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ESTABILIDADE E COMPLICAÇÕES PÓS-OPERATÓRIAS EM OSTEOTOMIA LE FORT I ASSOCIADA AO USO DE SUBSTITUTOS ÓSSEOS - REVISÃO SISTEMÁTICA

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Orientador: Prof. Dr. Eduardo Rolim Teixeira
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Dedico este trabalho:

Dedico este trabalho a Deus. Agradeço-o por me proporcionar saúde, capacitação, sustento, perseverança e permitir que eu conclua mais uma etapa importante da minha vida.

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RESUMO

Essa revisão sistemática foi conduzida para avaliar a estabilidade e complicações pós-operatórias da osteotomia Le Fort I (OLFI) com uso de enxertos ósseos com intuito de melhorar o entendimento dessa técnica e averiguar a necessidade de novas metodologias sobre o assunto. A busca sitemática foi efetuada nas bases de dados PubMed, EMBASE, Biblioteca Cochrane, literatura cinza (OpenGrey, registros de ensaios clínicos and Google Scholar) e busca manual, obtendo 1748 artigos publicados até 2019. Destes, 72 foram selecionados para leitura na íntegra, mas apenas 23 foram incluídos nessa revisão. O nível de concordância entre os autores para seleção dos estudos e para elegibilidade foi considerado excelente (k= 0.891 e k= 0.907 respectivamente). A qualidade metodológica foi considerada baixa, tendo todos estudos incluídos alto potencial de vieses. Mesmo assim, o estudo destaca que o enxerto ósseo reduz a taxa de recidiva fornecendo resultado das medidas estáveis nos planos sagital e vertical da maxila. Esses resultados de estabilidade perimitiram organizar uma categorização estratificada dos movimentos cirúrgicos em ambos os planos da maxila, afirmando que o enxerto ósseo pode estar bem indicado para avanço maxilar > 5 mm e reposicionamento inferior ≥ 3 mm. As complicações pós-operatórias mais freqüentes foram o deslocamento do bloco HA, propagação da cicatriz do local doador e sinusite. Os enxertos alogênicos e aloplásticos apresentaram maior prevalência em relação às complicações, com taxas de 6.1% e 5% repectivamente. Portanto essa técnica de enxertia apresenta baixa taxa de

complicação sendo considerada segura. Apesar das diretrizes propostas nesta revisão sistemática, houve amostras pequenas de alguns estudos, heterogeneidade em métodos e resultados, poucos ensaios clínicos com grupo controlado e uso de sobreposição 2D das alterações cirúrgicas. Isso indica a necessidade de pesquisas mais sólidas baseada em evidências para dar suporte a esses resultados.

Palavras-chave: Revisão sistemática. Cirurgia ortognática. Osteotomia Le Fort I. Enxertos ósseos. Estabilidade. Complicações

ABSTRACT

This review systematic was conducted to evaluate the stability and postoperative complications of Le Fort I osteotomy with the use of bone grafting in order to improve the understanding of this technique and to investigate the need for new methodologies on the subject. The systemmatic search was carried out in PubMed, EMBASE, Cochrane Library databases, grey literature (Opengrey, Register of clinical trials and Google scholar) and manual search, yielding 1748 articles published up until 2019. Of these, 72 articles were selected for full-text screening, but only 23 articles were included. The level of agreement between the authors for study selection and for eligibility was considered excellent (κ = 0.891 and κ = 0.907 respectively). Methodological quality was considered low, with all studies including high bias potential. Even so, the study highlights that the bone grafting reduces the rate of relapse by providing results of stable measurements in the sagittal and vertical planes of the maxilla. These stability results allowed us to organize a stratified categorization of the surgical movements in both planes of the maxilla, stating that the bone graft may be well indicated for maxillary advancement > 5 mm and inferior repositioning ≥ 3 mm. The most frequent postoperative complications were HA block displacement, donor site scarring and sinusitis. The allogeneic and alloplastic grafts presented a higher prevalence regarding complications with rate of 6.1% and 5% respectively. Therefore, this grafting technique presents a low complication rate and is considered safe. Despite the guidelines proposed in this systematic review, there were small samples in some studies, heterogeneity in methods and results, few clinical trials with

controlled group and use of 2D overlap of surgical changes. This indicates that more robust, evidence-based research is needed to support these results.

Keywords: Systematic review. Orthognathic surgery. Le Fort I osteotomy. Bone grafting. Stability. Complications.

LISTA DE ILUSTRAÇÕES

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ARTIGO

Subtitle: DBM, human demineralized bone matrix; F, female; HA, hidroxiapatite; IP, interpositional graft; M, male; NR, not reported by the authors.
[a] Total sample (*N*), Le Fort I osteotomy with bone graft sample (*n*).
[b] Monomaxillary surgical procedure (M), bimaxillary surgical procedure (B).
[c] Non-rigid fixation (N), rigid fixation (R).

Subtitle: CBCT, cone beam computed tomography; CR, cephalometric radiographs; D, stability analysis by dental measurement; NR, not reported by the authors; S, stability analysis by skeletal measurement; SD, standard deviation.
[a] T1 = mean surgical changes; T2 = mean stability changes. Sagittal: (-) retrusion/(no sign) protrusion. Vertical: (-) intrusion/(no sign) extrusion.
[b] Landmark: 1 = measurements at A-Point; 2 = measurements at Anterior Nasal Spine (ANS); 3 = measurements at Posterior Nasal Spine (PNS); 4 = measurements at Nasopalatine canal; 5 = distance Condilion (Co) to A-Point.
[c] 1 = group treated with combined wire fixation; 2 = group treat with rigid internal fixation.
[d] 1 = group with use of heterologous bone grafts; 2 = group with use of autologous bone grafts.
[e] 1 = group receiving interpositional xenogenic bovine bone grafting (Bio-Oss®); 2 = group receiving Bio-Oss® in onlay position; 3 = group receiving interpositional autogenous iliac crest bone grafting.
[f] 1 = maxillary impaction cases with Biopex®; 2 = maxillary advancement cases with Biopex®.

Subtitle: aBG, autologous bone graft; hBG, heterologous bone graft; msLeF, multi-segmental Le Fort I osteotomy; nRF, non-rigid fixation; opLeF, one-piece Le Fort I: RF, rigid fixation.
[a] Comparison between different treatments modalities (control group vs. test group – controlled study).
[b] Comparison between different surgical techniques (test group vs. test group – comparative study).
[c] Risk of bias: high, 0–5 ‘yes’ responses; medium, 6–7 ‘yes’ responses; low, 8 ‘yes’ responses.

LISTA DE ABREVIATURAS, SIGLAS, SÍMBOLOS

CO	Cirurgia Ortognática
OLFI	Osteotomia Le Fort I
K	Teste Kappa
>	Maior que
≥	Maior ou igual
mm	milímetros
≤	Menor ou igual
HA	Hidroxiapatita
FIR	Fixação interna rígida
2D	Two-dimensional
3D	Three-dimensional
eg	Example
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyse
PROSPERO	International prospective register of systematic reviews
MeSH	Medical Subject Headings
Emtree	Descritores de assunto do EMBASE
MFSM	Marcelo Fernandes Santos Melo
ASAM	Adriele Silveira Araújo Melo
RBO	Rogério Belle de Oliveira
SD	Standard-deviation
DBM	human demineralized bone matrix;
F	female

IP	interpositional graft;
M	male
NR	not reported by the authors.
(*N*)	Total sample
(M)	Monomaxillary surgical procedure
(B)	Bimaxillary surgical procedure
(N)	Non-rigid fixation
(R)	rigid fixation
CBCT	cone beam computed tomography
CR	cephalometric radiographs
D	stability analysis by dental measurement
S	stability analysis by skeletal measurement
T1	mean surgical changes
T2	mean stability changes.
(-)	Sagittal: retrusion sign
(-)	Vertical: intrusion sign
ANS	Anterior Nasal Spine
PNS	Posterior Nasal Spine
Co	Condilion
aBG	autologous bone graft
hBG	heterologous bone graft
msLeF	multi-segmental Le Fort I osteotomy
nRF	non-rigid fixation
opLeF	one-piece Le Fort I

SUMÁRIO

1 INTRODUÇÃO

A cirurgia ortognática (CO) é o tratamento de eleição para correção das deformidades dento-esqueléticas que envolvem a face[1]. Diversas técnicas cirúrgicas para o tratamento das alterações esqueléticas da maxila são reportadas, mas o procedimento mais comum é a osteotomia Le Fort I (OLFI).

Nesse contexto, os movimentos cirúrgicos permitidos por meio da OLFI são avanço ou recuo, impacção ou reposicionamento inferior e alteração transversa da maxila se associada à segmentação. Com relação a esses procedimentos, uma extensiva busca na literatura tem sido feita para melhorar os resultados cirúrgicos a longo prazo[2-6]. Apesar dos resultados satisfatórios e previsíveis da cirurgia ortognática, os efeitos adversos observados de instabilidade são preocupantes.

Ossificação incompleta entre os segmentos ósseos maxilares no local da linha da osteotomia é um dos principais problemas da técnica cirúrgica[7]. Pesquisas dentro da base biológica e filosofia cirúrgica da OLFI refinaram as técnicas cirúrgicas e progrediram na anestesia geral, nos métodos de fixação rígida e nos exames de imagem, tornando os procedimentos mais estáveis[8]. No entanto, alguns autores relatam que a fixação interna rígida (FIR) sozinha para a maxila osteotomizada, pode ser insuficiente e/ou inadequado se o tamanho do defeito entre o segmento distal avançado e o segmento proximal for grande o suficiente para não permitir adequada cicatrização óssea. O *gap* cirúrgico (espaço entre as linhas da osteotomia) pode gerar uma falha de cicatrização óssea na região e promover a formação de tecido fibrótico ao invés

de osso estável ao longo da linha da osteotomia[7,9]. Alguns estudos[1,10,11] relatam que quanto maior o movimento cirúrgico da maxila, maior o risco de recidiva esquelética e interposição de tecido fibroso (pseudoartrose maxilar)[12,13]. Já outros autores, não encontraram correlação entre a magnitude do movimento maxilar e o nível de recidiva[14].

