperdivergent retrognathic patients who underwent counterclockwise maxillomandibular advancement surgery (CMMA) were enrolled in this study. Patients were consecutively operated on by the same surgeon (LMW), using rigid internal fixation. Inclusion criteria included female patients at least 15 years old and male patients at least 17 years old. Patients may present with no TMJ abnormalities or with TMJ disc displacement assessed by clinical examination and magnetic resonance imaging [MRI] interpreted by 2 experienced and calibrated doctors [LMW and JRG]. This study required CBCT images obtained before surgery (T1), immediately after surgery (3-9 days) (T2), and at a minimum 6 months follow-up (T3). The exclusion criteria included craniofacial syndromes, systemic degenerative conditions such as rheumatoid arthritis, and previous TMJ intervention.

A total of 98 condyles were analyzed. 11 condyles were excluded due to previous arthroplasty. The final sample was composed of 87 condyles divided into 2 groups: CMMA-Drep (n= 63), condyles from patients diagnosed with pre-surgical

TMJ articular disc displacement who underwent articular disc repositioning using the Mitek® anchor technique [24] concomitantly with the orthognathic surgery; CMMA (n= 24), condyles from patients who underwent double-jaw surgery and no TMJ intervention. The CMMA group was subdivided into 2 groups: CMMA-1 (n= 16), condyles from patients with pre-surgical bilateral TMJ articular disc displacement with minimal to no pre-surgical symptoms; CMMA-2 (n= 8), condyles from patients with healthy TMJs (no TMJ- related signs or symptoms). All patients signed an informed consent form for hospital admission, surgical procedures, and release of information for research purposes. This study was approved by the university institutional review board and is in compliance with the Helsinki Declaration.

Surgical technique

CMMA technique included traditional Le Fort I osteotomy and bilateral sagittal split ramus osteotomies with internal rigid fixation. Maxilla was stabilized with 4 bone plates fixated with 2.0-mm screws and sagittal split osteotomies fixated with 1 bone plate at the corpus region followed by 2 or 3 bicortical 2.0-mm bone screws at the retromolar region on each side. Articular disc repositioning surgery using the Mitek® anchor (Mitek® Products, Inc, Westwood, MA) technique is an open joint procedure that was performed simultalneously with the orthognathic procedure, when indicated. Detailed description of the surgical procedure was previously published.[24]

Image acquisition and 3D analysis

CBCT images were obtained in the same machine (i-Cat® CBCT, 120 kV, 5 mA, Imaging Sciences, Hatfield, PA). The scanning protocol involved 17 x 23 cm extended field of view protocol, during an 17.8 second scan, with 0.3 mm isotropic voxel size. Images were resampled to 0.5mm isotropic voxel size for proceeding the segmentation of anatomic structures of interest (CMF Registration, 3D slicer software, www.slicer.org). 3D models of the cranial base, maxilla and mandible were constructed by outlining the cortical boundaries using semi-automatic discrimination procedures (ITK-SNAP software, www.itksnap.org). The program allowed the operator to check out slice-by-slice the effectiveness of the segmentation procedure and perform manual editing in the three planes of space. A previously validated 3D cephalometric analysis was conducted to determine facial skeletal pattern before surgery (T1) and assess surgical changes (T1-T2) for sample characterization (Fig 1) (Q3DC, 3D slicer software, www.slicer.org).

ITK-SNAP software was used for separating and cropping part of the ramus and mandibular condyle from each side (Fig 2). This model, called mask, indicated the registration program (CMF Registration, 3D slicer software, www.slicer.org) the specific place where we wanted the different time-point models to be superimposed. The regional registration method consists of a fully automated voxel-wise rigid registration that compares and matches the intensities of the voxel grey scales at the mask region between different time-points and relocates the image with 6 degrees of freedom. This method has been previously

validated.[30] The current study included a small modification in the mask design. Voxels at the superior aspect of the condyle were not considered for the registration procedure.

In order to analyze specific condylar remodeling changes, superposed models were simultaneously cropped (Easy Clip, 3D slicer software, www.slicer.org). All left condyles were mirrored in the sagittal plane to form right condyles to facilitate outcomes analysis (Fig 3). Then, the condylar models were compared by subtraction to compute post-surgical changes by using shape correspondence analysis (SPHARM-PDM, 3D slicer software, www.slicer.org).

SPHARM-PDM generated a mesh with 4002 correspondent points, via spherical mapping and spherical parameterization of each input volumes. Five specific regions of interest (ROIs) were selected as representative of each condylar pole, i.e., superior, anterior, posterior, medial and lateral poles. 37 correspondent points were used for analyzing changes in the anterior, superior and posterior poles, whereas 19 points were selected as representatives for analyzing changes in the lateral and medial poles (Fig 4). Referred ROIs were marked in post-surgical 3D models and propagated to the respective follow-up (Pick 'n Paint, 3D slicer software, www.slicer.org) (Fig 5). 3D point-wise linear distances between each time-point were then used to calculate remodeling changes in millimeters (Model to model distance, 3D slicer software, www.slicer.org). Positive and negative signals represented outward and inward movement, respectively. Thus, positive values indicated bone apposition and negative values indicated bone

resorption. Condylar volume changes were also calculated in cubic millimeters by using the ITK-SNAP software.

Semi-transparent overlays were used to visually compare condylar changes. The computed 4002 vector differences were also displayed on the condyle surface, scaled according to the magnitude of the difference and pointing in the direction of the change (vector maps).

Intra- and inter-observer errors in segmentation of the mandibular condyles were tested by two calibrated observers, using a randomly selected sample of 10 CBCT volumetric datasets. Systematic differences between the observers were assessed using a Hotelling T2 test in a multivariate analysis of covariance software (ShapeAnalysisMANCOVA).[31]

Kolmogorov–Smirnov and Shapiro–Wilk tests were used to check for the normality of data distribution in each group. Descriptive statistics reported pre-surgical (T1), surgical (T1-T2) and post-surgical changes (T2-T3) in each group. For normally distributed data, the differences among the groups were tested by using a one way analysis of variance (ANOVA) followed by Hochberg's GT2 post-hoc, appropriate for unequal sample sizes. Considering non-parametric data, Kruskal-Wallis was used to assess overall significance of the differences among the three groups and Mann-Whitney for between-groups comparisons. Independent sample t test and Mann-Whitney also checked for gender differences. Pearson and Spearman correlation coefficients evaluated the relationship between total volume changes and specific remodeling

characteristics in each pole of the mandibular condyles considering normally and non-normally distributed data, respectively. A significance level of $p \leq .05$ was applied. Statistics were calculated by using SPSS software (SPSS 16.0, Chicago, IL, USA).

RESULTS

The largest intra- and inter-observer differences in segmentation of the mandibular condyles were 0.14 mm (mean 0.05 mm; SD 0.02) and 0.15 mm (mean 0.07 mm; SD 0.02), respectively. These differences were found between the average models derived from each observer's condyle segmentations of CBCT scans. The significance maps showed no statistically significant differences for any of the 4002 points in study during both intra- ($p > 0.98$) and inter-observer reproducibility ($p > 0.84$) (Fig 6).

Demographic characteristics of the sample are listed in Table 1. The three groups in study showed similar mean age and follow-up period. All patients presented with a hyperdivergent craniofacial pattern and mandibular retrognathism. On average, maxillary retrusion was also observed. The amount of counterclockwise rotation and maxillary advancement was similar in the three groups. However, patients in CMMA-Drep group experienced greater mandibular advancement.

Table 2 evaluated gender differences on remodeling condylar changes. Female patients were prevalent in the two major groups: CMMA-Drep and CMMA (73% and 58%, respectively). Although it was not observed statistically significant

gender differences in none of the two groups, female patients into CMMA-Drep showed greater amount of resorption at the lateral and superior poles. The overall volume change in this group was also quite different. On average, females showed volume reduction whereas male patients showed volume increase. Considering CMMA group, more females also experienced condylar resorption.

There were highly statistically significant differences regarding anterior pole remodeling changes in CMMA-Drep group compared to both CMMA groups ($p \leq 0.001$). On average, patients submitted to disc replacement surgery showed bone apposition on the anterior pole during the follow-up period. It was not found statistically significant differences between CMMA-1 and CMMA-2 ($p > 0.05$). Statistically significant differences were also observed considering overall volume changes. CMMA-1 group experienced larger volume reduction when compared to CMMA-Drep and CMMA-2 groups ($p \leq 0.05$). No statistically significant differences were observed between CMMA-Drep and CMMA-2 (Tables 3 and 4).

The highest percentage of condyles that suffered resorption was observed in CMMA-1 group, particularly when considering the superior and posterior poles. Bone apposition on the anterior pole was observed on 90% of the sample in CMMA-Drep group. About 95% of CMMA-1 group showed some volume reduction. Volume increase was observed in 55% of the sample in CMMA-Drep and 60% of CMMA-2 (Fig 7).

Fig 8 shows semitransparencies and signed-distances color-coded maps illustrating the remodeling changes. The distances observed in the maps were determined by subtracting each one of the 4002 corresponding surface points between T2 and T3 models. Fig 9 also illustrated condylar remodeling by showing vectors maps.

Table 5 shows correlation coefficients between condylar poles remodeling and volume changes in each group. Considering CMMA-Drep group, the overall volume reduction was mostly associated with superior ($p \leq 0.001$) and lateral ($p \leq 0.001$) poles resorption. Superior ($p \leq 0.01$) and posterior ($p \leq 0.05$) poles resorption were associated with volume reduction in CMMA-1 group. All condylar poles were correlated with overall volume reduction in CMMA-2 group, except for the posterior one.

DISCUSSION

Based on conventional x-rays, authors have found signs of condylar osteoarthritis in patients that underwent orthognathic surgery. However, to date, no details concerning dimensional condylar changes were given.[32] The present study is the first to investigate three-dimensional condylar remodeling changes following counterclockwise maxillomandibular advancement and TMJ articular disc repositioning by using shape correspondence analysis (SPHARM-PDM) and volume measurements in a sample of hyperdivergent retrognathic patients.

3D models were constructed through a semiautomatic discrimination procedure, by calibrated examiners. Our results showed excellent intra- and inter-observer reliability of the segmentation procedures, corroborating other studies.[1, 33, 34] Therefore, it is unlikely that any segmentation errors would have influenced the outcomes of this research.

Previous studies have reported condylar remodeling changes by using cranial-base registration.[22] However, for comprehensive evaluation of condylar surface changes, a method of superimposition over the condylar neck, mandibular notch, and posterior border of ramus is necessary.[30, 35] The information from such a regional superimpositions can differ from the conclusions obtained by cranial-base superimposition, which may only assess longitudinal displacements of the condyle in relation to the cranial fossa, but do not separate these displacements from bone remodeling.

In the present study, the two different methods of voxelwise rigid registration were performed. Cranial-base superimposition was used for sample characterization, whereas regional registration allowed analyzing specific condylar remodeling changes. Previous studies have shown high accuracy in both 3D automatic registration methods.[30, 36, 37]

Authors have assessed 3D condylar changes by using the interactive closest point.[22, 38-41] However, such algorithm measures the smallest surface distances between 3D models, which do not necessarily imply anatomical correspondence.[38]

Volume measurements and shape correspondence (SPHARM-PDM)[29] were employed in this study to quantify 3D condylar remodeling changes following CMMA with or without articular disc repositioning, investigating possible gender differences. SPHARM-PDM has been shown to provide a unique and symmetric point-to-point correspondence across all measured surfaces. Shape differences were calculated between each correspondent point on T2 and T3 models.

Progressive condylar resorption is a multifactorial phenomenon, and some of the risk factors involved in this condition are interrelated.[42, 43] It is reported to occur in systemic diseases such as rheumatoid arthritis, among other autoimmune problems.[44] Therefore, patients with these diseases have been excluded from this study.

It has been suggested that orthognathic surgery itself may exacerbate condylar resorption.[45, 46] Moreover, authors have observed that preoperative morphological characteristics such as a high mandibular plane angle, small SNB angle, short posterior facial height, and a small posterior-to-anterior facial height ratio are reported to be risk factors for developing condylar resorption after orthognathic surgery [5, 8, 9, 47-50] Therefore, to avoid biased outcomes, only hyperdivergent retrognathic patients composed the sample in study. Given the high incidence of temporomandibular disorders in such particular craniofacial pattern, the group formed of healthy condyles in the current research was quite small.

Although the high prevalence of disc displacement in orthognathic patients has been well documented,[32, 51] very few studies have associated disc displacement to condylar bony changes. In the majority of cases, this association was found by assessing qualitative changes such as bone flattening, bone erosion and osteophyte formation rather than by quantifying dimensional changes.[33, 35, 52-55]

Actual results concerning changes in TMJ symptoms after orthognathic surgery are still not conclusive.[56] Valladares-Neto et al. [57] found that mandibular advancement surgery did not affect the TMJ of patients with pre-existing disc displacement and crepitus. Madani and Mirmortazavi [58] noted significant reduction in pain in patients who underwent mandibular advancement surgery, corroborating other authors.[56, 57, 59-61]

Contrariwise, some investigators have advocated that untreated TMJ internal derangement could act as negative factors in postsurgical TMJ outcome.[32, 51, 62, 63] Wolford et al. [23] observed that exact repositioning of the TMJ disc leads to clinical improvement in many cases and that very significant relapse takes place in the absence of TMJ disc repositioning. Other authors also noted a worsening of signs and symptoms of TMJ dysfunction, particularly an increase in headaches and muscular and joint pain.[64-66] Goncalves et al. [21] stated that mandibular advancement surgery with counterclockwise rotation is a stable procedure for patients with healthy TMJs and for those who simultaneously undergo disc repositioning. However, patients with preoperative articular disc displacement experienced a significant relapse following surgery.

Several studies have shown a strong female predilection for condylar resorption,[5, 8, 9, 67] particularly following orthognathic surgery.[47, 49] It may be attributed to sex hormones, such as the estrogen, which mediate the metabolism of cartilage and bone in female TMJs,[67, 68] eventually predisposing these patients to an exaggerated response to loading of the joint after orthognathic surgery.[42]

On the other hand, Berger et al. stated that there is weak evidence to support the hypothesis that estrogen levels are associated with TMD.[69] Actually, the interpretation of the high proportion of females with condylar resorption following orthognathic surgery in the literature is still controversial. Authors found that gender did not have a statistically significant effect on the incidence of condylar resorption after mandibular advancement. They stated that more women showed resorption than men because more women underwent surgery.[70]

Although it was not observed statistically significant gender differences regarding condylar remodeling changes in the present study, the female predominance was evident, particularly in CMMA-Drep group. Female patients into CMMA-Drep showed greater amount of resorption at the lateral and superior poles. On average, they also showed volume reduction whereas male patients showed volume increase. Xi et al. [49] also observed that the reduction in condylar volume was significantly larger among female patients. Considering CMMA group, both female and male patients experienced condylar resorption, however, female condyles were the most affected ones. Therefore, condylar resorption not only occurs in women but also in men,[9] particularly when disc replacement surgery is not performed.