Há uma hierarquia de estabilidade entre os tipos de movimento cirúrgico que são possíveis com a cirurgia ortognática e foi baseada primariamente em número de pacientes que sofreram alteraçoes de pelo menos 2 mm (alterações < 2 mm são consideradas dentro do intervalo de erro metodológico e clinicamente insignificante; 2-4 mm, fora do intervalo do erro metodológico e potencialmente significante clinicamente; e > 4 mm, altamente significantes para recidiva)[(1)]. Particularmente, a estabilidade da maxila dependerá do tipo de técnica cirúrgica proposta para a deformidade dentofacial. Tradicionalmente, o reposicionamento inferior da maxila é considerado o movimento maxilar mais instável devido à alta susceptibilidade de recidiva do componente vertical dentro das primeiras semanas pós-cirúrgicas, em que as forças oclusais tendem a empurrar o segmento para cima, antes da cicatrização óssea completa[1,15]. Os movimentos horizontais para avanço da maxila associados ou não à osteotomia sagital da mandíbula, são considerados ainda estáveis se fixados com FIR e ≤ 8 mm. Demais movimentos cirúrgicos foram relatados na escala de hierarquia de Proffit et al.[1] e recentemente atualizado com a criação de nova escala hierarquizada de estabilidade baseada em evidência (critérios metodológicos claros e análise estatística) realizados por Haas Junior et al[16].

Há abordagens lógicas para manter a posição estável da maxila até sua

cicatrização: fixação rígida pesada, o uso de enxertos ósseos (de preferência com menor capacidade de reabsorção) no defeito e cirurgia simultânea da mandíbula para diminuir a força oclusal[17].

Há estudos que reportam o uso de enxertos ósseos em maxila osteotomizada em pacientes com fissuras palatinas e que apresentam resultados estáveis e satisfatórios[18,19]. Pacientes com fissura labiopalatina frequentemente apresentam distúrbios de crescimento dos maxilares (maloclusão dento-esquelética), o que demanda correção orto-cirúrgica[20]. A OLFI em paciente fissurado torna-se um desafio para estabilidade dento-esquelética, por causa da presença de fístulas cicatriciais, palatais ou alveolares, hipoplasia maxilar devido a tensão muscular da região, dentes e vascularização dos segmentos comprometidos[21]. Para esse estudo torna-se um grupo heterogêneo com influência de variáveis clínicas adicionais que afetam a estabilidade esquelética pós-operatória e, por isso, não incluído na amostra.

Fatores que podem interferir na estabilidade da OLFI incluem: a distância dos segmentos ósseos, ortodontia pré-operatória inadequada, cirurgia monomaxilar versus cirurgia bimaxilar, cicatrização da ferida inadequada, mobilização óssea da maxila incompleta, segmentações maxilares, comprometimento vascular, força mastigatória e respiratória excessiva, método de fixação inapropriado, tensão e mobilização ou retração dos tecidos moles, interferência com o septo nasal, presença de fissuras palatinas e não uso de substitutos ósseos[2,7,22-24].

Para defeitos ósseos maiores que 3 mm entre os segmentos ao longo da

linha da osteotomia, indica-se o uso de enxertos ósseos entre os *gaps* para melhorar a estabilidade óssea e consequentemente diminuir o risco de recidiva[7,22,25]. A OLFI é bem descrita na literatura, mas apenas um número limitado de estudos faz uma análise comparativa (retrospectiva ou prospectiva) do uso dos enxertos ou substitutos ósseos no *gap* da linha da osteotomia da maxila para promover essa estabilidade[26-30]. Para grandes avanços de maxila (variação > 8-10 mm), alguns estudos[30] defendem o uso de enxertos ósseos nesses gaps, mas ainda não há um estudo bem controlado que defenda a técnica de enxertia para grandes avanços da maxila. Já para reposicionamento inferior da maxila, se a distância for menor que 2-3 mm, fragmentos ósseos obtidos durante a cirurgia e misturados com tecido de colágeno são utilizados para preencher o gap da ostetotomia. Mas se a maxila extende inferiormente mais que 3 mm, enxertos com osso sólido ou bloco de hidroxyapatita são geralmente indicados[15].

As vantagens do uso desses substitutos ósseos em osteotomia maxilar incluem: a capacidade de atuar como barreira mecânica para prevenir recidiva, fornecer uma matriz para ossificação e prevenir migração do tecido mole para a área osteotomizada. Todos esses fatores ajudam a acelerar a união óssea e reduzir as taxas de recidiva[24,26].

Uma variedade de biomateriais foi utilizada para preencher o *gap* entre os segmentos ósseos, incluindo enxertos autógenos, enxertos heterólogos, enxertos aloplásticos (HA sólido e poroso, cimento de fosfato de cálcio), fatores de crescimento e substitutos ósseos liofilizados humanos[5,31,32]. Portanto, torna-se importante a escolha do tipo de substituto ósseo para preenchimento do *gap*

formado após a OLFI, levando em consideração suas propriedades osteogênicas, melhor manejo do material enxertado, e as possíveis complicações cirúrgicas e pós-operatórias que podem ocorrer com o substituto ósseo selecionado[28,29,32].

Técnicas de enxerto ósseo autógeno são consideradas padrão-ouro devido à capacidade osteogênica e ausência de reações imunológicas. Por outro lado, existem também algumas desvantagens do seu uso, tais como: (1) procedimento cirúrgico aditivo em área doadora; (2) tempo cirúrgico prolongado; (3) aumento de dor/morbidade; (4) aumento de risco de infecção; (5) restrição de movimento no membro inferior ou extremidade; (6) aumento de custo; (7) reabsorção imprevisível do enxerto que pode levar à instabilidade óssea ou recidiva[33,34].

Deve-se ressaltar a importância da vascularização para o segmento ósseo distal ou linha da osteotomia, pois parece ser o principal fator para determinar se o substituto ósseo pode ser *in situ.* Técnicas cirúrgicas interposicional e onlay são as mais relatadas na literatura, sendo assim, técnicas previsíveis e adequadas[5,26,29,35].

Possíveis complicações com a utlização de enxertos ósseos na maxila osteotomizada podem limitar seu uso na cirurgia ortognática. As complicações relatadas na literatura são: infecção, sinusite do seio maxilar, deiscência da mucosa sobre o enxerto, exposição do implante ósseo, não-união ou união tardia, reabsorção, instabilidade ou deslocamento do enxerto para outra região anatômica, propriedades de difícil manuseio. Não há um estudo que sumarize esses dados e compare qual o risco mais acometido associado ao tipo de

enxerto, técnica de enxertia, magnitude do movimento maxilar e área anatômica receptora[10,26,27,30,36,37].

A literatura relata estudos que avaliam a utilização de enxertos ósseos em OLFI, mas não há uma padronização de condutas definida sobre a melhor forma de tratamento para esse tipo de técnica cirúrgica. Para estabelecer uma diretriz de indicação do uso de material de enxertia óssea para OLFI em CO e obtenção de melhores resultados, devem ser avaliados estudos de intervenção. Ensaios clínicos randomizados são a melhor forma de evidência científica. Caso esse tipo de estudo não esteja disponível na literatura, outros tipos de estudos podem ser utilizados para se avaliar uma intervenção ou gerar hipóteses a respeito[38,39].

Diretrizes de tratamento devem ser estabelecidas somente após a elaboração de revisões sistemáticas e metanálises sobre o assunto[38,39]. Portanto, uma revisão sistemática e metanálise de estudos observacionais ou de intervenção tornam-se uma importante ferramenta para ajudar a compreender as indicações e resultados cirúrgicos obtidos com o uso de substitutos ósseos no *gap* da OLFI em termos de estabilidade e complicações pós-operatórias. Com isso, pode-se também avaliar a necessidade de novos estudos sobre o assunto.

Desta forma torna-se necessário avaliar a literatura existente em busca de evidências científicas que demonstrem resultados mais previsíveis e/ou aumentem a estabilidade da OLFI com ou sem substitutos ósseos, bem como a tentativa de propor uma padronização de condutas para promover resultados esqueléticos mais estáveis da OLFI de acordo com o tipo de técnica cirúrgica,

magntitude e direção do movimento da maxila osteotomizada em único segmento. De forma secundária, ressalta a importância de avaliar as possíveis complicações pós-operatórias e suas prevalências nos estudos selecionados, com objetivo de creditar se a técnica cirúrgica descrita aumenta os riscos de complicações.

2 PROPOSIÇÃO

2.1. Objetivos gerais

Realizar uma revisão sistemática da literatura, respondendo a seguinte questão: “O uso de enxerto ósseo em OLFI em CO promove melhor estabilidade maxilar a longo prazo?”. Como objetivo secundário, serão avaliadas as possíveis complicações pós-operatórias do uso de enxertos ósseos nessa condição.

2.1 Objetivos específicos

- Avaliar e quantificar a estabilidade da maxila após OLFI com uso de substituto ósseo através de mensurações quantitativas clínicas e/ou imaginológicas em intervalos pré e pós-operatório. Medidas baseadas em evidências de recidiva (padrão clinicamente estável $\leq$ 2 mm);

- Descrever as possíveis complicações pós-operatórias com uso de enxerto ósseo utilizado em OLFI e técnica cirúrgica selecionada, em intervalos de tempo regulares;

- Avaliar a necessidade de novas metodologias sobre o assunto;

3 DESENVOLVIMENTO

3.1 Artigo Científico:

STABILITY AND POSTOPERATIVE COMPLICATIONS IN LE FORT I OSTEOTOMY ASSOCIATED WITH THE USE BONE GRAFTING SUBSTITUTES – SYSTEMATIC REVIEW

M. F. S. Melo, A. S. A. Melo, R. B. de Oliveira, E. R. Teixeira

ABSTRACT

After maxillary Le Fort I osteotomies, bone grafting can be required to fill the osteotomized gaps providing better long-term stability. This systematic review was conducted to evaluate the stability and postoperative complications of one-piece Le Fort I osteotomy with the use of bone grafting, aiming to improve the understanding of this intervention. The search was divided into a main search (PubMed, Embase, and Cochrane Library databases) that yielded 1738 articles published up until march 2019, and a secondary search was conducted by grey literature and manual search adding more 10 articles. After eligibility screening, 23 studies were included in the final sample. The level of agreement between the authors was considered excellent (κ = 0.891 for study selection and κ = 0.907 for study eligibility). Methodological quality was evaluated according to seven criteria related to study design, measurements, statistical analysis, and

follow-up. The risk of bias was considered potentially high in all studies. Even so, this review highlights that the bone grafting minimizes the rate of the relapse by providing stable measure outcomes in the sagittal and vertical planes, and is indicated for maxillary advancement greater than 5 mm and inferior repositioning ≥ 3 mm. The most frequent postoperative complications were HA block displacement, scar spread of donor site and sinusitis. Allogeneic and alloplastic grafts presented more complications with rate of 6.1% and 5%, respectively. In general, grafting technique presents a low complication rate. Despite the guidelines proposed in this detailed systematic review, many studies had small samples, heterogeneity in methods and outcomes, there were few clinical trials with controlled group, and use of 2D superimposition rather than 3D superimposition of the surgical changes. This indicates that more solid, evidence-based, long-term research is needed to support these results.

Keywords: orthognathic surgery; Le Fort I osteotomy; bone grafting; stability, complication; systematic review.

Introduction

Orthognathic surgery combined with orthodontic treatment is the most predictable approaches to correct dentofacial deformity and to achieve satisfactory outcomes with long-term bone stability[1,2]. The most common, safe and versatile surgical orthognathic procedure is the Le Fort I osteotomy that allow maxillary reposition in all 3 planes of movement (horizontal, vertical and transverse changes), restoring the function and facial esthetics, correcting skeletal and occlusal discrepancies, and treating the obstructive sleep apnea in patients with facial deformities[3-5].

However, gaps or continuity defects are created between the proximal and distal bone segments at the osteotomy site, and incomplete ossification of these segments has proven to be a major problem in these patients[5-7]. Factors that may be of concern in the stability of Le Fort I osteotomy include distance or contact of the osteotomy walls, presurgical orthodontic problems, inappropriate mobilization, intraoperative complications, excessive masticatory and respiratory forces, inappropriate fixation methods, type and amount of surgical movements, tension and mobilization of soft tissues, presence of fissures or clefts, segmentalization and inappropriate or no use of bone grafts[8-11]. Failure to graft these gaps can result in instability, relapse, and non-union of bone structures with subsequent relapse or worsening of the original deformity. Therefore, interpositional bone grafts in the osteotomy gap has proven an effective strategy for promoting bone union and reduction, acting as mechanical stops and preventing soft tissue herniation[8,12,13].

Grafting maxillary osteotomy gaps will depend of the type and magnitude of surgical movement, and type of fixation system used. Previous studies and clinical impressions of rigid fixation techniques indicate that there is improved stability of this system when compared to non-rigid fixation[14-17]. In orthognathic surgery, a combination of rigid internal fixation and application of bone grafts has shown good and stable results[3,18]. The requirement for grafting in maxillary advancement is still controversial in literature, but some studies relate the amount of maxillary advancement to necessity of grafting[6,18,19]. According Proffitt et al.[2], the maxillary advancement becomes stable with rigid internal fixation (RIF) until movements ≤ 8mm, and inferior reposition is the less stable movement. There is as yet no protocol on the required amount of osteotomized maxilla movement to standardize the use of the bone graft substitutes into the gaps.

If the defect size between the advanced inferior maxillary segment and the superior segment exceeds 3 mm at the levels of piriform rim and zygomaticomaxillary junction following Le Fort I osteotomy, use of a bone graft can become necessary for stabilization[7,20]. Other studies declare that measures between 3-5 mm[3,8,9,21,22] or more[6,11,12,19,23-25] of the bone fragments gap should be filled along the line of osteosynthesis for postoperarive stability. For maxillary inferior repositioning, if the distance is less than 2-3 mm, bony fragments gathered during the surgery mixed with tissue glue are used to fill gap, but if the distance is greater than 3 mm, grafting with solid bony or hydroxyapatite blocks is usually indicated[26]. The larger the defect size between bone segments the greater possibility of proliferation of fibrous tissue rather than bone tissue along

the osteotomy, and consequently the greater relapse[8,12,25,27,28]. However, there are no well-controlled study in which the maxilla is advanced to a large distance with and without bone grafting.

Various interpositional grafting materials and autogenous bone from different harvest sites have been advocated to maintain stables the repositioned segments and to allow successful early healing[4,28,29]. Each of these choices has inherent advantages and drawbacks or risks. Several autologous bone grafting (eg, calvarium, iliac crest, genial bone) still plays a significant role in orthognathic surgery, but many bone substitutes (eg, porous or block alloplastic grafts) have been developed to decrease the morbidity associated with donor sites and the postoperative bone graft resorption leading to osseous instability[21,25,30,31]. Allogenic bone (eg, demineralized bone matrix or freeze dried bone) are also a biological alternative to autologous grafts, but carry a small and real risk of transmission of disease. Alloplastic materials (eg, synthetic tricalcium phosphate) has been recognized as a useful bone alternative material[32], but may present an increased risk of infection[21,33]. Thereby, doubts about safety of the use of bone grafts in Le Fort I osteotomy, in turn, are based on the increased risk of postoperative complications, as following: signs and symptoms of infection, maxillary sinusitis, hematoma formation, wound dehiscence, changes in the overlying soft tissues, difficult handling properties, the need for a second operation, instability of the implant with resorption and/or poor healing at the osteotomy gap[13,34-36].

There are limited studies that discuss the use of graft materials in maxillary osteotomy Le Fort I with homogeneous demographic data and/or

satisfactory methodological quality for surgical intervention. Research into the long-term stability and postoperative complications of the Le Fort I osteotomy technique associated with use of bone graft could help patients, orthodontists, and surgeons to estimate the benefit of an elective operation versus its iminente risks, as well as prevent the occurrence of complications and facilitate their management. Within this context, systematic reviews are particularly relevant, as they are able to summarize and organize data from interventional studies – thus improving effect estimates – and analyze the risk of bias in the published literature.

This systematic review was conducted to evaluate the stability and postoperative complications related to the Le Fort I osteotomy combined with bone grafts in maxillary osteotomy gaps and to establish an evidence-based hierarchy of stability about these surgical topics. The two specific questions for which answers were sought were the following: (1) Can the maxillary Le Fort I osteotomy with use bone graft substitutes provide and maintain stability in the post-operative period? (2) What are the main postoperative complications?

Materials and methods

This systematic review was based on the PRISMA guidelines[37] and was registered at the PROSPERO (International prospective register of systematic reviews) - http://www.crd.york.ac.uk/PROSPERO - under the protocol number CDR42018090617. It was also aproved by the Sipesq CCE ECS – Pontífica Universidade Católica do Rio Grande do Sul, protocol number 8670.

Three comprehensive literature searches for systematic reviews were conducted until March 2019: the main search, which covered the PubMed, Embase, and Cochrane Library databases; a search of the grey literature was conducted through of the System for Information on Grey Literature in Europe (http://www.opengrey.eu/), clinical trials registry (http://www.clinicaltrials.gov/), and Google Scholar; and a hand-search of the reference lists of all articles retrieved through the main search and grey literature strategy. The PICO strategy was designed in: P (population): dentofacial deformity or orthognathic surgery; I (intervention): Le Fort I osteotomy; C (comparison): use of the bone graft substitutes in gaps osteotomies; O (outcome): maxillary stability and/or complications. No limits were applied for year of publication or language, and Boolean operators (OR and AND) were used for the combinations of thesaurus terms related to dentofacial deformity, Le Fort I osteotomy, bone substitutes, stability and postoperative complications.

Search Strategy

For main search, the medical subject heading (MeSH) terms (and their entry terms) and non-MeSH terms were used to search PubMed, as following:

(((“Dentofacial Deformities”[mh] OR "Deformities, Dentofacial” OR “Deformity, Dentofacial” OR “Dentofacial Deformity” OR “Dentofacial Abnormalities” OR “Abnormalities, Dentofacial” OR “Abnormality, Dentofacial” OR “Dentofacial Abnormality” OR “Dentofacial Dysplasia” OR “Dentofacial Dysplasias” OR “Dysplasia, Dentofacial” OR “Dysplasias, Dentofacial” OR “Adult”[mh] OR “Adults” OR “Young Adult”[mh] OR “Maxilla”[mh] OR “Maxillas” OR “Maxillary Bone” OR “Bone, Maxillary” OR “Bones, Maxillary” OR “Maxillary Bones” OR “Maxillae”)) AND (“Osteotomy, Le Fort"[mh] OR “Le Fort Osteotomy” OR “Osteotomy, LeFort” OR “LeFort

Osteotomy" OR "Maxillary Osteotomy"[mh] OR "Maxillary osteotomies" OR "Osteotomies, Maxillary" OR "Osteotomy, Maxillary" OR "Le Fort I Osteotomy" OR "Le Fort I osteotomies" OR "Maxillary Advancement" OR "Orthognathic Surgery"[mh] OR "Orthognathic Surgeries" OR "Orthognathic Surgical Procedures"[mh] OR "Orthognathic Surgical Procedure" OR "Jaw Surgery" OR "Jaw Surgeries" OR "Maxillo-Mandibular Surgery" OR "Maxillo-mandibular Surgeries")) AND ("Bone Substitutes"[mh] OR "Replacement Material, Bone" OR "Replacement Materials, Bone" OR "Materials, Bone Replacement" OR "Bone Substitute" OR "Substitute, Bone" OR "Substitutes, Bone" OR "Bone Replacement Material" OR "Material, Bone Replacement" OR "Bone Replacement Materials" OR "Bone Matrix"[mh] OR "Bone Matrices" OR "Matrices, Bone" OR "Matrix, Bone" OR "Durapatite"[mh] OR "Hydroxyapatites"[mh] OR "Hydroxyapatites Derivatives" OR "Derivatives, Hydroxyapatites" OR "Hydroxylapatite" OR "Calcium Hydroxyapatite" OR "Calcium Phosphates"[mh] OR "Phosphates, Calcium" OR "Bone Transplantation"[mh] OR "Grafting Bone" OR "Bone Graft*" OR "Transplantation, Bone" OR "Bone Regeneration"[mh] OR "Bone Regenerations" OR "Regeneration, Bone" OR "Regenerations, Bone" OR "Transplantation, Autologous"[mh] OR "Autotransplantation" OR "Autotransplantations" OR "Autografting" OR "Autograftings" OR "Autologous Transplantation" OR "Autologous Transplantations" OR "Transplantations, Autologous" OR "Transplantation, Heterologous"[mh] OR "Heterografting" OR "Xenotransplantation" OR "Xenograft Transplantation" OR "Transplantation, Xenograft" OR "Xenografting" OR "Heterograft Transplantation" OR "Transplantation, Heterograft" OR "Heterologous Transplantation" OR "Demineralized Bone Matrix" OR "Bone Morphogenetic Proteins"[mh] OR "Morphogenetic Proteins, Bone" OR "Bone Morphogenetic Protein" OR "Morphogenetic Protein, Bone" OR "Biocompatible Materials"[mh] OR "Materials, Biocompatible" OR "Biomaterials" OR "Hemocompatible Materials" OR "Materials, Hemocompatible" OR "Osteogenic Materials" OR "Interpositional Graft")).