Abubaker et al. [71] reported that immunodetectable estrogen receptors were found five times more often in symptomatic than in asymptomatic patients. This implies that symptomatic females may have different responses to estrogen levels, based on target receptors within the TMJ. In the current study, although the CMMA-Drep group was composed of symptomatic patients, it was observed less condylar volume reduction in this group for both female and male patients, which may suggest some protective effect provided by the disc replacement surgery.

Gonçalves et al. [22] reported that resorption on the anterior condylar surface was more frequent in the group that did not undergo disc replacement surgery. Bone apposition was observed after TMJ articular disc repositioning, which corroborate our findings. In the current study, highly statistically significant differences regarding anterior pole remodeling changes were observed in CMMA-Drep group compared to both CMMA groups. On average, patients submitted to disc replacement surgery showed bone apposition on the anterior pole during the follow-up period.

Gonçalves et al. [22] also reported that patients who underwent disc replacement surgery experienced resorption at the upper lateral quadrant of condylar posterior surface, adjacent to the area of bone anchor placement. Colour map analysis in the current study confirmed such observation. However, this localized resorption did not negatively influence the overall condylar remodeling in this group. Condyles from patients with pre-surgical bilateral TMJ articular disc displacement

that did not undergo TMJ intervention (CMMA-1) experienced larger volume reduction when compared to CMMA-Drep and CMMA-2 groups.

Statistically significant correlation coefficients suggested that most part of the volume reduction in CMMA-Drep was due to superior and lateral poles resorption. Such findings corroborated a previous research, which reported superior pole resorption and significant flattening of the lateral pole in condyles presenting with osteoarthritis, regardless the surgical procedure.[11] Superior and posterior poles resorption contributed the most with volume reduction in CMMA-1 group. Strong correlation coefficients indicated that volume reduction in CMMA-2 group was associated with the resorption of all condylar poles, except the posterior one. Caution is necessary when analyzing the results of correlation tests in this group given the fact that it is relatively easy to obtain perfect associations by chance given small sample size. On the other hand, for large samples, even weak statistically significant correlations may be relevant.

Post-orthognathic surgery stability and relapse can be influenced by the TMJ,[72, 73] in the sense that surgical correction of skeletal deformities requires soft-tissue responses and condylar remodeling to adapt to the new environment.[74] Large mandibular advancement and counterclockwise rotation have been reported as contributing surgical factors to condylar resorption,[5, 8, 9, 41, 42, 45-47, 70, 75] which occurs when mechanical stimuli exceed the adaptive capacity of the condyle.[5, 8, 76]

Patients in CMMA-Drep group would be expected to show higher levels of condylar resorption because they presented with symptomatic pre-surgical TMJ articular disc displacement and have also experienced greater mandibular advancement and counterclockwise rotation of the maxillomandibular complex. A large number of patients in this group showed condylar osteoarthritis signs, with important flattening of condylar surface, subchondral cysts, erosions and/or osteophytes, generating a considerable deformation of the condylar structure. Kobayashi et al. [42] observed a higher incidence of progressive postoperative condylar resorption in hyperdivergent retrognathic patients with preoperative erosion, condyle deformity, or both.

Therefore, ours findings brought relevant information given the controversies concerning open joint articular disc repositioning surgery.[21, 23-25, 77] It was shown that appropriate TMJ disc repositioning surgery may provide patients with previous TMJ disorders similar outcomes as those observed in patients with healthy TMJs, corroborating other studies.[21, 22] On the other hand, patients presenting with preoperatory disc displacement that did not undergo disc replacement surgery before or simultaneously with orthognathic surgery may show larger risk of surgical relapse given greater condylar resorption.[21]

More longitudinal studies with larger control groups would be necessary to confirm the importance of conducting TMJ disc repositioning surgery in patients at increased risk of developing condylar resorption following orthognathic surgery.

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FIGURES

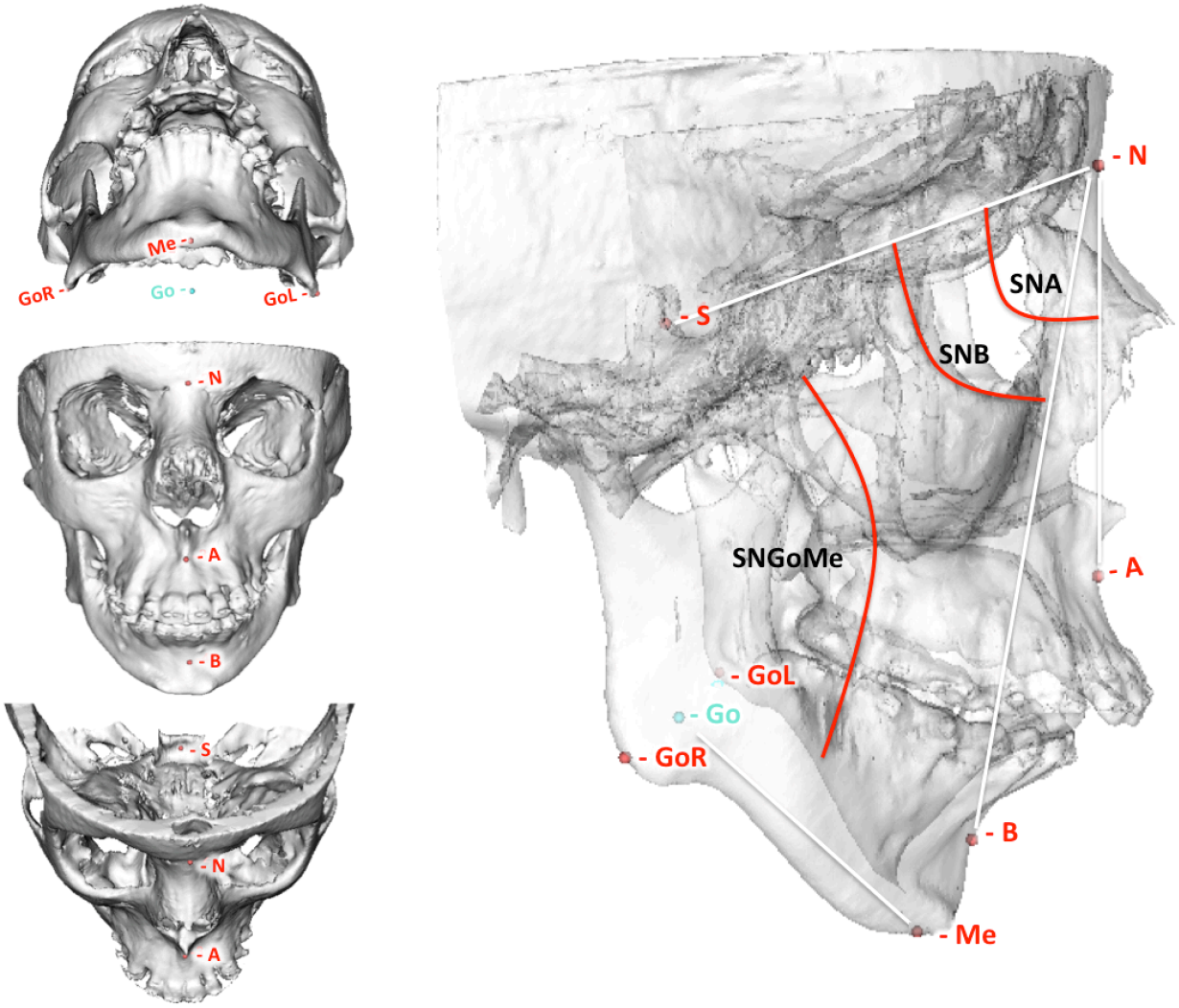

Fig 1. 3D Cephalometric analysis. SNA, angle obtained by the intersection of SN and NA lines. It reflects anteroposterior position of the maxilla relative to the cranial base; SNB, angle obtained by the intersection of SN and NB lines. It reflects anteroposterior position of the mandible relative to the cranial base; SNGoMe, angle obtained by the intersection of SN and the mandibular plane defined by GoMe line. It reflects the mandibular plane inclination relative to the cranial base. Go is obtained by the mean distance between the right (GoR) and left (GoL) sides

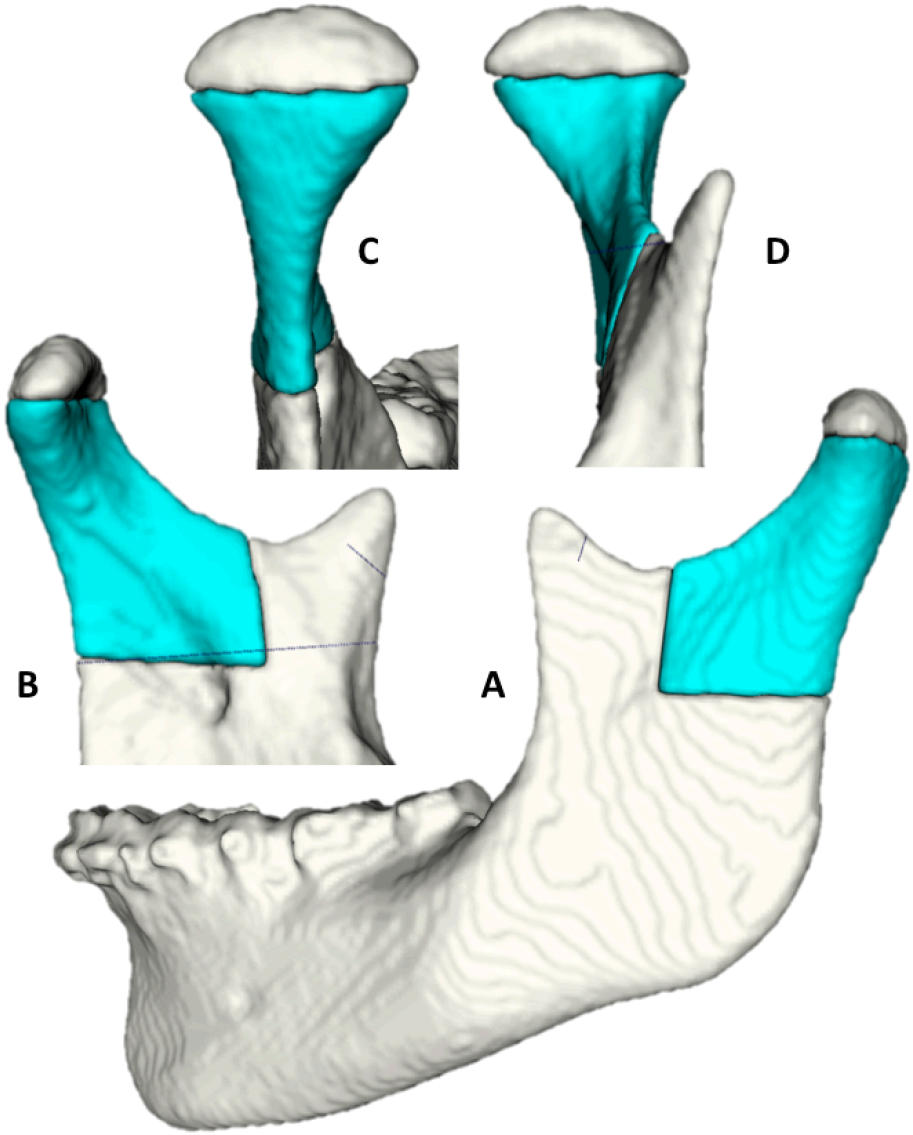

Fig 2. 3D model of the mandible constructed from the segmentation process. Registration mask is shown in blue. A, lateral view; B, medial view; C, posterior view; D, anterior view