For Embase, the PICO search strategy was employed, with the following Emtree terms and their synonyms: "dentofacial deformity", "maxilla", "Le Fort osteotomy", "orthognathic surgery", "bone transplantation", "bone graft",

“hydroxyapatite”, “biomaterial”, “calcium phosphate”, “bone morphogenetic protein”. The specific search query was the following:

[(‘dentofacial deformity’/exp OR 'dentofacial deformities' OR 'dentofacial deformity' OR 'dentofacial malformition’ OR ’maxilla’/exp OR ‘jaw, upper’ OR 'maxilla’ OR ’maxillary’ OR 'maxillofacial skeleton’ OR ’upper jaw') AND (‘le fort osteotomy’/exp OR 'le fort maxillary osteotomy’ OR 'le fort osteotomy' OR ’lefort osteotomy' OR ’maxillary osteotomy le fort' OR 'osteotomy le fort' OR 'osteotomy lefort' OR 'osteotomy, le fort' OR 'orthognathic surgery'/exp) AND ('bone transplantation'/exp OR 'bone grafting' OR 'bone reimplantation' OR 'bone transplantation' OR 'transplantation, bone' OR 'bone graft'/exp OR 'autograft, bone' OR 'autograft, spongy bone' OR 'autologous bone graft' OR 'bone autograft' OR 'bone flap' OR 'bone flaps' OR 'bone graft' OR 'bone grafts' OR 'bone transplant' OR 'compact bone autograft' OR 'free bone graft' OR 'graft, bone' OR 'osseous flap' OR 'osseous flaps' OR 'osseous graft' OR 'osseous grafts' OR 'osteoarticular graft' OR 'rib autograft' OR 'spongy bone autograft' OR 'viable bone graft' OR 'bone substitutes' OR 'hydroxyapatite'/exp OR 'algipore' OR 'alveoform' OR 'alveograf' OR 'calcitite' OR 'calcium hydroxyapatite' OR 'calcium hydroxylapatite' OR 'calcium phosphate hydroxide' OR 'decacalcium dihydroxide hexakis (orthophosphate)' OR 'durapatite' OR 'hydroxy apatite' OR 'hydroxyapatite' OR 'hydroxyapatites' OR 'hydroxyl apatite' OR 'hydroxylapatite' OR 'osteograf' OR 'ostim' OR 'periograf' OR 'biomaterial'/exp OR 'biocompatible materials' OR 'biologic material' OR 'biological material' OR 'biomaterial' OR 'calcium phosphate'/exp OR 'basic tricalcium phosphate' OR 'beta tricalcium phosphate' OR 'ca phosphate' OR 'calcium orthophosphate' OR 'calcium phosphate' OR 'calcium phosphate tribasic' OR 'calcium phosphates' OR 'neutral calcium phosphate' OR 'phosphate, calcium' OR 'tribasic calcium phosphate' OR 'tricalcium phosphate' OR 'triple phosphate' OR 'ca orthophosphate' OR 'bone morphogenetic protein'/exp OR 'bone morphogenetic protein' OR 'bone morphogenetic proteins' OR 'bone morphogenic protein')].

The Cochrane Library search strategy was based on MeSH terms: [(“Dentofacial Deformities” OR “Maxilla” AND “Orthognathic Surgery” OR “Osteotomy. Le Fort” OR “Maxillary Osteotomy” AND “Bone Substitutes” OR “Bone Matrix” OR “Hydroxyapatites” OR “Calcium Phosphates”)].

In addition, a secondary search (grey literature) and hand-search were conducted. With regard to the grey literature search, an effort to identify potentially relevant unpublished, articles published in non-indexed journals or ongoing trials was made by wide-ranging searching of Google Scholar, Open Gray, and clinical trials registry (http://clinicaltrials.gov/).

After the main search and secondary search were completed, a detailed hand-search of the references of the eligible articles was conducted for additional relevant papers.

Study Selection

The systematic literature search was performed by one author (MFSM), while studies were selected independently by two authors (MFSM and ASAM) based on titles and abstracts. Studies that met the following criteria were selected for full-text reading. The inclusion criteria were: (1) intervention and/or observational study; (2) studies performed in adults, non-growing, non-syndromic and without pain or pathology in the temporomandibular joint; (3) includes analysis of stability and/or complications after maxillary osteotomy Le Fort I associated with the use of bone graft substitutes in osteotomy gaps; (4) studies with at least 6 months of follow-up. The exclusion criteria were: (1)

edentulous patients; (2) letters and review articles; (3) case report; (4) cleft lip and palate; (5) segmental Le Fort I osteotomy.

Articles for which the title and abstract were evaluated and accepted in the first round of the selection process were screened for eligibility. Articles that did not meet all of these prerequisites were excluded. In the case of disagreement between the authors, the study was selected for full-text reading and was resolved by consensus between the two observers.

The kappa statistic (κ) was used to measure inter-rater agreement for title and abstract selection between MFSM and ASAM. According to Landis and Koch,[38] the level of inter-observer agreement is very good if the value of κ is 0.81–1.00, good if κ is 0.61–0.80, moderate if κ is 0.41–0.60, fair if κ is 0.21–0.40, and poor if is < 0.20.

Study eligibility

The same two authors performed the eligibility assessment independently, applying the inclusion criteria separately. To facilitate and maintain consistency in the analysis of articles after full-text reading, a standardized form was created and used to check studies against the following inclusion criteria: (1) the research topic is Le Fort I osteotomy associated with bone graft substitutes; (2) the study reports data on long-term stability (≥ 6 months) and/or postoperative complications after this type of technique; (3) the article reports an original study.

Any disagreement or doubt between two independent authors regarding the eligibility of the study was resolved by discussion with a more experience

author (RBO). Publications that did not meet the eligibility criteria were excluded from further analysis and the reason for exclusion was recorded. Studies meeting the eligibility criteria were undergone to data extraction and quality assessment. To avoid bias through duplicate publications, special attention was paid to identifying multiple reports from the same study. No language restriction was applied.

Again, the kappa statistic (k) was used to evaluate the level of agreement between the first two investigators.

Data extraction

Standardized data extraction tables were created to collect and organize the information from the eligible studies. The same two authors (MFSM and ASAM) independently extracted demographic and methodological data, and data on stability outcomes and/or postoperative complications involving maxillary osteotomy Le Fort I and use of bone graft substitutes in the osseous gaps (Table 1 and 2). In the event of disagreement, the article was discussed with a third author (RBO); if doubts persisted or in case of inability to extract all necessary information, efforts were made to contact the authors for clarification.

Analysis of surgical stability

Stability of the surgical procedure was assessed using the mean and standard deviation (SD) of dental and/or skeletal recurrence in the anterior and posterior segments of the maxilla, between the immediate postoperative period (mean surgical changes – T1) and the moment of the last follow-up (mean stability changes – T2) of at least 6 months post-surgery. Results were

expressed in millimeters (mm). Surgical movement in the sagittal and vertical planes was take into account. Additional data (eg, surgical movement in the transverse plane) regarding procedures such segmental osteotomy Le Fort I or modified techniques for maxillary osteotomy were removal or reshaping when also recorded.

Analysis of postoperative complications

The following complications were assessed: signs and symptoms of infection, maxillary sinusitis, hematoma formation, wound dehiscence, changes in the overlying soft tissues, difficult handling properties, instability of the implant with resorption and/or poor healing at the osteotomy gap (non-union), relapse, and increased pain and morbity of the grafted site. The prevalence of each complication was assessed in relation to the sample reported by the authors.

Methodological quality assessment and risk of bias

The methodological quality of the selected publications was assessed independently by two revisers (MFSM and ASAM) using an adaptation of the bias analysis for small intervention proposed by Clementini et al[39]. The criteria used were sample selection, comparison of intervention effects, blinding of outcome assessors, validation of measures, statistical analysis, definition of inclusion and exclusion criteria, and postoperative follow-up. Studies were classified as having a low risk of bias if all items were present, as having a medium risk of bias if one or two items were missing, and as having a high risk of bias if three or more items were missing (Table 3).

Results

The protocol of this systematic review is summarized in the PRISMA flow diagram (Figure 1), giving an overview of the selection process.

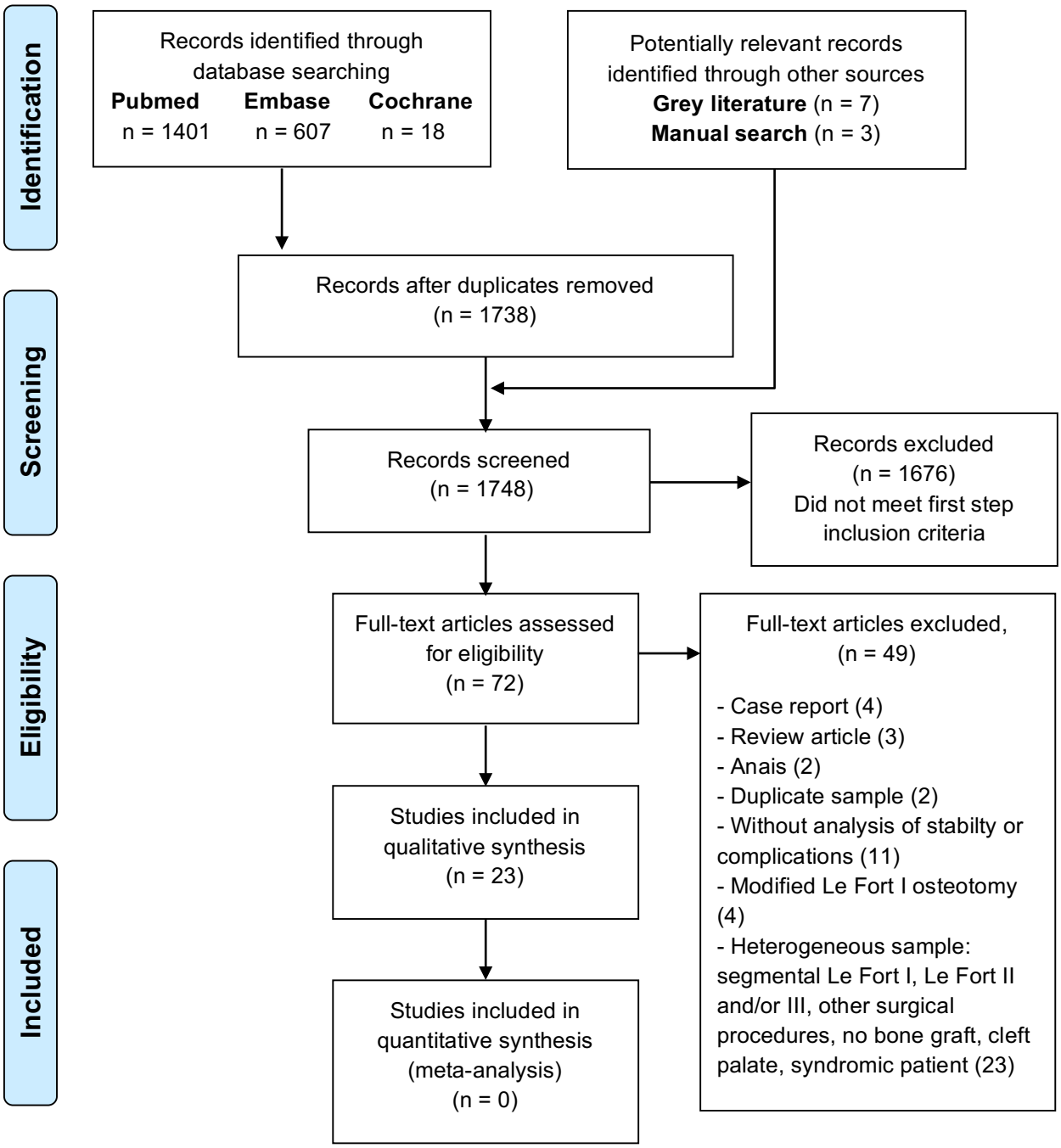

Figure 1. Flowchart of the methodological search and study selection process.

Search strategy

A total of 1738 studies were identified (Pubmed, *n* = 1401; Embase, *n* = 607; Cochrane Library, *n* = 18), with overlap among databases. The grey literature search and hand-search of the references revealed ten[4,27,35,36,40-45] additional articles, but only three[35,36,42] of them were included in this systematic review.

Study Selection

The titles and abstracts of the 1748 retrieved articles were read independently by two authors (MFSM and ASAM) with an excellent level of inter-rater agreement coefficient (κ = 0.891, 95% confidence interval 0.809-0.953). After eliminating duplicate records and those with non-relevant titles and abstracts, 1676 studies were excluded and 72 studies were selected for eligibility.

Study eligibility

The same two authors independently evaluated the full texts of 72 articles (62 selected from the main search strategy, 7 from the grey literature and 3 from the hand-search). After this step, 23 articles met the inclusion criteria and were included in this review: 20[6,18,19,21,22,24,25,28,29,32,46-55] from the main search, 3[35,36,42] from the grey literature and 0 from manual search. The remaining 49 articles (42 from the main search, 4 from the grey literature and 3 from manual search) were excluded for the following reasons: 4 studies were case report[3,40,56,57]; 3 studies were review article[4,27,44]; 2 studies were

ANAIS[58,59]; 2 studies presented duplicate sample[30,60]; 11 studies did not report an analysis of stability or complications after Le Fort I osteotomy one-piece with use bone graft substitute[7,8,41,61-68]; 4 studies performed only modified Le Fort I osteotomy in the sample[69-72]; and 23 studies presented heterogeneous sample (segmental Le Fort I, Le Fort II and/or III, other surgical procedures, no bone graft, cleft palate, and syndromic patient) for the same stability and/or complication analysis[9,11,13,14,20,34,43,45,73-87].

The level of inter-rater agreement was considered excellent with κ = 0.907 (95% confidence interval 0.8-1).

Data extraction

After the study inclusion process, 23[6,18,19,21,22,24,25,28,29,32,35,36,42,46-55] articles were selected for data extraction and qualitative synthesis. This information was standardized in the Tables 1, 2, and 3, referring respectively to demographic data/complications, analysis of surgical stability, and analysis of methodological quality.

A meta-analysis of the results was planned if individual studies provided the data required for analysis and if the heterogeneity of the included studies was low, what was not the case.

Table 1. Demographic data for the studies included.

Author, Year	Study Type	Sample[a]	Age (years) Mean ± SD (range)	Gender	Mono or bimaxillary surgery[b]	Non-rigid or rigid fixation[c]	Type of bone graft	Technique of bone graft	Site of bone graft	Stability and/or complications analysis
Araujo et al., 1978[19]	Clinical trial Retrospective	*N* = 21 *n* = 3	26 (17-41)	NR	M (NR) B (NR)	N (21)	Freeze-dried bone	IP	Pterigomaxillar	Stability: sagittal and vertical Complications: infection
Arpornmaeklong et al., 2003[46]	Clinical trial Retrospective	*N* = 26 *n* =11	22.3 (13-38) Total sample	M (8) F (18)	NR	N (0) R (26)	Iliac crest or local bone from maxilla	IP	Anterior and lateral bony walls	Stability: sagittal and vertical
Carlotti et al., 1987[47]	Clinical trial Retrospective	*N* = 30	NR	NR	M (18) B (12)	N (30)	Iliac crest	IP	NR	Stability: sagittal and vertical
Christian et al., 1982[36]	Case series	*N* = 12 *n* = 2	NR	NR	M (2)	NR	Frozen femoral head allogenic bone	NR	NR	Stability: sagittal and vertical Complications: none (*n* = 2)
Costa et al., 2005[48]	Case Series	*N* = 6	NR	NR	M (3) B (3)	N (0) R(6)	Medial ilium	IP	Lateral to the piriform area	Stability: vertical Complications: none
Egbert et al., 1995[49]	Clinical trial Retrospective	*N* = 25	Group A = 31 (20-49) Group B = 26 (20-34)	M (10) F(15)	M (25)	N (12) R (13)	Iliac crest	IP	Defects in the anterior and lateral sinus walls	Stability: sagittal and vertical
Eser et al., 2015[50]	Clinical trial Retrospective	*N* = 80	22.1 ± 4.1 (15-36)	M (25) F (55)	M (29) B (51)	N (0) R (80)	Heterologou Osteoplan-Flex (42) Autologous Iliac crest (38)	IP	NR	Stability: sagittal and vertical Complications: none
Kent et al., 1986[35]	Case series	*N* = 98 *n* = 29	NR	NR	NR	N (66) R (0)	HA block alone or with autogenous iliac crest	IP	Maxillary lateral wall and pterygoid plate	Stability: sagittal and vertical Complications: HA block displacement (3) with postsurgical mobility + reintervention (1) Dehiscence over HA block (1)
Kerawala et al., 2001[18]	Clinical trial Retrospective	*N* = 112	26 (15-48)	M (45) F (67)	M (36) B (76)	N (0) R (112)	Iliac crest	IP	Lateral antral walls	Stability: sagittal and vertical Complications: scar spread of donor site (3)

Table 1 (*Continued*)

Author, Year	Study Type	Sample[a]	Age (years) Mean ± SD (range)	Gender	Mono or bimaxillary surgery[b]	Non-rigid or rigid fixation[c]	Type of bone graft	Technique of bone graft	Site of bone graft	Stability and/or complications analysis
Kuvat et al., 2009[6]	Case Series	*N* = 10	21.7	M (4) F (6)	B (10)	N (0) R (10)	DBM + Bovine bone collagen-protein extracts (Colloss)	IP	Anterior maxillary wall	Stability: sagittal and vertical Complications: none
Lee JY et., 2015[51]	Clinical trial Retrospective	*N* = 15	22.2	M (7) F (8)	B (15)	N (0) R (15)	Maxilla Propeller graft of reduction side	IP	Augmentation canting through Le Fort I osteotomy	Stability: sagittal vertical and transverse
Lye et al., 2008[25]	Clinical trial Retrospective	*N* = 113 *n* = 65	33.11 (17-73)	M (57) F (56) Total sample	NR	N (0) R (113)	DBM with variables (cadaveric tibial bone, collagen membranes, iliac or mandibular bone)	IP	Anterior maxilla	Complications: Maxillary sinusitis (2); infection (2)
Marx et al., 1981[52]	Case series	*N* = 36 *n* = 3	(18-19)	M (2) F (1)	M (3)	NR	Freeze-dried bone allograft (corticocancelous ilium)	NR	Pterigoid-maxillary area; lateral wall maxilla	Complications: none
Mayrink et al., 2014[42]	Case series	*N* = 8	NR	M (5) F (3)	M (3) B (5)	N (0) R (8)	Calcium phosphate cement	IP	NR	Stability: sagittal Complications: none
Naros et al., 2019[24]	Clinical trial Prospective	*N* = 25	26.1 ± 9.7 (17-55)	M (12) F (14)	NR	N (0) R (25)	Anterior iliac crest (8) Bovine bone substitute (Bio-oss®) (17)	Iliac crest IP = 8 Bio-oss® IP = 12 Onlay = 5	NR	Stability: sagittal and maxillary inclination Complications: late pseudarthrosis and abscess (1 - Bio-oss IP)
Persson et al., 1986[29]	Clinical trial Retrospective	*N* = 16	24.8 (17-41)	M (11) F (5)	M (9) B (7)	N (0) R (16)	Cancellous iliac bone strips	Onlay	Along the osteotomy sites	Stability: sagittal and vertical Complications: Sinusitis (1)

Table 1 (*Continued*)

Author, Year	Study Type	Sample[a]	Age (years) Mean ± SD (range)	Gender	Mono or bimaxillary surgery[b]	Non-rigid or rigid fixation[c]	Type of bone graft	Technique of bone graft	Site of bone graft	Stability and/or complications analysis
Posnick et al., 2015[28]	Case Series	*N* = 50 *n* = 17	32 (15-60)	M (11) F (6)	B (17)	N (0) R (50)	Freeze-dried Allogenic corticocancelllous (iliac)	IP	Between the pyriform rim and zygomatic buttress	Complications: none
Quejada et al., 1987[53]	Case series	*N* = 10	21 (15-32)	M (4) F (6)	M (6) B (4)	N (10) R (0)	Autogenous	IP	NR	Stability: vertical
Ragaey et al., 2017[21]	Clinical trial Retrospective	*N*= 438 *n* = 71	NR	NR	NR	N (0) R (438)	B-tricalcium phosphate	IP	NR	Complications: Delayed union /no union (1)
Rosen et al., 1990[54]	Case Series	*N* = 9	20.9 (15 – 44)	M (2) F (7)	M (5) B (4)	N (0) R (9)	Porous HA block (Interpore-200)	IP	anterolateral maxilla	Stability: vertical Complications: none
Rosen et al., 1991[55]	Case Series	*N* = 76 *n* = 28	25 (14–58) Total sample	M (31) F (45) Total sample	NR	R	Porous HA block (Interpore-200)	IP	Anterolateral maxilla and lateral nasal wall; Zygomatic tuberosity	Stability: sagittal and vertical Complications: none (28)
Ueki et al., 2013[32]	Clinical trial Retrospective	*N* = 45 *n* = 23	25.5 ± 7.6 (16-48) Total sample	M (18); F (27) Total sample	B (45)	N (0) R (45)	α-tricalcium phosphate (Biopex®)	IP	Anterior and lateral maxilla	Stability: sagittal and vertical Complications: none
Waite et al., 1996[22]	Clinical trial Retrospective	*N* = 22 *n* = 11	43 (32-54)	M (19) F (3)	B (22)	N (0) R (22)	Genial bone	IP	Maxillary lateral wall	Stability: sagittal and vertical

DBM, human demineralized bone matrix; F, female; HA, hidroxiapatite; IP, interpositional graft; M, male; NR, not reported by the authors.