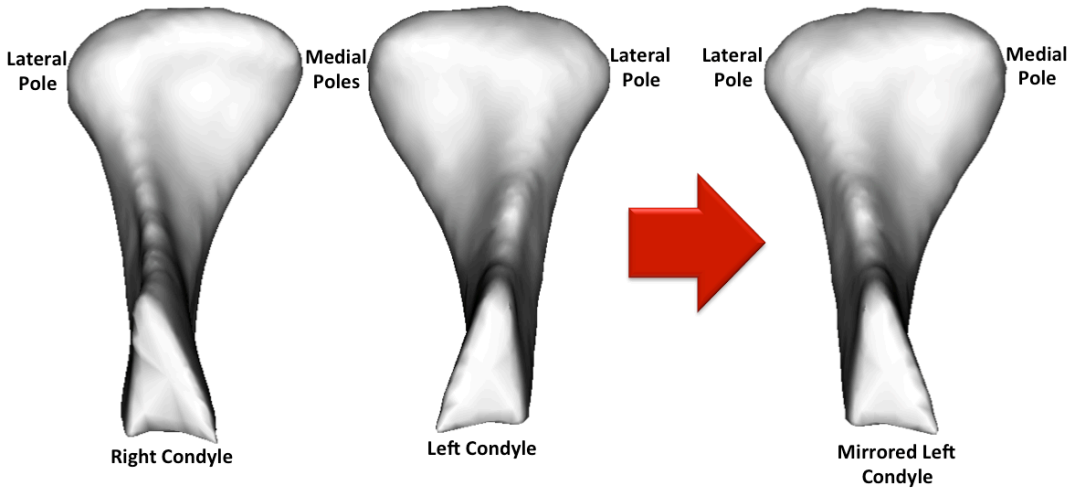

Fig 3. All left condyles were mirrored as right condyles

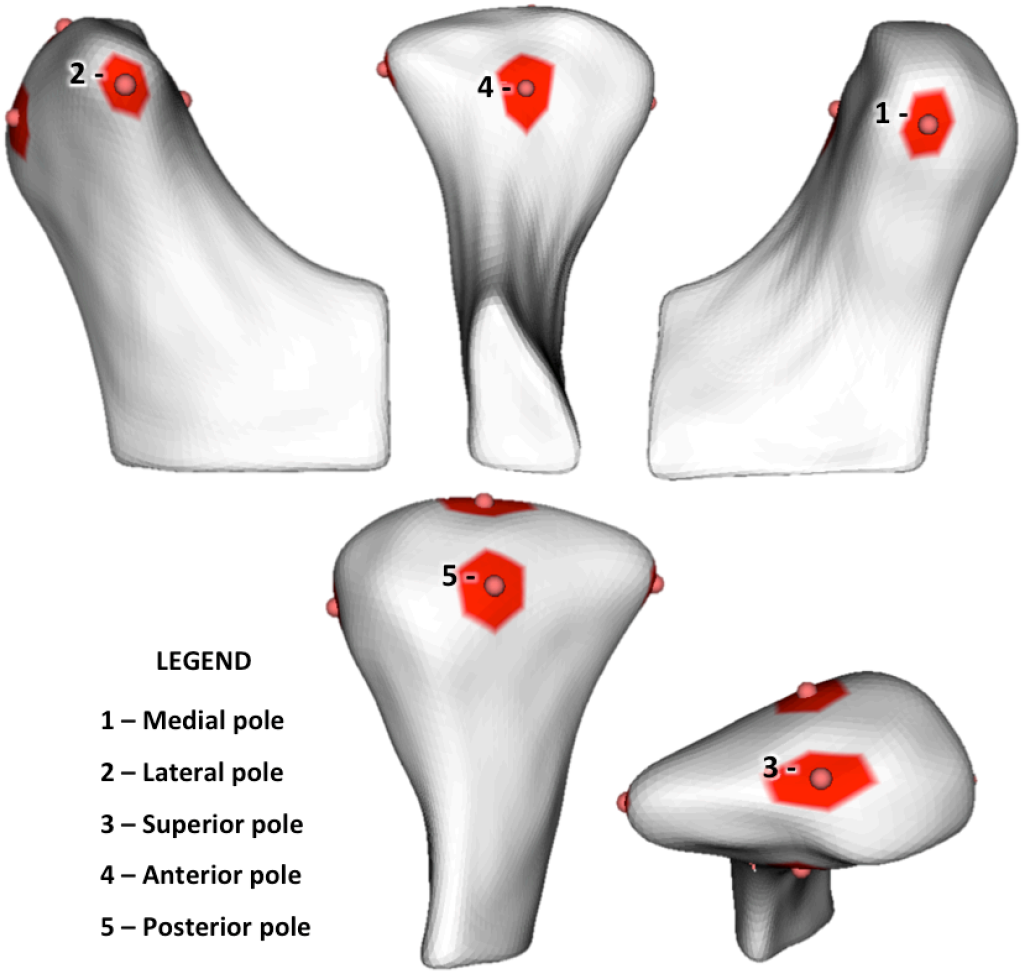

Fig 4. Regions of interest (ROIs) for the study

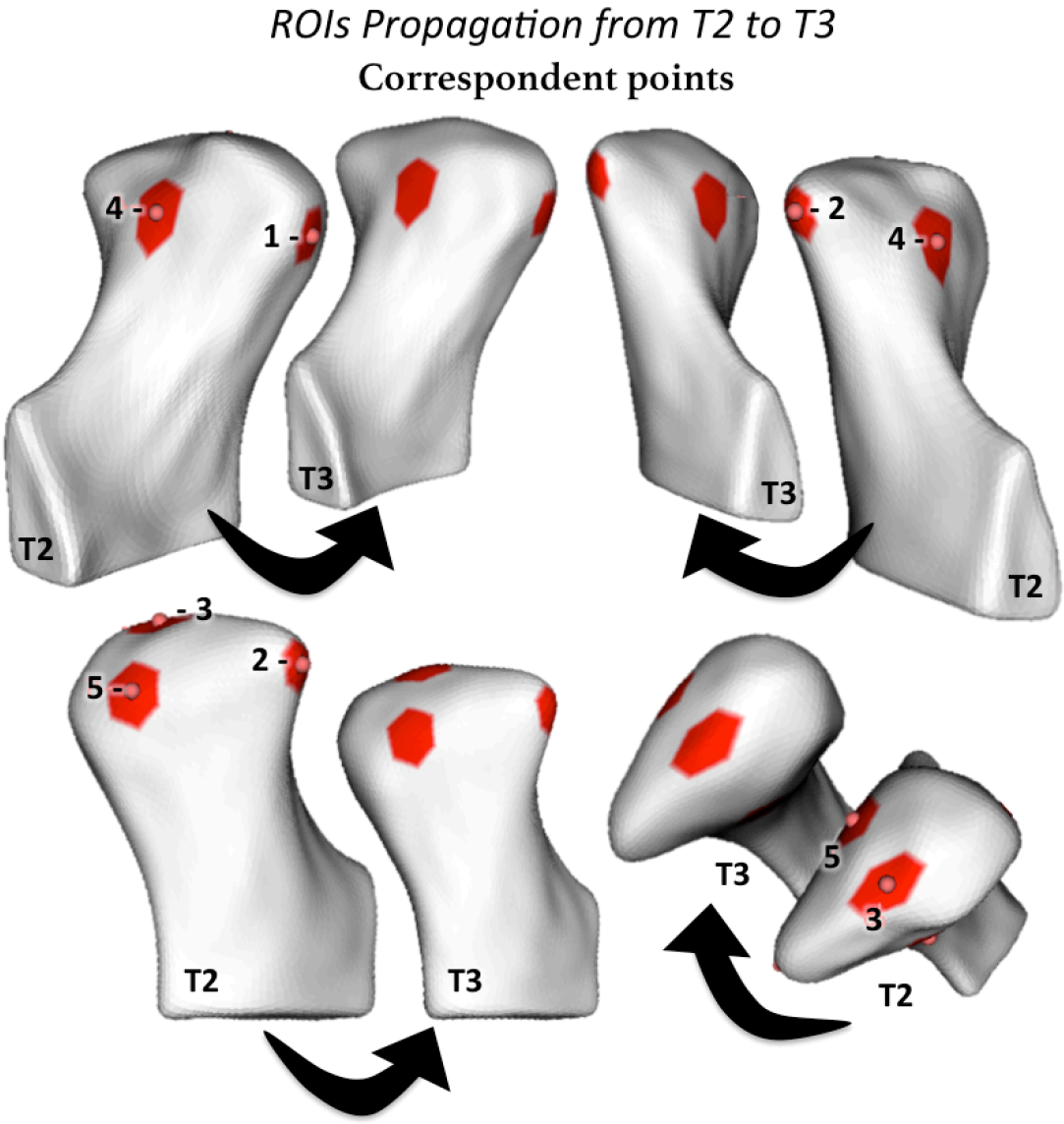

Fig 5. ROIs were propagated from the T2 to T3 model by correspondent surface mesh points

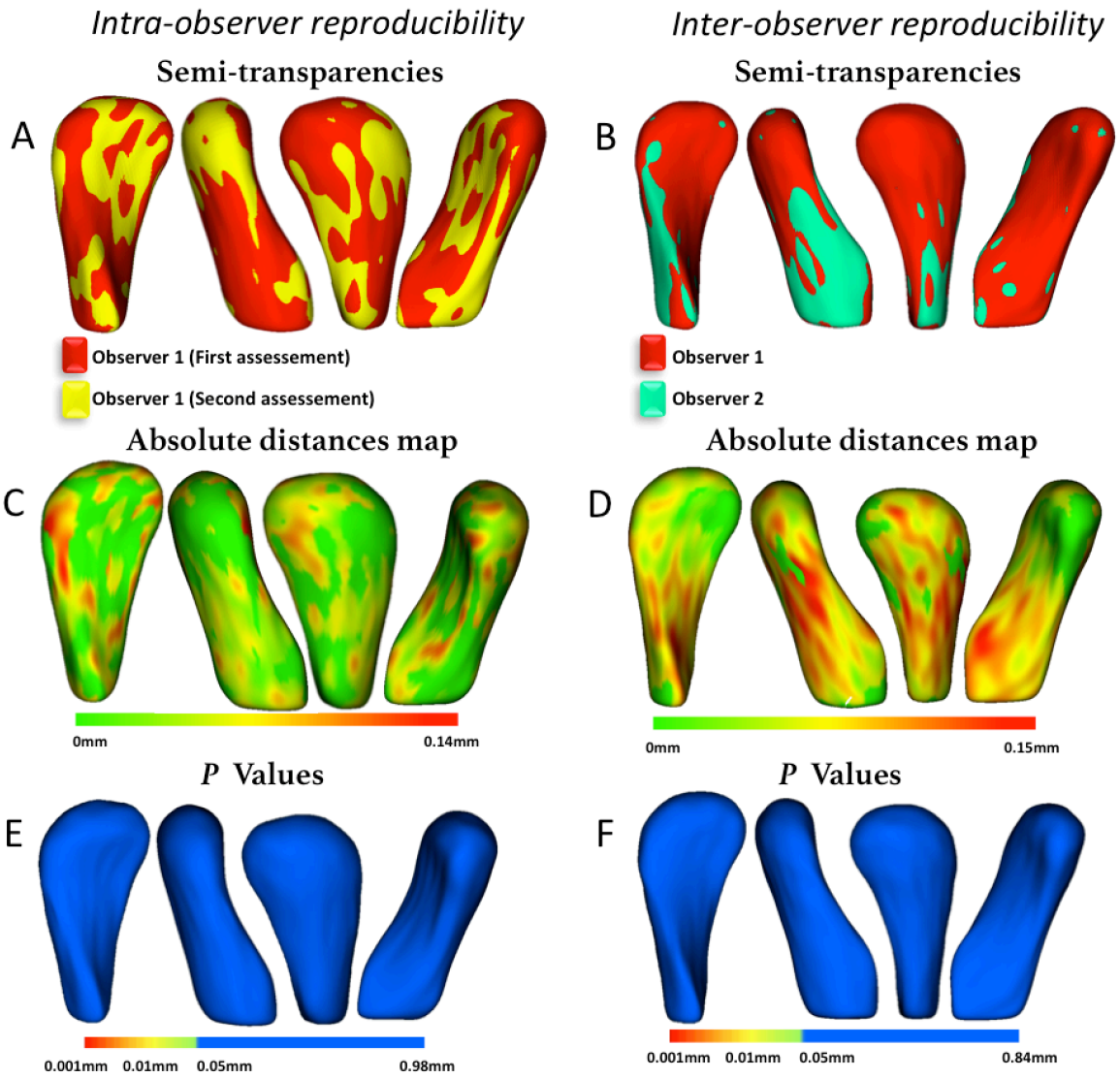

Fig 6. Intra- and inter-observer reproducibility results. A and B, Overlay of the average models constructed by the observers for 10 cone beam computed tomography images randomly selected. C and D, Absolute distances map obtained after subtracting the average models constructed from the segmentations of two independent observers. E and F, Significance map shows P > .05 for the whole condylar surface considering both intra- and inter-observer reproducibility

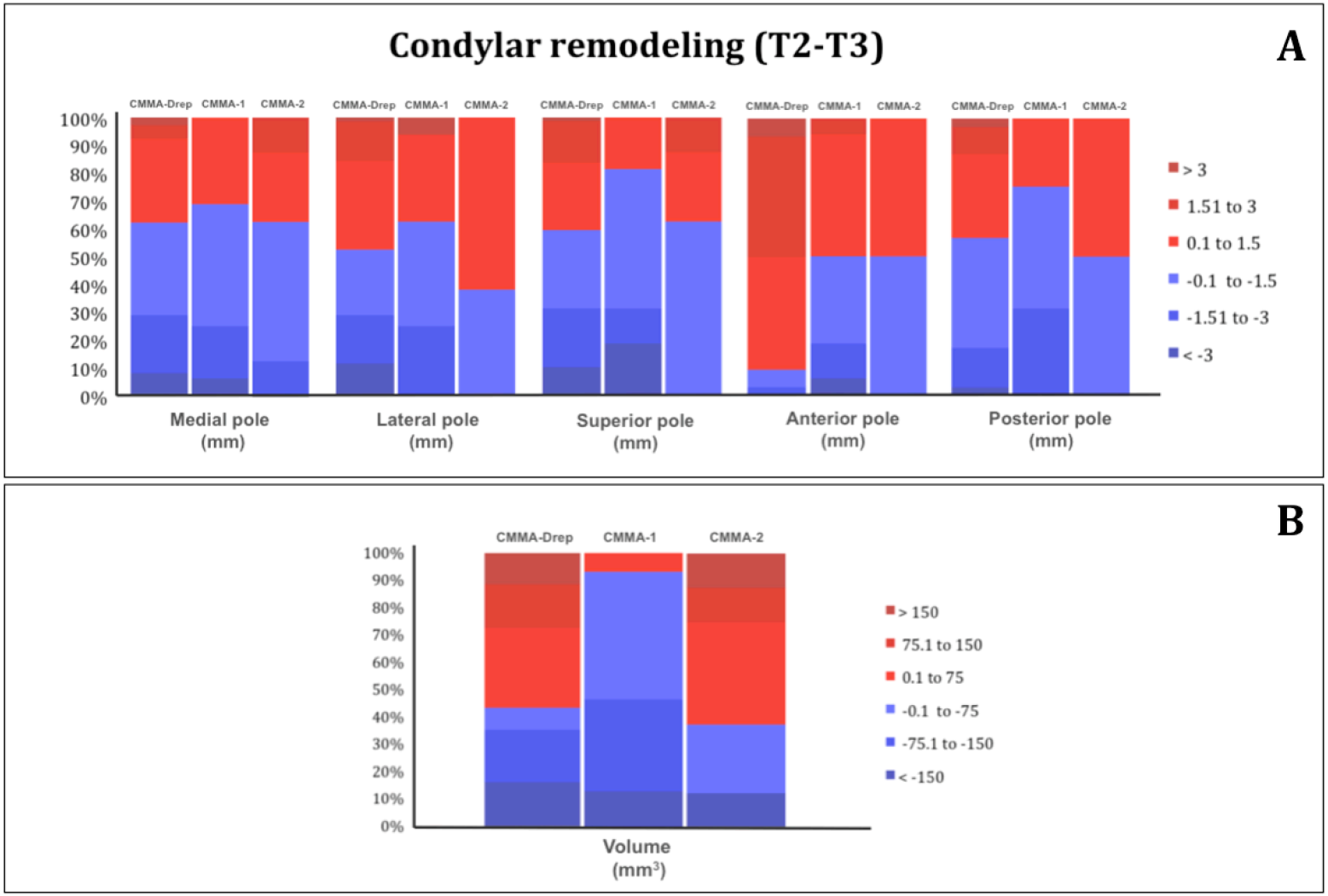

Fig 7. Percentage of patients according to condylar remodeling changes (T2-T3). A, Changes in each condylar pole; B, Overall volume changes