[a] Total sample (*N*), Le Fort I osteotomy with bone graft sample (*n*).

[b] Monomaxillary surgical procedure (M), bimaxillary surgical procedure (B).

[c] Non-rigid fixation (N), rigid fixation (R).

Table 2. Analysis of the studies reporting stability as the outcome.[a]

Author, Year	Method of Analysis	Follow-up (months)	Sagittal[b] Mean (SD), mm				Vertical[b] Mean (SD), mm			
			Anterior maxilla		Posterior maxilla		Anterior maxilla		Posterior maxilla	
			T1	T2	T1	T2	T1	T2	T1	T2
Araujo et al., 1978[19]	CR	31	S: 6	S[1]: -1.8 S[2]: -1.4 D: 0,7	NR	S: NR D: -0.3	NR	S[1]: -2 S[2]: -0,4 D: 0,9	NR	S[3]: -0.5 D: 0.1
Arpornmaeklong et al., 2003[46]	CR	25.7 (12 - 84) Total Sample	S[1]: 5.9 (1.4) S[2]: 6.1 (1.3) D: 4.0 (2.1)	S[1]: -1.1 (0.8) S[2]: -1.0 (1.8) D: 0.5 (0.8)	S[3]: 6.2 (1.4) D: NR	S[3]: -1.3 (1.4) D: NR	S[1]: -2.9 (3.5) S[2]: -3.3 (3.8) D: -3.1 (3.9)	S[1]: 1.2 (1.2) S[2]: 1.2 (0.8) D: 1.2 (1.5)	S[3]: 0.1 (0.6) D: NR	S[3]: 0.4 (0.9) D: NR
Carlotti et al., 1987[47]	CR	15.4 (5 - 28)	S: 7.4 (3 - 11)	S[1]: -0.5 D: -0.2	NR	NR	NR	S[1]: -0.1 D: -0.1	NR	NR
Christian et al., 1982[36]	CR	18 and 38 (n = 2)	S[2]: 8	S: No relapse	NR	NR	S[2]: 7	S[2]: -2	NR	NR
Costa et al., 2005[48]	CR	12	NR	NR	NR	NR	S[1]: 5.0 (1.44) S[2]: 5.66 (1.36) D: NR	S[1]: -0.16 (1.63) S[2]: -0.41 (1.56) D: NR	S[3]: 0.33 (1.25) D: NR	S[3]: 0.08 (1.11) D: NR
Egbert et al., 1995[49,c]	CR	≥ 12	S[2]: 8.7 (1.8)[1] S[2]: 6.9 (2.7)[2] D: NR	S[2]: -1.2 (0.88)[1] S[2]: -0.4 (0.7)[2] D: NR	NR	NR	S[2]: -0.1 (2.1)[1] S[2]: -1.4 (2.4)[2] D: NR	S[2]: -0.9 (1.3)[1] S[2]: 0.2 (1.0)[2] D: NR	NR	NR
Eser et al., 2015[50,d]	CR	12	S[1]: 4.8 (4.6)[1] S[1]: 4.1 (4.1)[2] D: NR	S[1]: -0.4 (0.6)[1] S[1]: -0.4 (0.6)[2] D: NR	NR	NR	S[1]: 3.8[1] S[1]: 3.0[2] D: NR	S[1]: -0.4[1] S[1]: -0.5[2] D: NR	NR	NR
Kent et al., 1986[35]	CR	14.2 (6 - 33)	5.5 (4 - 8)	< 20%	NR	NR	5.5 (3 - 9)	< 20%	NR	NR
Kerawala et al., 2001[18]	CR	≥ 12	S: 3.8 (2.1) D: NR	S: -0.1 (0.4) D: NR	S: 4.3 (2.1) D: NR	S: -0.1 (0.4) D: NR	S: 3.9 (1.5) D: NR	S: -0.2 (0.3) D: NR	S: 4.6 (1.6) D: NR	S: -0.1 (0.2) D: NR
Kuvat et al., 2009[6]	CR	14.5	S[1]: 5.7 D: NR	S: 0 D: NR	NR	NR	S[2]: -1.8 D: NR	S[2]: 0 D: NR	S[3]: -2.3 D: NR	S[3]: 0 D: NR
Lee JY et., 2015[51]	CBCT	6	S[4]: 0.57 (2.28) D: -0.52 (1.90)	S[4]: 0.18 (0.95) D: 0.36 (1.62)	S[3]: 0.51 (1.23) D: -0.59 (3.10)	S[3]: 0.41 (1.89) D: -0.61 (1.28)	S[4]: 0.52 (2.72) D: 2.27 (1.71)	S[4]: -0.66 (2.35) D: -0.66 (3.01)	S[3]: 0.28 (1.94) D: 1.83 (3.75)	S[3]: -0.49 (2.58) D: -1.25 (2.78)
Mayrink et al., 2014[42]	CR	≥ 6	S: 6.25 ± 2.43	S[5]: -2.73 S[1]: -3.44	NR	NR	NR	NR	NR	NR
Naros et al., 2019[24,e]	CR	≥ 6 (5.7 - 11.6)	S[1]: 3.58 (1.22)[1] S[1]: 4.7 (3.47)[2] S[1]: 2.35 (1.15)[3]	S[1]: - 0.73 (0.37) 20.5%[1] S[1]:- 1.43 (0.96) 30.3%[2] S[1]: - 0.78 (0.59) 33%[3]	NR	NR	NR	NR	NR	NR

Table 2 (*Continued*)[a]

Author, Year	Method of Analysis	Follow-up (months)	Sagittal[b] Mean (SD), mm				Vertical[b] Mean (SD), mm			
			Anterior maxilla		Posterior maxilla		Anterior maxilla		Posterior maxilla	
			T1	T2	T1	T2	T1	T2	T1	T2
Persson et al., 1986[29]	CR	6	S[1]: 2.3 (2.31) D: 0.8 (3.36)	S[1]: -0.1 (1.71) D: NR	NR	NR	S[2]: 7.1 (2.83) D: 6.6 (3.20)	S: NR D: -1.5 (1.69)	S[3]: 0.6 (2.93) D: NR	S[3]: -0.0 (0.78) D: NR
Quejada et al., 1987[53]	CR	12	S[1]: 1.3 D: NR	S[1]: NR D: NR	NR	NR	S: NR D: 8.9 (2.2)	S: NR D: -2 (1.2)	S[3]: 0.7	S[3]: NR
Rosen et al., 1990[54]	CR	19.6 (11 - 28)	NR	NR	NR	NR	S[2]: 6.2 (4.9 - 7.5)	S[2]: ≅ -0,5 (4.3%)	NR	NR
Rosen et al., 1991[55]	CR	16.3 (6 - 46)	S: 9.2 (8 -13)	S: ≤ -1	NR	NR	S: 6.5 (4.5 -7.5)	S: ≤ -0.5 (4.5%)	NR	NR
Ueki et al., 2013[32,f]	CR	12	S[1]: -1.0 (1.6)[1] S[2]: 0.2 (2.0)[1] D: -1.0 (3.3)[1] S[1]: 3.7 (2.9)[2] S[2]: 3.4 (2.7)[2] D: 4.4 (4.7)[2]	S[1]: 0.8[1] S[2]: 0.3[1] D: -0.4[1] S[1]: -0.5[2] S[2]: -0.7[2] D: -0.9[2]	S[3]: -1.0 (2.1)[1] S[3]: 2.8 (3.2)[2] D: NR	S[3]: 0.8[1] S[3]: 1.2[2] D: NR	S[1]: 0.3 (3.1)[1] S[2]: 0.7 (2.7)[1] D: 1.1 (1.2)[1] S[1]: -0.5 (3.5)[2] S[2]: -0.3 (3.1)[2] D: 0.4 (1.2)[2]	S[1]: -0.3[1] S[2]: -1.0[1] D: -0.2[1] S[1]: -0.5[2] S[2]: -0.6[2] D: 0.1[2]	S[3]: -1.8 (2.4)[1] S[3]: -0.9 (1.4)[2] D: NR	S[3]: -0.2[1] S[3]: 0.3[2] D: NR
Waite et al., 1996[22]	CR	10.5 (≥ 6)	S[1]: 9.9 (3.7) S[2]: 10.7 (3.7) D: 9.7 (3.3)	S[1]: -0.8 (0.8) S[2]: -0.7 (0.6) D: -0.7 (0.6)	S[3]: 9.1 (2.8) D: NR	S[3]: -0.7 (0.7) D: NR	S: NR D: 0.5 (1.8)	S: NR D: -0.1 (0.8)	NR	NR

CBCT, cone beam computed tomography; CR, cephalometric radiographs; D, stability analysis by dental measurement; NR, not reported by the authors; S, stability analysis by skeletal measurement; SD, standard deviation.

[a] T1 = mean surgical changes; T2 = mean stability changes. Sagittal: (-) retrusion/(no sign) protrusion. Vertical: (-) intrusion/(no sign) extrusion.

[b] Landmark: 1 = measurements at A-Point; 2 = measurements at Anterior Nasal Spine (ANS); 3 = measurements at Posterior Nasal Spine (PNS); 4 = measurements at Nasopalatine canal; 5 = distance Condilion (Co) to A-Point.

[c] 1 = group treated with combined wire fixation; 2 = group treat with rigid internal fixation.

[d] 1 = group with use of heterologous bone grafts; 2 = group with use of autologous bone grafts.

[e] 1 = group receiving interpositional xenogenic bovine bone grafting (Bio-Oss®); 2 = group receiving Bio-Oss® in onlay position; 3 = group receiving interpositional autogenous iliac crest bone grafting.

[f] 1 = maxillary impaction cases with Biopex®; 2 = maxillary advancement cases with Biopex®.