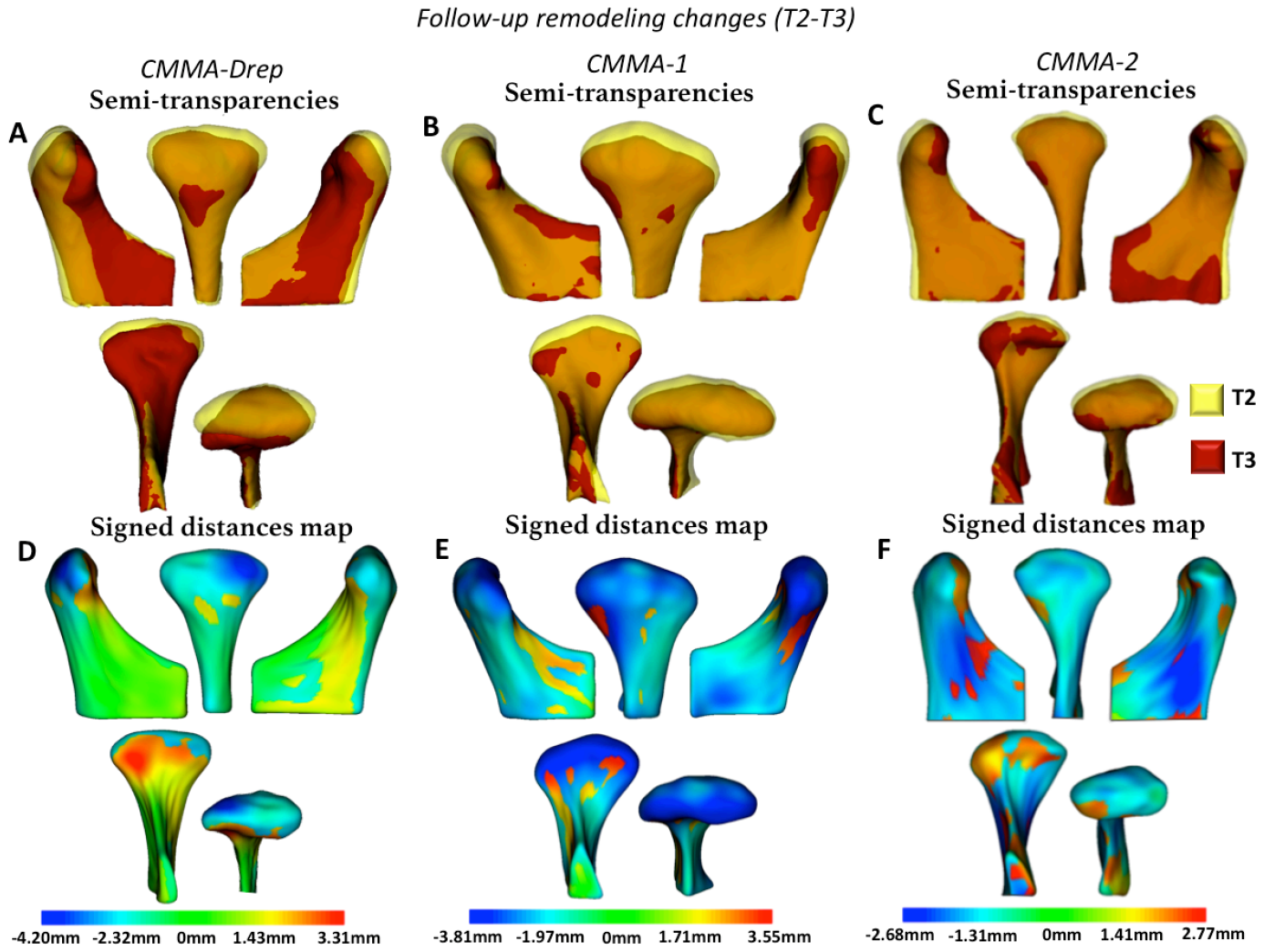

Fig 8. Right condyle models of patients randomly selected from CMMA-Drep and CMMA groups. A, B, C, Semi-transparency overlays showing condylar displacement during surgery (T1-T2). D, E, F, Respective color-coded signed distances maps of surgical changes (T1-T2)

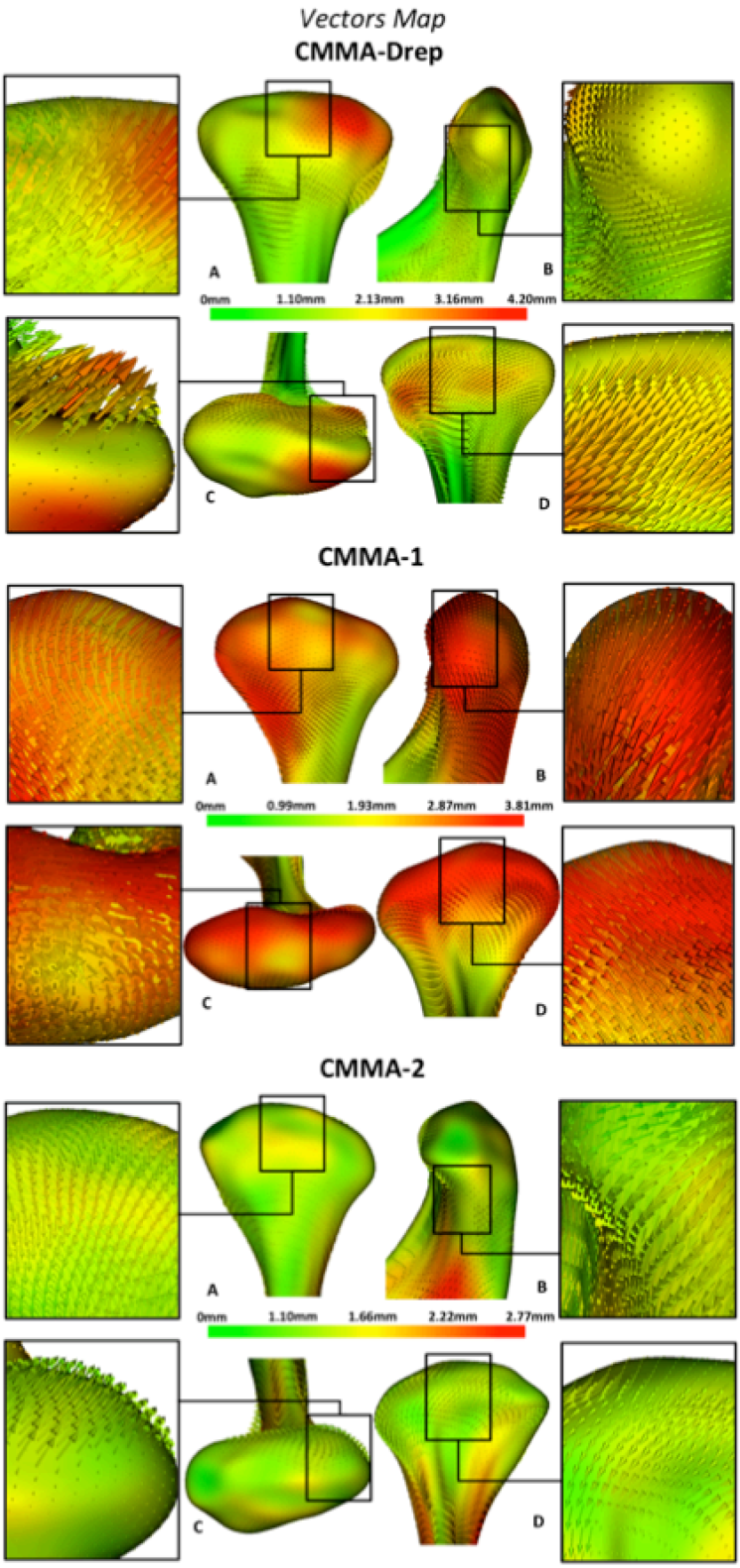

Fig 9. Vectors map showing changes from T1 to T2 in randomly selected patients from CMMA-Drep and CMMA groups. A, Posterior view. B, Medial view. C, Superior view. D, Anterior view

TABLES

Table 1. Demographic data

		CMMA-Drep (n= 63)				CMMA (n= 24)							
						CMMA-1 (n= 16)				CMMA-2 (n= 8)			
		Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
	Age (yr)	25.3	11.1	16.0	49.0	29.6	11.0	15.0	46.0	26.5	13.7	15.0	48.0
	Follow-up (mo)	16.1	7.1	8.0	36.0	16.1	8.8	7.0	39.0	10.8	3.5	8.0	16.0
Before Surgery (T1)	SNGoMe (°)	44.7	5.1	37.7	61.0	41.4	3.0	37.1	47.4	44.7	3.0	40.1	47.3
	SNA (°)	78.2	3.7	69.5	85.8	78.6	2.9	72.7	83.8	75.3	4.8	67.7	78.8
	SNB (°)	72.6	4.0	59.4	78.3	75.4	2.8	69.6	78.7	74.5	2.9	71.7	78.1
Surgical Changes[a] (T1-T2)	SNGoMe (°)	7.0	3.7	0.7	14.6	5.5	2.8	2.6	11.2	6.5	2.5	2.8	9.0
	SNA (°)	-3.2	2.2	-8.0	1.2	-3.9	2.1	-7.1	-0.4	-3.9	1.5	-6.0	-2.2
	SNB (°)	-6.6	2.3	-12.6	-0.6	-5.1	1.4	-8.2	-3.5	-4.0	1.2	-5.1	-2.8

Abbreviations: SD, Standard deviation; Min, Minimum; Max, Maximum; SNGoMe, sella-nasion to mandibular plane angle; SNA, sella-nasion to A point angle; SNB, sella-nasion to B point angle

[a] Positive values indicate counterclockwise rotation and negative values indicate clockwise rotation for SNGoMe measurements; Considering SNA and SNB measurements, negative values indicate the maxilla/mandible moved anteriorly and positive values indicate it moved posteriorly

Table 2. Gender differences on remodeling condylar changes

Condylar changes[a] (T2-T3)	CMMA-Drep (n= 63)							CMMA (n= 24)						
	Female (n= 46)			Male (n= 17)				Female (n= 14)			Male (n= 10)			
	Mean	SD	Med	Mean	SD	Med	P value	Mean	SD	Med	Mean	SD	Med	P value
Medial Pole (mm)	-0.7	1.8	-0.7	-0.5	1.6	-0.8	0.730*	-0.2	1.5	-0.4	-0.7	0.9	-0.5	0.355*
Lateral Pole (mm)	-0.6	1.9	-0.9	0.2	1.8	0.4	0.137*	-0.6	1.2	-0.6	0.3	1.6	0.4	0.097*
Superior Pole (mm)	-0.7	2.0	-1.3	-0.3	1.5	-0.4	0.285‡	-0.8	1.5	-0.7	-0.9	1.7	-0.5	0.861‡
Anterior Pole (mm)	1.3	1.2	1.5	1.6	1.1	1.5	0.816‡	0.0	1.2	0.1	-0.4	1.5	0.0	0.499*
Posterior Pole (mm)	-0.3	1.7	-0.8	0.2	1.3	0.7	0.193‡	-0.8	1.1	-0.5	-0.6	1.2	-0.1	0.446‡
Volume (mm^3)	-29.6	136.9	2.1	69.2	188.9	24.0	0.109‡	-60.4	159.2	-44.5	-67.5	209.9	-12.0	0.349‡

[a]Negative values indicate bone resorption and positive values indicate bone apposition
Abbreviations: SD, Standard Deviation; Med, Median
* Independent sample t test, ‡Mann-Whitney
Significant if $P \leq 0.05$

Table 3. Descriptive statistics and group comparisons relative to remodeling condylar changes. Effect of simultaneous articular disc repositioning surgery

Condylar changes [a] (T2-T3)	CMMA-Drep (n= 63)					CMMA-1 (n= 16)					CMMA-2 (n= 8)					
	Mean	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*Mean*	*SD*	*Med*	*Min*	*Max*	*P value*
Medial Pole (mm)	-0.6	1.8	-0.8	-5.3	3.3	-0.6	1.4	-0.6	-3.3	1.3	0.0	1.1	-0.3	-1.5	2.2	0.609*
Lateral Pole (mm)	-0.4	1.9	-0.7	-4.6	3.2	-0.4	1.6	-0.6	-2.6	3.7	0.1	0.8	0.3	-1.3	1.4	0.717*
Superior Pole (mm)	-0.6	1.8	-0.9	-5.4	3.0	-1.2	1.6	-0.9	-5.1	1.3	0.0	1.0	-0.2	-1.3	2.0	0.191‡
Anterior Pole (mm)	1.4	1.2	1.5	-2.5	4.7	-0.3	1.6	0.1	-4.0	2.4	0.1	0.7	0.1	-1.1	1.2	**0.000‡**
Posterior Pole (mm)	-0.2	1.6	-0.7	-3.2	4.6	-1.0	1.2	-0.7	-3.0	0.9	-0.3	0.8	0.0	-1.4	0.4	0.221‡
Volume (mm^3)	-2.9	157.4	13.9	-320.6	647.1	-107.7	175.8	-44.0	-634.5	26.0	25.3	155.2	34.9	-245.0	307.0	**0.051‡**

[a]Negative values indicate bone resorption and positive values indicate bone apposition
Abbreviations: SD, Standard Deviation; Med, Median; Min, Minimum; Max, Maximum
* ANOVA, ‡ Kruskal-Wallis
Significant if $P \leq 0.05$

Table 4. Mann-Whitney Post-hoc comparisons of condylar remodeling changes (T2-T3) between groups

Condylar Changes [a] (T2-T3)	CMMA-Drep – CMMA-1		CMMA-Drep – CMMA-2		CMMA-1 – CMMA-2	
	Median Difference	*P value*	*Median Difference*	*P value*	*Median Difference*	*P value*
Anterior Pole (mm)	1.4	**0.000**	1.4	**0.001**	0.0	0.540
Volume (mm^3)	57.9	**0.026**	21.0	0.604	78.9	**0.037**

Significant if P ≤ 0.05

Table 5. Correlation coefficients between volume changes in the long-term follow-up and the amount of condylar remodeling in each pole

		Condylar pole remodeling changes (T2-T3) *Correlation coefficients/ Significance*									
		Med	*Sig*	*Lat*	Sig	*Sup*	Sig	*Ant*	*Sig*	*Post*	*Sig*
Volume changes (T2-T3)	**CMMA-Drep (n= 63)**	0.120	0.350*	0.414	**0.001***	0.529	**0.000‡**	0.027	0.834‡	0.234	0.065‡
	CMMA-1 (n= 16)	0.444	0.085‡	0.171	0.528‡	0.653	**0.006‡**	0.397	0.128‡	0.509	**0.044‡**
	CMMA-2 (n= 8)	0.919	**0.001***	0.969	**0.000***	0.867	**0.005***	0.883	**0.004***	0.108	0.799‡

Abbreviations: Sig, Significance; Med, Medial pole; Lat, Lateral pole; Sup, Superior pole; Ant, Anterior pole; Post, Posterior pole

* Pearson, ‡ Spearman

Significant if P ≤ 0.05

3.3 Publicação 3

Counterclockwise maxillomandibular advancement surgery and disc repositioning. Can clinical and surgical factors predict condylar remodeling in the long-term follow-up?*

L. R. Gomes, L. H. Cevidanes, M. R. Gomes, A. C. Ruellas, D. P. O. Ryan, B. Paniagua, L. M. Wolford, J. R. Gonçalves

ABSTRACT

This study investigated whether specific clinical and surgical factors may predict condylar-remodeling changes in patients receiving counterclockwise maxillomandibular advancement and disc repositioning surgery (CMMA-Drep). 75 condyles from 41 female patients treated with CMMA-Drep had cone beam computed tomography (CBCT) scans taken pre-surgery, immediately after surgery and, on average, 16 months post-surgery. Pre- and postsurgical 3D models were superimposed using automatic voxel-based registration on the cranial base to evaluate condylar displacements after surgery, and regional registration to access condylar remodeling in the follow-up period. 3D-Cephalometrics, shape correspondence analysis (SPHARM-PDM) and volume measurements were applied to quantify the changes. Statistical framework

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included Pearson product–moment correlations and stepwise multiple linear regression analysis. Weak but statistically significant correlation coefficients were observed between some clinical and surgical variables with condylar remodeling changes in the follow-up period. Highly statistically significant correlation showed that older patients were more susceptible to overall condylar volume reduction following CMMA-Drep ($p \leq .001$). Counterclockwise rotation of the maxillomandibular complex was associated with larger bone resorption at the superior pole but lower resorption at the posterior one. On average, CMMA-Drep caused the condyles to translate slightly downward (1mm ± 1.3), medially (1.5mm ± 1.8) and rotate in a medial (medial roll, 5.2º ± 7.3), lateral (lateral yaw, 4.5º ± 6.0), and counterclockwise direction (upward pitch, 7.5º ± 8.0). Displacement condylar changes generated by CMMA-Drep did not seem to be associated with greater condylar resorption in the follow-up period. Such changes showed, on average, opposite direction from those correlated with greater risk of condylar resorption. Moreover, positional changes were only weakly associated with remodeling in the follow-up period, suggesting that other risk factors may play a role in condylar resorption.

INTRODUCTION

Postoperative instability of counterclockwise maxillomandibular advancement due to condylar displacement changes during the surgical procedure and/or subsequent long-term condylar resorption remains an area of concern.[1, 2] Authors have suggested that such factors may lead to sagittal relapse and anterior bite opening.[3, 4]

Current literature regarding treatment effectiveness and options for preventing degenerative condylar changes after bimaxillary surgical advancement is controversial. Although some investigators believe that orthognathic surgery alone reduces or eliminates TMJ dysfunction and symptoms,[5-7] others have reported that performing orthognathic surgery in the presence of TMJ disorder may cause further harmful effects to the TMJ. [8, 9]

Some studies have shown that simultaneous surgical correction of coexisting dentofacial deformities and TMJ pathology by repositioning and stabilizing the articular disc provides high-quality treatment outcomes for most patients.[10-13]

On the other hand, specific condylar displacement changes during articular disc repositioning surgery might be investigated as a potential factor inducing condylar remodeling in the long-term follow-up.[14] Moreover, it has been reported that the degree of mandibular advancement performed may also contribute to skeletal relapse and condylar resorption.[11] Patients with presurgical TMJ symptoms requiring large mandibular advancement appear to be at increased risk.[15, 16]

The use of cone beam computed tomography (CBCT) and new three-dimensional (3D) tools allow for a comprehensive analysis of surgical and post-surgical skeletal changes. Such technologies have the potential of identifying individual variability and highlight associations between structural changes and the stability of surgical correction.[17, 18]

This study investigated whether specific clinical and surgical factors may predict condylar-remodeling changes in patients receiving counterclockwise maxillomandibular advancement and disc repositioning surgery.

MATERIALS AND METHODS

CBCT scans from 41 female patients presenting with disc displacement and TMJ osteoarthritis (OA) who underwent counterclockwise maxillomandibular advancement (CMMA) associated with disc repositioning surgery were enrolled in this study (Fig 1). Patients were consecutively operated on by the same surgeon (LMW), using rigid internal fixation. Articular disc displacement was assessed by clinical examination and magnetic resonance imaging [MRI] interpreted by 2 experienced and calibrated doctors [LMW and JRG]. TMJ OA was assessed on the CBCTs by using diagnostic criteria for temporomandibular disorders.[19]

The current study required CBCT images obtained before surgery (T1), immediately after surgery (3-9 days) (T2), and at a minimum 6 months follow-up (T3). Archives from patients presenting with craniofacial syndromes, systemic degenerative conditions such as rheumatoid arthritis or who underwent previous TMJ intervention were excluded.

A total of 82 condyles were analyzed. Seven condyles were excluded due to previous arthroplasty. The final sample was composed of 75 condyles. All patients signed an informed consent form for hospital admission, surgical

procedures, and release of information for research purposes. This study was approved by the university institutional review board and is in compliance with the Helsinki Declaration.

Surgical technique

CMMA technique included traditional Le Fort I osteotomy and bilateral sagittal split ramus osteotomies with internal rigid fixation. Maxilla was stabilized with 4 bone plates fixated with 2.0-mm screws and sagittal split osteotomies fixated with 1 bone plate at the corpus region followed by 2 or 3 bicortical 2.0-mm bone screws at the retromolar region on each side. Articular disc repositioning surgery using the Mitek® anchor (Mitek® Products, Inc, Westwood, MA) technique is an open joint procedure that was performed simultalneously with the orthognathic procedure. Detailed description of such surgical procedure was previously published.[10]

Image acquisition and 3D analysis

CBCT images were obtained using a 17 x 23 cm extended field of view protocol, during an 17.8 second scan, with 0.3 mm isotropic voxel size (i-Cat® CBCT, 120 kV, 5 mA, Imaging Sciences, Hatfield, PA). Images were resampled to 0.5mm isotropic voxel size for proceeding the segmentation of anatomic structures of interest (CMF Registration, 3D slicer software, www.slicer.org). 3D models of the cranial base, maxilla and mandible were constructed by outlining the cortical boundaries using semi-automatic discrimination procedures (ITK-SNAP software,

www.itksnap.org). 3D cephalometric analysis was conducted to determine facial skeletal pattern before surgery (T1) and assess surgical changes (T1-T2) for sample characterization (Q3DC, 3D slicer software, www.slicer.org).

The present study required the different time-point images to be superimposed by using two specific voxel based registration methods (CMF Registration, 3D slicer software, www.slicer.org). Cranial base registration [17] was applied to assess condylar displacement changes, whereas regional registration [20] was used to analyze condylar remodeling. Both procedures were conducted through 3D Slicer software (CMF Registration, 3D slicer software, www.slicer.org).

All left condyles were mirrored in the sagittal plane to form right condyles to facilitate outcomes analysis. Superposed models were simultaneously cropped (Easy Clip, 3D slicer software, www.slicer.org) and compared by subtraction to compute surgical (T1-T2) and post-surgical (T2-T3) changes by using shape correspondence analysis (SPHARM-PDM, 3D slicer software, www.slicer.org).

Shape correspondence made it possible to mark the interest regions in one condyle and propagate such regions for the other surgical time-points, obtaining x,y,z coordinates for each point (Pick ’n Paint, 3D slicer software, www.slicer.org). Then, math formulas were applied considering the different correspondent points in the condylar surface, which allowed measuring both translational (antero-posterior, vertical and lateral) and rotational (pitch, roll and yaw) displacements. Each condylar translational displacement was measured in

millimeters and rotational changes in degrees. Positive or negative signs indicated displacement direction (Fig 2).

Five specific regions of interest (ROIs) were selected as representative of each condylar pole, i.e., superior, anterior, posterior, medial and lateral poles. 37 correspondent points were used for analyzing changes in the anterior, superior and posterior poles, whereas 19 points were selected as representatives for analyzing changes in the lateral and medial poles (Fig 3). Referred ROIs were marked in post-surgical 3D models and propagated to the respective follow-up (Pick 'n Paint, 3D slicer software, www.slicer.org). 3D point-wise linear distances between each time-point were then used to calculate remodeling changes in millimeters (Model to model distance, 3D slicer software, www.slicer.org). Positive and negative signals represented outward and inward movement, respectively. Thus, positive values indicated bone apposition and negative values indicated bone resorption. Condylar volume changes were also calculated in cubic millimeters by using the ITK-SNAP software.

Descriptive statistics were used to report clinical characteristics before surgery (T1), as well as surgical (T1-T2) and post-surgical changes (T2-T3). Pearson product–moment correlations were used to identify the relationship of clinical and surgical factors with condylar remodeling in the follow-up period. Stepwise multiple linear regression analysis showed the independent variables that best predict condylar remodeling in specific sites. A significance level of $p \leq .05$ was applied. Statistics were calculated by using SPSS software (SPSS 16.0, Chicago, IL, USA).

RESULTS

Clinical demographic characteristics are listed in Table 1. Sample was composed mostly of hyperdivergent retrognathic patients. 15% of the subjects presented with SNGoMe angle lower than 33.2º and/or SNB angle greater than 79º. Maxilla was on average retruded as well. All patients underwent mandibular advancement and counterclockwise (CCW) rotation of the maxillomandibular complex simultaneously with disc repositioning surgery. The mean CCW rotation and advancement at the B point were 5.6º ± 3.1 and 6.0mm ± 2.3, respectively. Descriptive statistics of surgical displacement changes are shown in Table 2.

On average, during the surgical procedure (T1-T2) the proximal segment moved backward, downward and medially. However, it was observed that such translational displacement occurred in small magnitude (from 0.1 to 0.9mm) for the great majority of the patients in study (Fig 4). About 30% of the sample showed forward, upward and lateral displacement of the mandibular condyle. Taking into account the rotational displacements, it was noticed lateral Yaw, medial Roll and upward Pitch for most of the condyles in our sample.

During the follow-up period (T2-T3) is was observed condylar remodeling changes. Medial, lateral, superior and posterior poles of the mandibular condyle experienced bone resorption. However, a small percentage of the patients showed resorption greater than 1.5mm. Lateral and superior poles were the most affected ones. On the other hand, the anterior pole showed bone apposition. It

was also noticed that although most of the ROIs in study showed bone resorption, 42% of the sample did not experienced reduction in the overall condylar volume, i.e., bone resorption was compensated for by bone apposition. About 18% of the sample showed more than 75mm^3 volume increase (Table 3; Fig 5).

Pearson product–moment correlations aimed to identify the relationship of clinical and surgical factors with condylar remodeling in the follow-up period. Among the clinical characteristics studied, age and facial pattern before surgery showed weak but statistically significantly correlation with condylar remodeling. The older the patient, the greater the bone resorption at the lateral pole ($p \leq .05$) and the overall condylar volume reduction ($p \leq .001$). The more vertical the patient's facial pattern (i.e., high SNGoMe angle at T1), the lower the bone resorption at the anterior pole ($p \leq .05$) and the overall volume reduction ($p \leq .05$). Maxillary and mandibular retrusion (i.e., low SNA and SNB angle at T1, respectively) were associated with larger medial pole resorption ($p \leq .05$). The greater the mandibular retrognathism, the lower the anterior pole resorption ($p \leq .01$). The follow-up period in months showed no statistically significant correlations with condylar remodeling.

Among the surgical changes (T1-T2), the amount of CCW rotation (SNGoMe) and mandibular advancement (SNB) showed weak but statistically significant correlation with condylar remodeling in the follow-up period. The greater the amount of CCW rotation, the lower the overall volume reduction ($p \leq .05$) and bone resorption at the lateral ($p \leq .05$) and posterior poles ($p \leq .001$). On the other

hand, CCW rotation was associated with larger bone resorption at the superior pole ($p \leq .05$). It was also observed that the greater the mandibular advancement, the larger the bone resorption at the superior pole ($p \leq .05$) and the lower the condylar resorption at the posterior pole ($p \leq .05$).

Condylar displacement changes during surgery (T1-T2) also showed some weak but statistically significant correlations with remodeling changes (T2-T3). Upward condylar displacement correlated with greater condylar resorption at the posterior pole ($r=0.26$, $p \leq .05$). Lateral and anterior condylar displacement correlated with greater condylar resorption at the lateral ($r=0.3$, $p \leq .01$) and anterior poles ($r=0.29$, $p \leq .05$), respectively. Medial displacement was correlated with greater overall volume reduction ($p \leq .05$). Lateral roll and medial yaw correlated with greater condylar resorption at the posterior ($r=-0.26$, $p \leq .05$) and lateral poles ($r=-0.26$, $p \leq .05$), respectively.

Stepwise multiple linear regression analysis showed the independent variables (clinical characteristics and/or surgical changes) that best predict condylar remodeling in specific sites. Mandibular position relative to the cranial base in T1 (SNB) was the independent variable that better explained condylar remodeling at the medial and anterior poles. For each degree of mandibular retrognathia, it would be observed an increase in medial pole resorption and anterior pole apposition of about 0,09mm. However, such prediction models explained only 5% of the medial pole changes and 9% of the anterior pole changes.

Condylar lateral displacement better explained condylar remodeling at the lateral pole. For each millimeter of lateral displacement, it was suggested an increase in lateral pole resorption of about 0,30mm. Such prediction model explained 9% of the lateral pole changes. The superior pole remodeling was better explained by the association of two independent variables: Age and SNGoMe (T1-T2), expressing the amount of CCW rotation. For each year older and for each degree of CCW rotation, it was increased the superior pole resorption in 0,04mm and 0,22mm, respectively. The model explained 15% of the superior pole changes (r^2= 0,15). SNGoMe (T1-T2) also explained posterior pole remodeling changes. For each degree of CCW rotation, it was reduced the posterior pole resorption in 0,20mm (r^2= 0,14). Age better explained the overall volume changes. For each year older, the model suggested a volume reduction of 5,06mm^3. Age explained 21% of the overall changes in volume.

DISCUSSION

The exact cause of condylar resorption following orthognathic surgery remains unknown. Such occurrence has been attributed to specific clinical factors as well as to characteristics intrinsic to the surgical procedure. This study is the first to investigate the association between clinical and surgical factors with condylar remodeling in the follow-up period, using two different voxelwise rigid registration approaches as well as shape correspondence analysis (SPHARM-PDM) and volume measurements.

Cranial-base superimposition was used for quantifying condylar displacement changes during surgery whereas regional registration allowed analyzing specific condylar remodeling changes. Previous studies have shown high accuracy in both 3D automatic registration methods.[20-22]

Shape correspondence (SPHARM-PDM) [23] was employed to quantify 3D condylar displacement changes during CMMA-Drep and remodeling in the follow-up period. SPHARM-PDM has been shown to provide a unique and symmetric point-to-point correspondence across all measured surfaces. Shape differences were calculated between each correspondent point on T2 and T3 models. Besides measuring the depth of bony defects at specific sites, it was also computed the overall volume change.

Several studies have shown that the first signs of condylar resorption were apparent 6 months after mandibular advancement,[24-27] and it developed up to 2 years postoperatively.[24, 25, 28-30] In the present study, the follow-up period in months showed no statistically significant correlations with condylar remodeling, which may suggest that from 6 months on it is already possible to verify condylar remodeling changes as observed up to 52 months follow-up. Authors have stated that most of the condylar resorption is expected to occur during the first year after surgery.[31]

The current research also investigated the impact of age on the amount of condylar remodeling during the follow-up period. It was observed highly statistically significant correlation showing that the older the patient, the greater

the overall condylar volume reduction. Weak but statistically significant correlation was also observed suggesting greater lateral pole resorption in elderly patients.

Previous studies showed that high mandibular plane angle, mandibular retrognathism and female patients appeared to be some of the risk factors for condylar resorption, particularly following mandibular advancement surgery.[14, 27, 30-32] However, Hoppenreijis et al. [16] reported that the mandibular plane angle might be less important than what literature has assumed.[24, 30] Those authors found progressive condylar resorption in patients with open bite as well as deep bite.

Xi et al. [33] reported that preoperative mandibular plane angle was not correlated with surgical relapse. The authors stated that high-angle patients have significantly smaller condyles preoperatively in combination with a tendency for counterclockwise rotation of the proximal segment and a possibly larger average mandibular advancement. Therefore, those facts make high-angle patients more susceptible to condylar resorption and relapse rather than the high mandibular plane angle itself.

In the present study, greater condylar resorption was not associated with higher SNGoMe angle preoperatively. Hyperdivergent patients experienced lower bone resorption at the anterior pole and lower overall volume reduction. However, the most hyperdivergent patients in our sample were also the youngest ones, which may explain the lower overall volume reduction in this group.