Demographic data

The data are summarized in Table 1. With regard to the study design, these were essentially retrospective studies (only one used a randomized prospective design[24]) and had been published in the period of 1978 to 2019.

A total of 601 patients underwent one-piece Le Fort I osteotomy with the use of bone graft substitutes was included in this review. The most patients were male (59,2%), and mean age ranged from 18,5 to 43 years. Orthognathic surgeries were mostly bimaxillary[6,22,28,32,51] (*n* = 271) and employed rigid internal fixation[6,18,21,22,24,25,28,29,32,42,46,48,50,51,54,55] (*n* = 520).

Autogenous bone (*n* = 282) was the most commonly used grafting substitute, of which the iliac crest was the main donor site[18,24,29,46-49]. The second most commonly bone substitute was alloplastic grafts (*n* = 97)[21,32,35,42,54,55], followed by allogeneic graft (*n* = 77)[19,25,28,36,52], xenogeneic graft (*n* = 59)[24,50], and graft association(*n* = 10)[6]. The technique of bone grafting was essentially interpositional, with only two studies reporting employment of onlay graft[24,29].

Analysis of postoperative complications

The prevalence of each post-surgical complication was assessed in relation to the sample reported by the authors and the recorded complications regarding bone grafting in one-piece Le Fort I osteotomy sites were infection (3%)[19,25], scar spread of donor site (*2.7*%)[18], sinusitis (3.7%)[25,29], late abscess and pseudarthrosis (4%)[24], delayed union/non union (1.4%)[21], hydroxylapatite block displacement (10%)[35] with postoperative mobility and reintervention (*3.4*%)[35], dehiscence of the mucosa over HA block (3.4%)[35].

Allogeneic grafts (6.1%)[19,25], followed by alloplastic bone substitutes (5%)[21,35], were the graft materials that presented more postoperative complications, while autogenous grafts (2.3%)[18,29] presented a lower prevalence of complications, followed by xenogeneic grafts (4%)[24]. Others ten studies[6,28,32,36,42,48,50,52,54,55] also evaluated postoperative complications, however none complication was identified in their samples (*n* = 186).

Analysis of Surgical Stability

Data refer to Table 2. A total of 445 patients (75% of the overall sample included in the systematic review) who underwent one-piece Le Fort I osteotomy with use of bone grafting in the gaps were included in this stability analysis[6,18,19,22,24,29,32,35,36,42,46-51,53-55.]

Essentially, the method used for analysis of post-surgical stability was by means of superimposition of cephalometric radiographs with an average of 14.4 months follow-up (ranging 6 to 31 months)[6,18,19,22,24,29,32,35,36,42,46-50,53-55]. Only the study of Lee et al.[51] compared the pre- and post-operative outcomes using cone beam computed tomographic (CBCT) through superimposition and 3-dimensional analysis (x, y, z coordinate system), using skeletal landmarks.
The surgical change (T1), and stability/relapse (T2) for the surgical movements are shown in table 2. Only sagittal and vertical analysis were included this review.

Sagittal and vertical stability

The majority of the studies evaluated post-surgical stability in both sagittal and vertical planes as an outcome

measure[6,18,19,22,29,32,35,36,46,47,49,51,53,55]. Three studies evaluated post-surgical movement only in the vertical plane[42,48,54] and one study assessed the surgical movement in the sagittal plane[24].

According to the type of graft used, the sagittal stability varied from -0.1[18,29] to -1.2 ± 0.88 mm[49] for cases grafted with autogenous bone, from -0.7[32] to -3.44 mm[42] for alloplastic graft, from 0[36] to -1.8 mm[19], from -0.4 ± 0.6[50] to -1.43 ± 0.96 mm[24] for xenogeneic bone substitutes, and for association grafts only the study of Kuvat et al.[6] was considered, presenting a recurrence of 0 mm. In relation to vertical stability, the recurrence ranged from -0.16 ± 1.63[48] to -2 ± 1.2 mm[53] for autogenous grafts, from approximately -0.5[54,55] to -1.2 mm[35] for alloplastic grafts, and for allogeneic and xenogeneic grafts, only the studies of Chrintian et al. and Eser et al., respectively, were founded, showing a relapse of -2 mm[36] and -0.4 mm[50].

Based on literature[21,26], the studies of this review were categorized according to skeletal maxillary surgical movements: (1) advancement – minor (<5 mm), medium (5-8 mm), and major (> 8 mm); and (2) inferior repositioning – measure < 3 mm and measure ≥ 3 mm. Six studies presented minor mean maxillary advancement[18,24,29,32,50,51], eight were classified in the medium category[6,19,35,36,42,46,47,49], and in three studies the maxilla was advancement more than 8 mm[22,49,55].

In patients undergoing mean maxillary advancement < 5 mm, the skeletal recurrence (T2) ranged from -0.1 ± 0.4 mm[(18)] to -1.43 ± 0.96 mm[24]. For advancement between 5 mm and 8 mm, the relapse ranged from 0 mm[6,36] to -3.44 mm[42]. For major advancements (> 8 mm), the recurrence ranged from -0.7 ± 0.6 mm[22] to -1.2 ± 0.88 mm[49]. The categorization was based on the

alterations measured by the skeletal reference points, since the dental points may undergo modifications coming from the orthodontic treatment besides the relapse. Analyzing the scatterplot (Figure 2) that correlates the mean magnitude of maxillary advancement and postoperative recurrence reported in the articles included in this review, there was no correlation trend between the two variables. According to the determination coefficient (r^2), 9.14% of the relapse is influenced by the magnitude of the advancement in this sample.

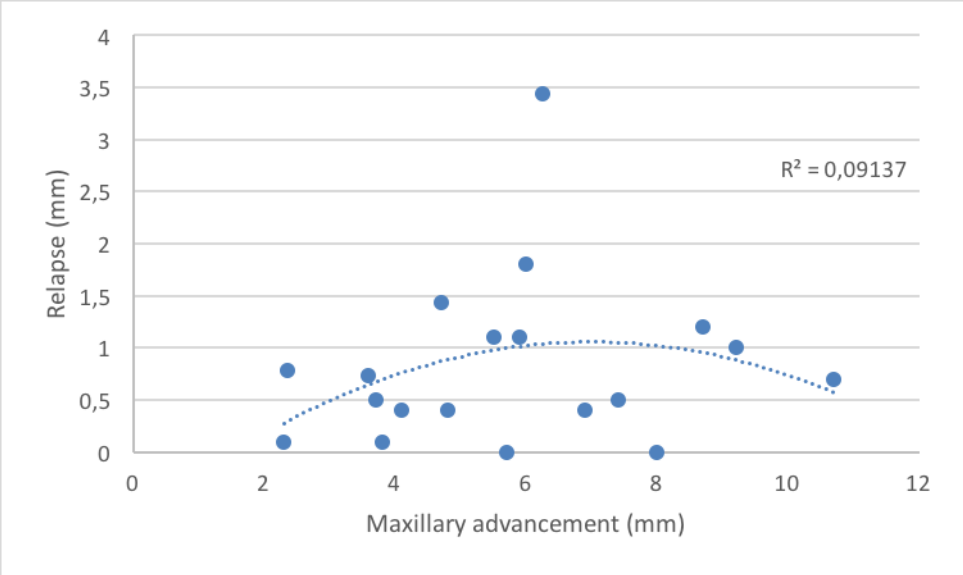

Figure 2. Scatterplot relating the variable magnitude of the maxillary advancement and the recurrence presented in the articles included in the systematic review.

Regarding inferior repositioning, the anterior maxilla was downgrafted ≥ 3 mm in nine studies[18,29,35,36,48,50,53-55]. The relapse for this vertical surgical movement ranged from -0.16 ± 1.63 mm[48] to -2 mm[36,53]. Inferior repositioning < 3 mm was related in the study of Lee et al[51] due to canting correction in facial

asymmetry. The dental landmark (upper canines) was downgrafted in the augmentation side 2.27 ± 1.71 mm, and relapsed -0.66 ± 3.01 mm.

Stratifying the sample according to the type of fixation, sagittal recurrence ranged from 0[6] to -3.44 mm[42] in cases where internal rigid fixation was employed, and from -0.5[47] to -1.8 mm[19] in cases of non-rigid fixation. In relation to orthognathic surgery type, if was a mono[36,49] or bimaxillary[6,22,32,51] procedure, the relapse in the sagittal plane ranged from 0[36] to -1.2 ± 0.88 mm[49] for surgeries involving only Le Fort I osteotomy, and from 0[(6)] to -0.8 ± 0.8 mm[22] for cases of bimaxillary surgeries. The majority of articles presented a sample with a combination of mono and bimaxillary procedures in the same evaluation[18,29,42,47,48,50,53,54].

Analysis of methodological quality

Data refer to Table 3. The risk of bias was considered high for all studies included in this systematic review. The main absent quality criteria was blind assessment, sample randomization and comparison between treatments.

In fact, none of included studies reported blind assessment. Two studies[35,52] had the highest risk – all criteria for methodological quality were ignored. Furthermore, due to the substantial heterogeneity of the included studies, it was no possible to perform a meta-analysis of the results.

Table 3. Quality assessment of included studies.

Study	Randomization or consecutive patients in a prospective study	Comparison between treatments[a]	Blind assessment	Validation of measurements	Statistical analysis	Defined inclusion and exclusion criteria	Report of follow-up (≥ 12 months)	Potencial Risk of bias[c]
Araujo et al., 1978[19]	No	Yes[a]	No	No	No	No	Yes	High
Arpornmaeklong et al., 2003[46]	No	No[b] opLeF vs. msLeF	No	Yes	Yes	Yes	Yes	High
Carlotti et al., 1987[47]	No	No	No	No	Yes	No	No	High
Christian et al., 1982[36]	No	No	No	No	No	No	Yes	High
Costa et al., 2005[48]	No	No	No	Yes	Yes	Yes	Yes	High
Egbert et al., 1995[49]	No	No[b] nRF vs. RF	No	Yes	Yes	Yes	Yes	High
Eser et al., 2015[50]	No	No[b] aBG vs. hBG	No	No	Yes	Yes	Yes	High
Kent et al., 1986[35]	No	No	No	No	No	No	No	High
Kerawala et al., 2001[18]	No	No	No	Yes	Yes	Yes	Yes	High
Kuvat et al., 2009[6]	No	No	No	No	Yes	No	Yes	High
Lee JY et., 2015[51]	No	No	No	Yes	Yes	Yes	No	High
Lye et al., 2008[25]	No	Yes[a]	No	No	No	Yes	No	High
Marx et al., 1981[52]	No	No	No	No	No	No	No	High
Mayrink et al.,2014[42]	No	No	No	Yes	Yes	Yes	No	High
Naros et al., 2019[24]	Yes	No[b] aBG vs. hBG	No	No	Yes	Yes	No	High
Persson et al., 1986[29]	No	No	No	No	Yes	Yes	No	High
Posnick et al.,2015[28]	No	No	No	No	No	Yes	Yes	High
Quejada et al., 1987[53]	No	No	No	No	Yes	No	Yes	High
Ragaey et al., 2017[21]	No	Yes[a]	No	No	Yes	Yes	No	High

Table 3 (*Continued*)

Study	Randomization or consecutive patients in a prospective study	Comparison between treatments[a]	Blind assessment	Validation of measurements	Statistical analysis	Defined inclusion and exclusion criteria	Report of follow-up (≥ 12 months)	Potencial Risk of bias
Rosen et al., 1990[54]	No	No	No	No	No	No	Yes	High
Rosen et al., 1991[55]	No	No	No	No	No	Yes	No	High
Ueki et al., 2013[32]	No	Yes[a]	No	Yes	Yes	No	Yes	High
Waite et al., 1996[22]	No	Yes[a]	No	No	Yes	Yes	No	High

aBG, autologous bone graft; hBG, heterologous bone graft; msLeF, multi-segmental Le Fort I osteotomy; nRF, non-rigid fixation; opLeF, one-piece Le Fort I: RF, rigid fixation.