Patients presenting with lower SNB angle at T1 were also associated with lower anterior pole resorption, but larger resorption at the medial pole. Considering that patients with a more severe hyperdivergent and retrognathic profile were also submitted to greater amount of surgical advancement and counterclockwise rotation, the associations found regarding such clinical and surgical characteristics may be interrelated.

Greater amount of CCW rotation was associated with lower bone resorption at the lateral and posterior poles as well as lower overall volume reduction. On the other hand, it was associated with larger bone resorption at the superior pole.

Worms et al. [34] and Hwang et al. [26] reported that condylar resorption was most apparent in mandibular advancement procedures that rotate the mandible in a counterclockwise direction. However, Xi et al. [33] did not found correlation between counterclockwise rotation of the distal segment and condylar remodeling or skeletal relapse.

Actually, the role of mandibular advancement in condylar resorption is controversial. Tension in the surrounding soft-tissue components after mandibular advancement produces a posteriorly directed force. This force causes the condyle to be retruded forcefully into the fossa, which generates pressure on the condylar head.[26, 28] Therefore, several authors have hypothesized that larger surgical advancements are associated with a higher incidence of condylar resorption.[2, 14, 16, 31]

Xi et al. [33] reported significant correlation between the amount of mandibular advancement and post- operative reduction in condylar volume, whereas other authors did not find a direct correlation with resorption of the mandibular condyle.[18, 26, 27] According to Huang et al. [26], after mandibular advancement and counterclockwise rotation, the posteriorly directed force does not appear to have a direct influence on the development of condylar resorption because it usually occurs on the anterior-superior surface of the condyle, not the posterior surface, which corroborate other literature findings.[25, 27, 30]

In the present study, the correlation between the amount of mandibular advancement and overall volume change was not significant. However, larger bone resorption at the superior pole was noticed. Lower resorption at the posterior pole was also observed with higher mandibular advancement. Such association may be explained by the fact that patients that underwent greater mandibular advancement also experienced more CCW rotation, i.e., such surgical changes are also interrelated.

Sagittal condylar displacement has been reported after orthognathic surgery, however, the role of condylar torque in the development of condylar resorption is also controversial. It has been advocated that an optimal intraoperative positioning of the proximal segments would ensure stability of the surgical results and reduce the chance of post-surgical condylar resorption.[2, 4, 31, 35] On the other hand, Dicker et al. [36] analyzing the static and dynamic loading of the condyles after surgical mandibular advancement observed that an increased postoperative

joint loading and sagittal rotation of the condyle were not a serious cause of condylar resorption or relapse.

In the present study, weak but statistically significant associations were observed between the magnitude of condylar displacement and remodeling changes in the follow-up period. Upward condylar displacement correlated with greater condylar resorption at the posterior pole. Lateral and anterior condylar displacement correlated with greater condylar resorption at the lateral and anterior poles, respectively. Lateral roll and medial yaw correlated with greater condylar resorption at the posterior and lateral poles, respectively.

Authors have suggested that a counterclockwise rotation of the proximal segments in combination with a posterior inclination of the condylar neck may increase the loading of the anterior-superior surface of the condyle, making it more prone to condylar resorption with subsequent skeletal relapse.[27, 29, 33, 37] However, the extent of condylar change that is compatible with normal function postsurgically is still unknown. In the present research, it was not found statistically significant correlation between CCW rotation of the proximal segment and condylar remodeling in the follow-up period. The literature supports our findings that small condylar rotations do not appear to have a functional compromise.[4, 38, 39]

Authors have described different patterns of condylar displacements considering two specific surgical protocols: maxillomandibular advancement only (MMA) and maxillomandibular advancement with disc repositioning surgery (MMA-Drep).

Condyles translated backward, upward and medially in patients treated with MMA only [4, 13, 18, 40] whereas it translated forward, downward, and medially in patients treated with MMA-Drep.[13] Medial rotation through the z axis (roll), lateral rotation through the y axis (yaw) and upward rotation through the x axis (pitch) occurred regardless of TMJ disc repositioning and at similar amounts and frequency.[13]

In the current study, on average, CMMA-Drep caused the condyles to translate slightly downward, posteriorly, medially and rotate in a medial (roll), lateral (yaw) and upward direction (pitch), partially corroborating Gonçalves et al. [13] findings. The only difference observed considered the anteroposterior displacement. These authors stated that the disc repositioning procedure generates forward condylar displacement.[13] 30% of the sample in the current study also experienced forward translation, but most of the cases showed, on average, 0,6mm of backward displacement, which is a very small change. Considering that our sample underwent expressive maxillomandibular advancement and counterclockwise rotation, part of the forward displacement generated by disc repositioning may have been annulled by muscular pressure.

Displacement changes generated by CMMA-Drep did not seem to be associated with greater condylar resorption in the follow-up period. Such changes showed, on average, opposite direction from the ones correlated with greater risk of condylar resorption. Moreover, positional changes were only weakly associated with remodeling in the follow-up period, suggesting that other risk factors may play a role in condylar resorption.

Among all clinical and surgical factors studied, the independent variable age composed the prediction model that better described the overall volume reduction. About 21% of volume reduction was explained by the age of the patient submitted to CMMA-Drep, showing that older patients were more susceptible to greater condylar resorption.

Another relevant observation is related to the amount of counterclockwise rotation of the maxillomandibular complex. The independent variable CCW rotation composed the prediction models that better described condylar remodeling changes at the superior and posterior poles. Higher CCW rotation seems to cause greater amount of resorption at the superior pole whereas protecting the posterior one. However, considering that most correlation coefficients found were weak, caution is needed when interpreting such results.

In conclusion, it was observed that older patients were more susceptible to overall condylar volume reduction following CMMA-Drep. The magnitude of the surgical procedure as well as condylar displacement changes were only weakly associated with remodeling in the follow-up period, suggesting that other risk factors may play a role in condylar resorption.

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COMPETING INTERESTS

None.

ETHICAL APPROVAL

This study was approved by the Human Research Ethics Committee of the Araraquara School of Dentistry, São Paulo State University and National Ethics Commttee, Plataforma Brasil (CAAE 01125412.2.0000.5416).

PATIENT CONSENT

All patients signed an informed consent form for hospital admission, surgical procedures, and release of information for research purposes.

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FIGURES

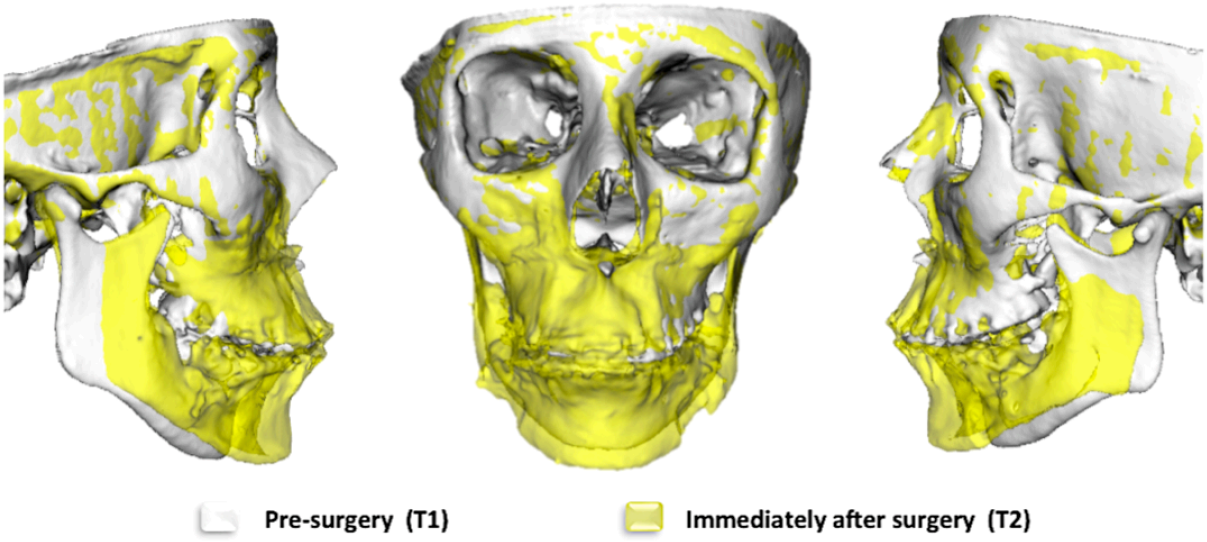

Fig 1. All patients underwent counterclockwise maxillomandibular advancement surgery. Images obtained from a randomly selected patient. The amount of surgical movement differed from one patient to another

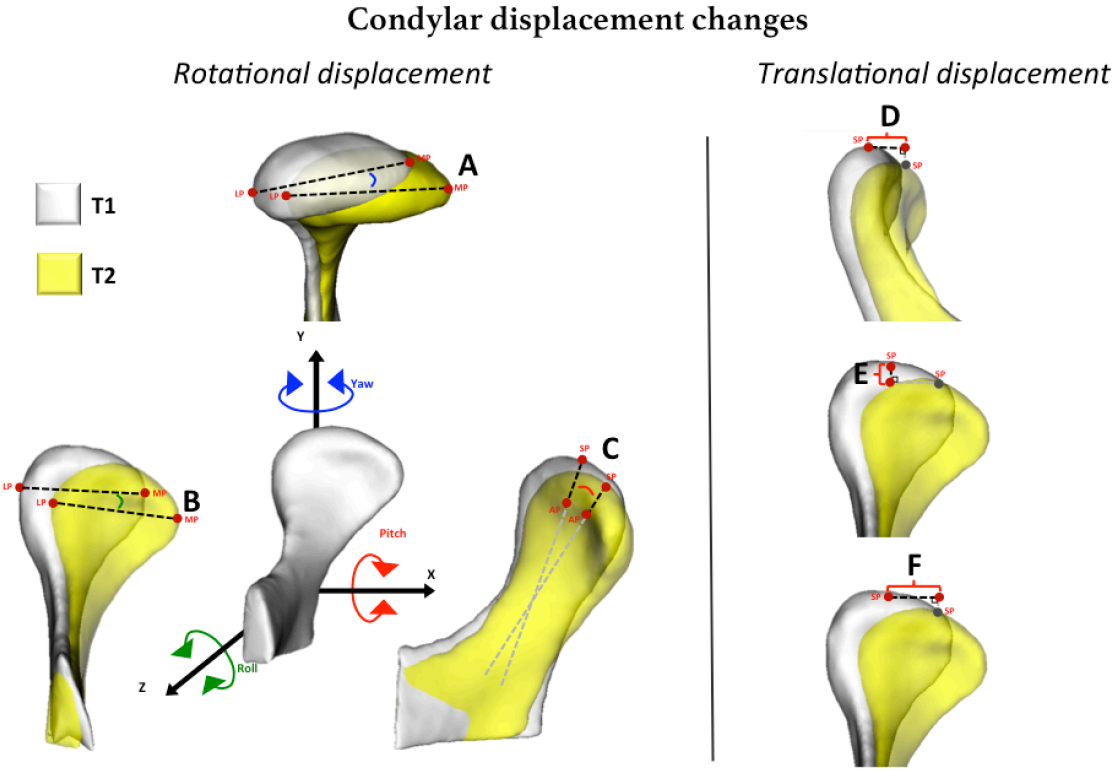

Fig 2. Rotational and translational measurements used to assess condylar changes. A, Yaw, rotation around the Y axis (axial view). B, Roll, rotation around the Z axis (coronal view). C, Pitch, rotation around the X axis (sagittal view). D, Antero-posterior displacement (sagittal view). E, Vertical displacement (coronal view). F, Lateral displacement (coronal view)

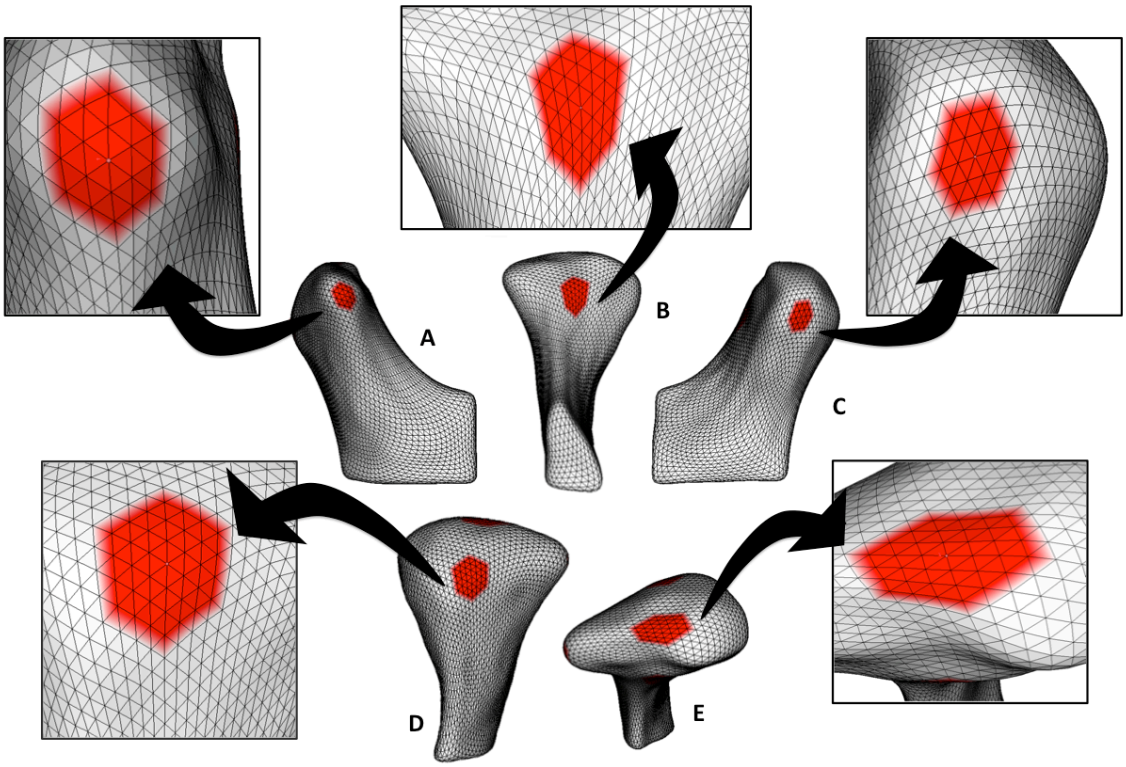

Fig 3. Regions of interest (ROIs) for investigating condylar remodeling changes. A, lateral pole; B, anterior pole; C, medial pole; D, posterior pole; E, superior pole

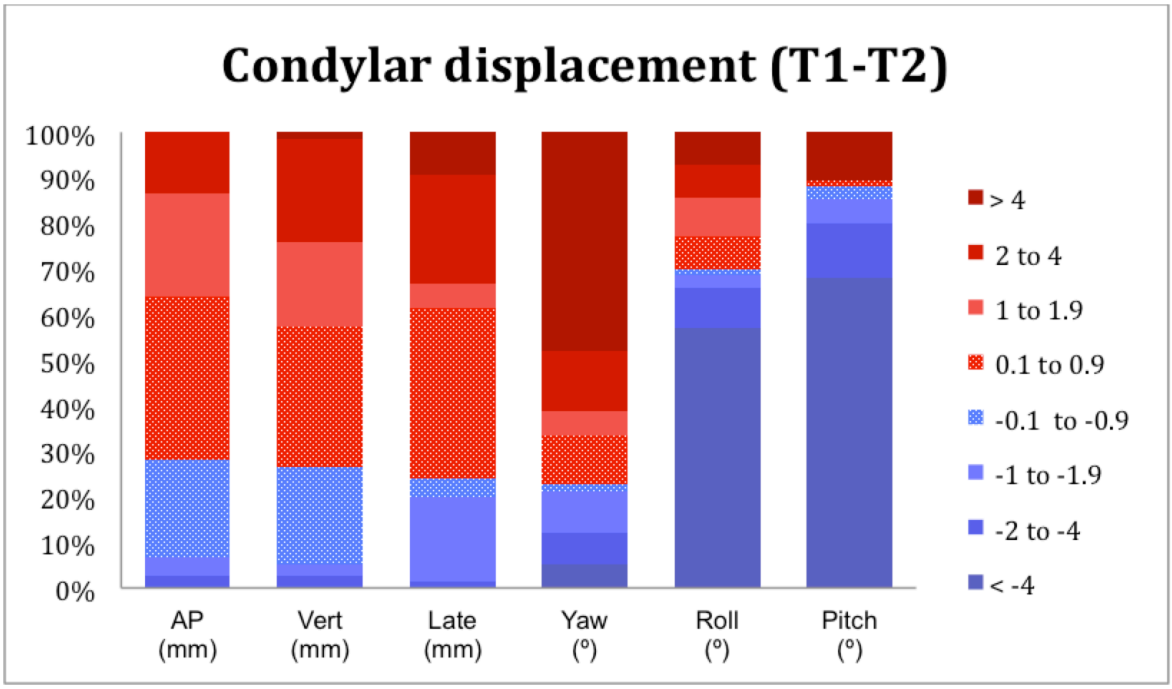

Fig 4. Percentage of patients according to direction and magnitude of condylar translational and rotational changes during surgery (T1-T2)

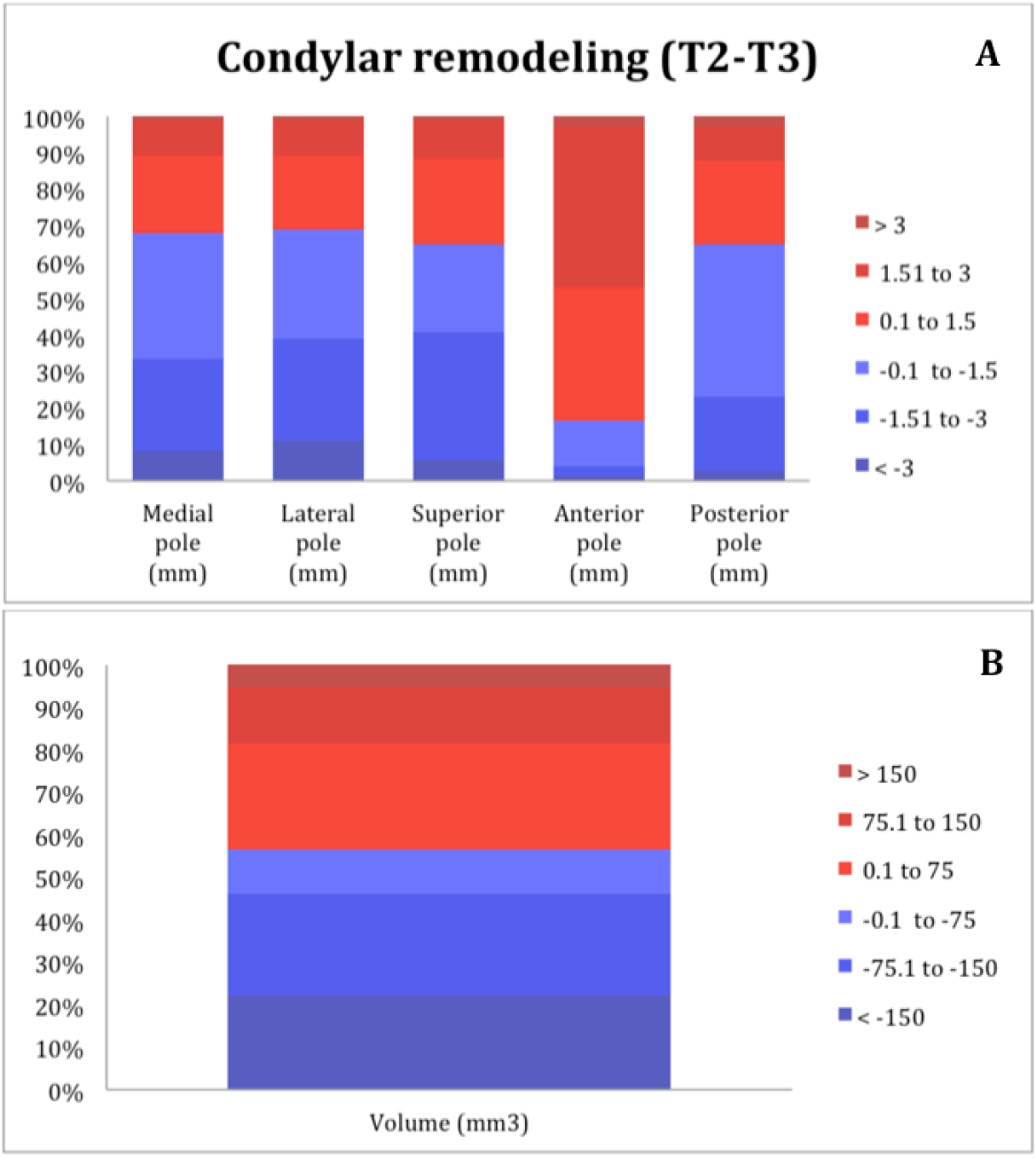

Fig 5. Percentage of patients according to condylar remodeling changes (T2-T3). A, Changes in each condylar pole; B, Overall volume changes

TABLES

Table 1. Demographic data. Clinical characteristics

			Before Surgery (T1)		
	Age (yr)	Follow-up (mo)	SNGoMe (°)	SNA (°)	SNB (°)
Mean	26.4	16.1	40.9	79.1	74.4
SD	12.5	8.2	7.4	3.7	4.6
Min	16.0	6.0	25.1	69.5	59.4
Max	58.0	52.0	61.0	85.8	81.6
Percentile					
15th	16.0	10.0	33.2	75.1	71.1
50th	21.0	14.0	41.4	79.4	74.9
85th	41.9	23.9	46.3	83.2	79.0

Abbreviations: SD, Standard deviation; Min, Minimum; Max, Maximum; SNGoMe, sella-nasion to mandibular plane angle; SNA, sella-nasion to A point angle; SNB, sella-nasion to B point angle

Table 2. Demographic data. Surgical changes (T1-T2)

	Magnitude of the surgical procedure			Condylar displacement changes					
	SNGoMe (°)	SNA (°)	SNB (°)	AP (mm)	Vert (mm)	Late (mm)	Yaw (°)	Roll (°)	Pitch (°)
Mean	5.6	-3.3	-6.0	0.6	1.0	1.5	4.5	-5.2	-7.5
SD	3.1	2.0	2.3	1.3	1.3	1.8	6.0	7.3	8.0
Min	0.7	-7.4	-12.6	-3.2	-2.3	-2.5	-11.8	-30.5	-32.3
Max	14.6	1.2	-1.8	3.5	5.0	7.3	18.3	8.7	14.0
Percentile									
15th	2.3	-5.5	-8.4	-0.6	-0.2	-0.6	-1.2	-11.4	-14.5
50th	5.4	-3.1	-5.7	0.8	0.9	1.2	3.5	-4.4	-7.8
85th	7.9	-1.4	-3.4	1.8	2.4	3.4	12.0	1.8	-1.3

Abbreviations: SD, Standard deviation; Min, Minimum; Max, Maximum

SNGoMe (sella-nasion to mandibular plane angle), Positive values indicate counterclockwise rotation and negative values clockwise rotation

SNA (sella-nasion to A point angle), Negative values indicate the maxilla moved anteriorly and positive values indicate it moved posteriorly

SNB (sella-nasion to B point angle), Negative values indicate the mandible moved anteriorly and positive values indicate it moved posteriorly

AP (antero-posterior displacement), Negative values indicate the condyle moved anteriorly and positive values indicate it moved posteriorly

Vert (vertical displacement), Negative values indicate the condyle moved upward and positive values indicate it moved downward

Late (lateral displacement), Negative values indicate the condyle moved laterally and positive values indicate it moved medially

Yaw (rotation around the Y axis), Negative values indicate posterior rotation of the medial pole and/or anterior rotation of the lateral pole; Positive values indicate anterior rotation of the medial pole and/or posterior rotation of the lateral pole

Roll (rotation around the Z axis), Negative values indicate the condyle moved medially and positive values indicate it moved laterally

Pitch (rotation around the X axis), Negative values indicate the condyle underwent counterclockwise rotation and positive values indicated it rotated clockwise

Table 3. Descriptive statistics for post-surgical condylar remodeling changes (T2-T3)

	Condylar remodeling changes [a]					
	Medial Pole (mm)	Lateral Pole (mm)	Superior Pole (mm)	Anterior Pole (mm)	Posterior Pole (mm)	Volume (mm^3)
Mean	-0.8	-0.9	-0.8	1.1	-0.5	-52.0
SD	1.8	1.8	1.9	1.3	1.6	137.8
Min	-5.3	-4.8	-5.4	-3.8	-3.6	-364.0
Max	3.3	3.2	3.6	4.2	4.6	243.2
Percentile						
15th	-2.5	-2.8	-2.4	-0.3	-2.0	-191.6
50th	-0.9	-1.2	-1.3	1.4	-0.8	-60.0
85th	1.2	1.3	1.4	2.1	1.0	86.3

[a]Negative values indicate bone resorption and positive values indicate bone apposition
Abbreviations: SD, Standard Deviation; Sig, Significance; NS, Not significant
* P ≤ .05; ** P ≤ .01; *** P ≤ .001

Table 4. Clinical characteristics (T1) and surgical changes (T1-T2) versus condylar remodeling in the follow-up period (T2-T3). Pearson correlation coefficients

		Condylar remodeling changes (T2-T3) *Correlation coefficients/ Significance*											
		Med	***(Sig)***	***Lat***	***(Sig)***	***Sup***	***(Sig)***	***Ant***	***(Sig)***	***Post***	***(Sig)***	***Vol***	***(Sig)***
Clinical characteristics	**Age (yr)**	0.06	NS	-0.27	*	-0.15	NS	-0.09	NS	-0.11	NS	-0.46	***
	Follow-up (mo)	-0.11	NS	-0.06	NS	-0.02	NS	0.05	NS	-0.02	NS	-0.07	NS
	Facial pattern before surgery (T1)												
	SNGoMe (°)	-0.20	NS	0.19	NS	-0.12	NS	0.27	*	0.21	NS	0.27	*
	SNA (°)	0.23	*	-0.08	NS	0.16	NS	-0.16	NS	-0.02	NS	0.03	NS
	SNB (°)	0.29	*	-0.22	NS	0.19	NS	-0.31	**	-0.10	NS	-0.20	NS
Surgical changes	***Magnitude of the surgical procedure (T1-T2)***												
	SNGoMe (°)	-0.07	NS	0.23	*	-0.28	*	0.22	NS	0.38	***	0.25	*
	SNA (°)	-0.04	NS	0.20	NS	0.01	NS	0.02	NS	-0.02	NS	0.07	NS
	SNB (°)	0.18	NS	-0.14	NS	0.27	*	-0.21	NS	-0.28	*	-0.05	NS
	Condylar displacement changes (T1-T2)												
	AP (mm)	-0.09	NS	0.11	NS	-0.09	NS	0.29	*	-0.06	NS	0.13	NS
	Vert (mm)	-0.16	NS	0.08	NS	-0.16	NS	0.03	NS	0.26	*	-0.03	NS
	Late (mm)	-0.05	NS	0.30	**	-0.04	NS	0.08	NS	0.20	NS	-0.25	*
	Yaw (°)	0.11	NS	0.24	*	0.11	NS	-0.10	NS	-0.00	NS	-0.13	NS
	Roll (°)	0.22	NS	-0.06	NS	0.15	NS	-0.11	NS	-0.26	*	-0.06	NS
	Pitch (°)	0.22	NS	-0.07	NS	0.07	NS	-0.12	NS	-0.23	NS	-0.15	NS

Abbreviations: Sig, Significance; Med, Medial pole; Lat, Lateral pole; Sup, Superior pole; Ant, Anterior pole; Post, Posterior pole; Vol, volume; SNGoMe, sella-nasion to mandibular plane angle; SNA, sella-nasion to A point angle; SNB, sella-nasion to B point angle; AP, Antero-posterior displacement; Vert, Vertical displacement; Late, Lateral displacement; Yaw, rotation around the Y axis; Roll, rotation around the Z axis; Pitch, rotation around the X axis
* P ≤ .05; ** P ≤ .01; *** P ≤ .001

Table 5. Stepwise multiple linear regression analysis

Dependent Variable (T2-T3)	Independent Variables	Unstandardized Coefficients B (95% CI)	Standardized Coefficients Beta	R^2	P value
Medial pole	SNB (T1)	0.09	0.23	0.05	0.05
Lateral pole	Late (T1-T2)	0.30	-0.30	0.09	0.008
Superior pole	SNGoMe (T1-T2)	-0.22	-0.37	0.15	0.002
	Age	-0.04	-0.27		0.020
Anterior pole	SNB (T1)	-0.09	-0.30	0.09	0.008
Posterior pole	SNGoMe (T1-T2)	0.20	0.38	0.14	0.001
Volume	Age	-5.06	0.46	0.21	0.000

Abbreviations: SNGoMe, sella-nasion to mandibular plane angle; SNB, sella-nasion to B point angle; Late, Lateral displacement

4 Considerações Finais

Fundamentados nos resultados e conclusões apresentados pelos artigos, podemos tecer as seguintes considerações finais:

Após cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular foi observado que, em média, os côndilos mandibulares sofreram deslocamento para posterior e medial, além de rotações nos três planos do espaço: para cima no plano sagital (upward pitch), para medial no plano coronal (medial roll) e para lateral no plano axial (lateral yaw). Diferença estatisticamente significante quanto ao deslocamento condilar em pacientes que sofreram ou não cirurgia de reposicionamento de disco articular foi observada considerando o deslocamento no sentido vertical. Côndilos de pacientes submetidos à cirurgia de reposicionamento de disco articular evidenciaram deslocamento para baixo, enquanto que os demais sofreram deslocamento para cima ($p \leq 0.001$).

Embora certo deslocamento condilar após cirurgia ortognática tenha ocorrido nos três grupos em estudo, de maneira geral, observou-se estabilidade no procedimento cirúrgico em longo prazo, principalmente no grupo de pacientes que sofreu cirurgia de reposicionamento de disco articular simultaneamente à cirurgia ortognática (Grupos 1), e no grupo de

pacientes com ATM saudável (Grupo 3). Os pacientes que apresentavam deslocamento de disco articular mas não foram submetidos à cirurgia de reposicionamento de disco (Grupo 2) apresentaram maior grau de recidiva na cirurgia ortognática. Além disso, o Grupo 2 também apresentou o maior percentual de pacientes que sofreram o problema.

Portanto, a cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular tem demonstrado ser um procedimento estável para pacientes com ATMs saudáveis, assim como para aqueles tratados com cirurgia de reposicionamento de disco articular.

Quanto à remodelação condilar durante o período de acompanhamento pós-cirúrgico, o Grupo 1 evidenciou aposição óssea no polo anterior do côndilo mandibular, diferença estatisticamente significante quando comparada aos demais grupos em estudo ($p \leq 0.001$). Observou-se maior redução em volume total do côndilo mandibular em pacientes do Grupo 2 ($p \leq 0.05$), enquanto que não foram encontradas diferenças estatísticas significantes quanto à alteração em volume entre os Grupos 1 e 3. Tal achado sugere que a cirurgia de reposicionamento de disco articular oferece certo efeito protetor à pacientes com distúrbios têmporo-mandibulares submetidos à cirurgia ortognática, proporcionando a estes pacientes resultados semelhantes, em termos de alteração total em volume, aos observados em pacientes com ATMs saudáveis.

Não foram observadas diferenças estatísticas significativas entre os gêneros feminino e masculino considerando remodelação condilar no período de acompanhamento pós-cirúrgico. Entretanto, notou-se que, em média, côndilos de pacientes do gênero feminino sofreram maior redução em volume.

Coeficientes de correlação fracos, no entanto, estatisticamente significantes foram observados considerando a relação entre variáveis clínicas e cirúrgicas com remodelação condilar. Quanto maior a idade do paciente, maior susceptibilidade à redução de volume condilar após cirurgia ortognática ($p \leq 0.001$). A rotação anti-horária do complexo maxilo-mandibular foi associada com maior grau de reabsorção no polo superior do côndilo mandibular, e menor reabsorção no polo posterior.

As alterações de deslocamento condilar geradas após a cirurgia de reposicionamento de disco simultaneamente à cirurgia ortognática não parecem estar associadas com maior reabsorção condilar no período de acompanhamento pós-cirúrgico. Tais alterações apresentaram, em média, sentidos opostos àquelas correlacionadas com maior risco de reabsorção condilar. Portanto, o deslocamento condilar para cima, o qual ocorre pela ação de forças musculares após cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular, pode ser prejudicial principalmente para

pacientes com distúrbios têmporo-mandibulares que não sofreram reposicionamento de disco articular. Como as alterações de deslocamento foram apenas fracamente correlacionadas com remodelação condilar pós-cirúrgica, outros fatores de risco devem desempenhar um papel importante na reabsorção.

Mais estudos se fazem necessários, considerando amostras maiores de pacientes não submetidos à cirurgia de reposicionamento de disco, para que possamos confirmar a necessidade da realização de tal procedimento previamente ou simultaneamente à cirurgia ortognática.

Os resultados apresentados no presente trabalho sugerem que o reposicionamento do disco articular seja um importante aliado à cirurgia ortognática de avanço e rotação anti-horária maxilo-mandibular, proporcionando um efeito de proteção ao côndilo mandibular acometido pela osteoartrite da ATM.

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ANEXO A Parecer da Comissão Nacional de Ética em Pesquisa (CONEP)

COMISSÃO NACIONAL DE ÉTICA EM PESQUISA

PARECER CONSUBSTANCIADO DA CONEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Osteoartrite da Articulação Temporomandibular. Padrão de Reabsorção Condilar e Variabilidade Morfológica, Influência da Osteotomia Sagital bilateral de Mandíbula para Avanço e Reposicionamento dos Discos Articulares

Pesquisador: João Roberto Gonçalves

Área Temática: Área 8. Pesquisa com cooperação estrangeira.

Versão: 2

CAAE: 01125412.2.0000.5416

Instituição Proponente: Faculdade de Odontologia de Araraquara - UNESP

Patrocinador Principal: Faculdade de Odontologia de Araraquara - UNESP

DADOS DO PARECER

Número do Parecer: 222.672

Data da Relatoria: 18/03/2013

Apresentação do Projeto:

Os sinais clínicos da osteoartrite apresentam-se de maneira bastante variável. Com frequência evoluem para reparação completa e adaptação morfológica mas podem apresentar curso adverso com agressiva degeneração, deformidade de estruturas relacionadas e comprometimento da função. As articulações temporomandibulares(ATMs) têm especial capacidade adaptativa em relação às demais articulações em função de seu revestimento fibrocartilaginoso. Por outro lado, o tecido ósseo do côndilo mandibular, por estar localizado logo abaixo da fibrocartilagem, o torna particularmente vulnerável a alterações morfológicas decorrentes de processos inflamatórios ou carga mecânica que ultrapasse o limiar adaptativo. Embora ainda seja motivo de discussão, a reabsorção condilar generalizada da ATM tem sido encarada como uma osteoartrite de baixo componente inflamatório. Este conceito está adequadamente inserido nas mais recentes revisões de classificação. Muito comumente, pacientes são submetidos a cirurgias ortognáticas que envolvem grandes avanços mandibulares para correção de maloclusões esqueléticas e problemas relacionados. Este procedimento, muito embora seja considerado o melhor protocolo para o tratamento das maloclusões esqueléticas, promove aumento da carga mecânica sobre ATMs devido ao estiramento dos músculos supra hioideos,tecido conjuntivo adjacente, ligamentos e fáscias musculares. Em função deste efeito colateral relacionado estes pacientes compõem assim, um grupo especialmente suscetível ao desenvolvimento de osteoartrite das ATMs ou agravamento

de processos préexistentes.

Objetivo da Pesquisa:

Objetivo Primário: Analisar retrospectivamente os côndilos mandibulares de pacientes submetidos a osteotomia sagital bilateral para avanços mandibulares com rotação anti-horária do complexo maxilo-mandibular, prevalência de torque condilar imediatamente após a cirurgia, remodelação condilar após 11 meses, estabilidade da posição maxilo-mandibular obtida e influência do reposicionamento simultâneo dos discos articulares das ATMs.

Objetivo Secundário: Caracterização da osteoartrite por índice de severidade e relação com sinais subjetivos e objetivos relatados pelos pacientes por ocasião da aquisição das imagens. Comparar a sintomatologia, sinais subjetivos e objetivos de 40 pacientes portadores de osteoartrite com 40 pacientes que não apresentavam sinais de osteoartrite, pareados por faixa etária e gênero.

Avaliação dos Riscos e Benefícios:

Riscos: Os indivíduos da amostra foram expostos à radiação para coleta das imagens tomográficas 3D entre novembro de 2008 e novembro de 2010, seguindo o protocolo de proteção com aventais de chumbo. É importante destacar que as tomografias foram tomadas exclusivamente por serem fundamentais para o planejamento cirúrgico e monitoramento clínico pós-cirúrgico dos pacientes. O presente projeto é um estudo retrospectivo dos dados arquivados destes pacientes obtidos com autorização formal de todos. O risco de identificação dos sujeitos da amostra foi inimizado através da remoção do nome dos indivíduos componentes deste estudo e substituição por códigos identificadores em todos os arquivos a serem utilizados. Somente o responsável pelo projeto têm os códigos identificados com o nome dos pacientes, que estão guardados em local seguro, sem acesso a outras pessoas.

Benefícios: A avaliação quantitativa precisa da osteoartrite das articulações temporomandibulares ajudará pacientes acometidos a terem diagnóstico precoce, aumentando as possibilidades de controle não cirúrgico, retardando ou mesmo interrompendo o curso da doença.

Comentários e Considerações sobre a Pesquisa:

A pesquisa se reveste de extrema relevância, pois, ao avaliar de forma quantitativa e precisa a osteoartrite das ATMs pode ajudar no diagnóstico precoce daqueles pacientes, aumentando as possibilidades de controle não cirúrgico, retardando ou mesmo interrompendo o curso da doença. Estudo bem fundamentado na literatura e seu desenho, bem como sua metodologia estão adequados para se alcançar os objetivos propostos.

COMISSÃO NACIONAL DE
ÉTICA EM PESQUISA

Considerações sobre os Termos de apresentação obrigatória:

Todos os termos foram apresentados, inclusive declaração do médico norte-americano autorizando a análise das tomografias de seus pacientes e informando que os mesmos assinaram Termo de Consentimento autorizando a utilização das tomografias para a pesquisa.

Recomendações:

Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:

No documento "PB PROJETO DE PESQUISA 11254.pdf" o cronograma, apesar de já ter sido solicitado a sua alteração, foi alterado para o início da coleta de dados no final de janeiro, mas o próprio pesquisador responsável explica que era uma data sugerida e que poderia alterar novamente conforme os trâmites do protocolo nesta CONEP. Recomenda-se a sua adequação.

Foi informado que o número de sujeitos que é (100), mas em outro lugar fala-se em 100 no Brasil e 100 nos EUA. Lendo-se o projeto entende-se que são os mesmos sujeitos, ou melhor, as mesmas tomografias obtidas nos EUA que serão analisadas no Brasil. A diferença real está entre o protocolo que indica 100 sujeitos e a Folha de Rosto que indica 120. Recomenda-se adequação.

Situação do Parecer:

Aprovado com Recomendação

Considerações Finais a critério da CONEP:

Diante do exposto, a Comissão Nacional de Ética em Pesquisa - CONEP, de acordo com as atribuições definidas na Resolução CNS 196/96, manifesta-se pela aprovação do projeto de pesquisa proposto, devendo o CEP verificar o cumprimento das questões acima, antes do início do estudo.

Situação: Protocolo aprovado com recomendação.

COMISSÃO NACIONAL DE
ÉTICA EM PESQUISA

BRASILIA, 19 de Março de 2013

Assinador por:
Aníbal Gil Lopes
(Coordenador)

Endereço: SEPN 510 NORTE, BLOCO A 1º SUBSOLO, Edifício Ex-INAN - Unidade II - Ministério da Saúde
Bairro: Asa Norte **CEP:** 70.750-521
UF: DF **Município:** BRASILIA
Telefone: (61)3315-5878 **E-mail:** conep@saude.gov.br

ANEXO B Parecer do Comitê de Ética em Pesquisa (CEP) da Faculdade de Odontologia de Araraquara

FACULDADE DE ODONTOLOGIA DE ARARAQUARA - UNESP

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Osteoartrite da Articulação Temporomandibular. Padrão de Reabsorção Condilar e Variabilidade Morfológica, Influência da Osteotomia Sagital bilateral de Mandíbula para Avanço e Reposicionamento dos Discos Articulares

Pesquisador: João Roberto Gonçalves

Área Temática: Área 8. Pesquisa com cooperação estrangeira.

Versão: 3

CAAE: 01125412.2.0000.5416

Instituição Proponente: Faculdade de Odontologia de Araraquara - UNESP

Patrocinador Principal: Faculdade de Odontologia de Araraquara - UNESP

DADOS DO PARECER

Número do Parecer: 228.240

Data da Relatoria: 26/03/2013

Apresentação do Projeto:

Maloclusões esqueléticas em adultos frequentemente exigem tratamento ortodôntico associado a tratamento cirúrgico.

Embora seja considerado o melhor protocolo para o tratamento das maloclusões esqueléticas, este procedimento promove aumento da carga mecânica sobre ATMs, fazendo destes pacientes um grupo especialmente suscetível ao desenvolvimento de osteoartrite das ATMs, caracterizada como a reabsorção condilar generalizada da ATM.

Com a pesquisa proposta, Dr. João Roberto Gonçalves, juntamente com seus colaboradores, buscará estudar a osteoartrite das articulações têmporomandibulares e suas relações com potenciais fatores predisponentes e/ou agravantes por meio de novas técnicas computacionais desenvolvidas para otimização do uso de imagens tridimensionais (tomografias computadorizadas e ressonância magnética).

O projeto está adequadamente apresentado.

Objetivo da Pesquisa:

Objetivo Primário: Analisar retrospectivamente os côndilos mandibulares de pacientes submetidos a osteotomia sagital bilateral para avanços mandibulares com rotação anti-horária do complexo maxilomandibular, prevalência de torque condilar imediatamente após a cirurgia, remodelação condilar após 11 meses, estabilidade da posição maxilo-mandibular obtida e influência do

Endereço: HUMAITA 1680
Bairro: CENTRO **CEP:** 14.801-903
UF: SP **Município:** ARARAQUARA
Telefone: 1633-0164 **Fax:** 1633-0164 **E-mail:** cep@foar.unesp.br; mnagle@foar.unesp.br

reposicionamento simultâneo dos discos articulares das ATMs.
Objetivo Secundário: Caracterização da osteoartrite por índice de severidade e relação com sinais subjetivos e objetivos relatados pelos pacientes por ocasião da aquisição das imagens. Comparar a sintomatologia, sinais subjetivos e objetivos de 40 pacientes portadores de osteoartrite com 40 pacientes que não apresentavam sinais de osteoartrite, pareados por faixa etária e gênero.

Avaliação dos Riscos e Benefícios:
Não se aplica. A pesquisa fará uso de tomografias realizadas em pacientes atendidos na Baylor University Medical Center em Dallas, TX - EUA, durante o período de Outubro de 2008 a Outubro de 2010, sob responsabilidade do Prof. Larry M. Wolford.

Comentários e Considerações sobre a Pesquisa:
A pesquisa é oportuna e poderá apresentar importante contribuição para a identificação do risco de osteoartrite em pacientes que se submetem a cirurgia para correção de maloclusões. O projeto está muito bem apresentado e a metodologia proposta é adequada aos objetivos da pesquisa.

Considerações sobre os Termos de apresentação obrigatória:
Todos os termos foram apresentados, inclusive declaração do médico norte-americano autorizando a análise das tomografias de seus pacientes e informando que os mesmos assinaram Termo de Consentimento autorizando a utilização das tomografias para a pesquisa.

Recomendações:
Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:
O projeto é oportuno e toda a documentação necessária para sua avaliação foi adequadamente apresentada, bem como os documentos solicitados em pendência da CONEP.

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

Considerações Finais a critério do CEP:
Projeto APROVADO pelo CEP, após análise de documentos apresentados. Encaminhe-se ao pesquisador para dar início a pesquisa.

FACULDADE DE ODONTOLOGIA DE ARARAQUARA - UNESP

ARARAQUARA, 25 de Março de 2013

Assinador por:
Maurício Meirelles Nagle
(Coordenador)

Endereço: HUMAITA 1680
Bairro: CENTRO **CEP:** 14.801-903
UF: SP **Município:** ARARAQUARA
Telefone: 1633-0164 **Fax:** 1633-0164 **E-mail:** cep@foar.unesp.br; mnagle@foar.unesp.br

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Araraquara, 10 de março de 2017.

LILIANE DE CARVALHO ROSAS GOMES