[a] Comparison between different treatments modalities (control group vs. test group – controlled study).

[b] Comparison between different surgical techniques (test group vs. test group – comparative study).

[c] Risk of bias: high, 0–5 'yes' responses; medium, 6–7 'yes' responses; low, 8 'yes' responses.

Discussion

The stability and predictability of the one-piece Le Fort I osteotomy varies according to the direction and magnitude of the surgical movement, the type of fixation and the surgical technique used, if the gaps between bone segments are bone-grafted or not[18]. Regarding the use of bone graft substitutes in Le Fort I osteotomy, there are in the literature articles that describe and study such procedure with methodological variations, analyzing long-term stability and postoperative complications.

Thereby, there were two main reasons to conduct this systematic review. First, there is no standardized guideline that determines and quantifies the limit of maxillary surgical displacement that from it is necessary the use of graft to fill the gap created by Le Fort I osteotomy to provide and maintain the postoperative stability; second, to answer this question through the analysis of data from studies that evaluated the stability of this technique and/or its post-surgical complications as outcomes.

There is a previous systematic review[88] regarding about the use of bone grafts in orthognathic surgery, but it did not present in detail the results addressing the stability of the surgical segments (amount of movement and relapse) in the extraction of data from the primary studies. In addition, the current review probably presented a broader and more sensitive search, and without restriction to the foreign language, since nine included studies[24,29,46-49,52-54] are missing in the previous review, with only one[24] of them being published after its search period.

All of the 23 studies included in this systematic review were of low methodological quality, resulting in high potential risk of bias. Thus, the founded

clinical results must be interpreted with caution because of limited quality; nevertheless, the authors are confident that the evidence published on the issue is presented in this systematic review. Of these articles, only five[19,21,22,25,32] was considered a controlled study where a comparison between groups with and without bone grafts was performed, three[19,22,32] of which assessed surgical stability. Araujo et al.[19], and Waite et al.[22] reported that bone grafting was beneficial for postoperative stability, while Ueki et al.[32] showed no significant difference between the use of Biopex (self-setting a-tricalcium phosphate) and nothing else other than hydroxyapatite resorbable plates for fixation. In this last research[32], the maxilla was advanced 3.7 mm, and relapsed 0.5 mm in both situations after 1 year follow-up. In the study of Araujo et al.[19] the average maxillary advancement was 6 mm, and skeletal relapse was 1.4 mm for the group with allogeneic bone graft, and 3.5 mm for group without grafts. Waite et al.[22] analyzed radiographic data of patients with obstructive sleep apnea syndrome that underwent approximately 10 mm of maxillary advancement with rigid fixation. The mean recurrence was 0.7 mm in patients that received autogenous bone graft from the mandibular symphyseal area, and 1.8 mm in the control group, with a statistical significant difference.

These data corroborate the indication of grafting only in cases of large surgical displacements, since stability can be achieved, regardless of grafting, in small maxillary movements, as seen in the work of Ueki et al.[32] According to Araujo et al.[19], the routine use of pterygomaxillary bone grafts for stability after maxillary advancement is not indicated, and not needed when there is adequate surgical mobilization and passive repositioning, sufficient skeletal and maxillomandibular fixation, ideal postoperative occlusion, and movements less than 5 mm. They

conclude by reporting that if one or two of these factors cannot be achieved, bone grafts should be employed for postoperative stability.

Analyzing the total sample of this review, the maximum recurrence for maxillary advancement greater than 5 mm was 3.44 mm[42], despite the use of interpositional grafts in the osteotomy gaps. This happened in the Mayrink et al.[42] study, the only one in which the mean recurrence exceeded the clinically relevant change (> 2 mm)[2]. Changes of 2-4 mm is considered potentially clinically significant, and >4 mm is clinically highly significant[2]. As the authors[42] themselves report, this can be explained by erros in a specific cephalometric measure (use of Nperp, thas is influenced by another landmark, the Frankfurt Horizontal Plane), since other landmarks did not express such a sagittal recurrence in the same sample. In all the others 149 patients, mean relapse not exceed 1.8 mm, showing the good performance of bone substitutes in relation to Le Fort I osteotomy stability.

Contradicting the above, Hoffman and Brennan[89] stated that degree of advancement, as well as other uncontrollable variables like patients age, sex, and simultaneous mandibular procedures, had no effect on postoperative skeletal stability. Also, Bhatia et al.[5] suggested no direct correlation between degree of advancement and relapse using rigid fixation without bone grafting. No correlation was found between magnitude of maxillary advancement and relapse when the data obtained in this review were evaluated, perhaps because of the heterogeneity of the studies, since there were differences in the type of fixation for example, or even because the use of bone substitutes in the osteotomy gaps reduced the rate of relapse in large maxillary advances. For Dowling et al.[90], one-piece Le Fort I advancement is relatively a stable surgery, however suggested that higher

advancements is a factors that can augment the relapse possibilities. An explanation for this is in the work of Waite et al.[22]; they affirmed that in large advancements there is usually minimal bone contact at the lateral wall of the maxilla. In their experience of large advancements with only rigid fixation, nonunion occurred due to fibrous tissue ingrowth into the maxillary gaps, resulting in malocclusion and relapse.

With this lack of consensus, some studies have associated the amount of maxillary advancement with the need of grafting[6,19,22,49,60,91], while other researches did not perform grafting in gap osteotomy and had a minimal skeletal relapse[5,89,90].

Taking into account that maxillary inferior repositioning is the most unstable and problematic surgical procedure[1,2], a published systematic review[26] on this topic suggests the use of bony fragments gathered and mixed with tissue glue to fill osteotomy gap in movements less than 2-3 mm, and grafting with solid bony or hidroxyapatite blocks for downgrafting that extends more than 3 mm. In the current review, studies that presented inferior repositioning of the anterior maxilla $\geq$ 3 mm showed a relapse rate for this vertical surgical movement ranged from -0.16 $\pm$ 1.63 mm[48] to -2 mm[36,53], finding a directly proportional relationship between magnitude of repositioning and recurrence. Relapse of maxillary downward movement with non-rigid fixation and no bone grafting of up to 100% has been reported in the literature[92]. In contrast, Convens et al.[26] reported relapse rates of between 0% and 35% with the use of bone grafts in some situations. Major et al.[14] confirmed that autogenous bone grafting with rigid internal fixation minimizes relapse after inferior repositioning. Proffit et al.[45] demonstrated that rigid fixation has improved stability in the horizontal plane but cannot prevent relapse in the vertical plane; for this reason, they advocated the use of interpositional bone grafts to enhance skeletal stability. It

was founded that the literature remains with pre-established surgical concepts that is necessary rigid internal fixation and bone grafting to minimize the relapse in cases of maxillary downward movement.

Another important issue is the need for rigid fixation, which appears to be the primary determinant of skeletal stability[10,26] since it overcomes the weaknesses of wire fixation. The study of Egbert et al.[49] compared the non-rigid versus rigid fixation, showing more stable results for the second group. The mean percent postsurgical change at 1 year for non-rigid fixation group was 14% and for rigid fixation group was 6%. Relapse in the posterior direction > 2 mm was observed in three patients, all from the non-rigid fixation group. The superiority of rigid internal fixation is already well understood in the literature, so that orthognathic surgeries are currently performed almost exclusively with this type of fixation, regardless of the use of bone grafts. With the exception of the work[49] described above, the most recent studies included in this review reporting the use of non-rigid fixation were published in 1987[47,53].

Postoperative complications were also analyzed in this systematic review. Seventeen studies that evaluated this outcome with a total sample of 507 patients were summarized[6,18,19,21,24,25,28,29,32,35,36,42,48,50,52,54,55]. Overall, only 14 patients (2.77%) were affected by some complication[18,21,24,25,29,35,36]. The most frequent occurrences of postoperative complications in this sample were HA block displacement (n = 3)[35], scar spread of donor site (n = 3)[18] and sinusitis (n = 3)[18,29]. Alloplastic[21,24,35] and allogeneic[19,25] bone substitutes were the grafts most associated with complications. Others studies[13,20,30,43,75,88,93] have also shown a higher

prevalence of post-surgical complications in orthognathic surgery with the use of porous HA, such as infections, sinusitis, exposure, and chronic inflammation.

Regarding to freeze-dried allografts, articles[52,94] reported, in theory, the possibility of disease transmission from donor to recipient, contaminated specimens causing infection and host incompatibility. Although autogenous bone grafting techniques are considered gold standard due to their osteogenic, osteoinductive and osteoconductive capacity, they carry limitations as donor area comorbidity, extending the duration of surgery, and they undergo bone remodeling and resorption during healing, which has been linked with significant graft loss[75]. Xenogeneic bone grafts have properties such as good biocompatibility and biomechanical stability. A major drawback of this bone substitute is the high cost ratio, the lack of osteoinductivity, and the subsequent long healing time[24,95], but your high porosity and large surface resembles the physiological bone structure and present lower resorption when compared to autogenous bone. In view of the low prevalence of postoperative complications found in this review, the use of bone grafts in maxillary osteotomy gaps can be used when indicated to improve long-term surgical stability.

Although the interpositional graft technique is the most used to fill the gaps between the bone segments, two studies[24,29] have reported the use of onlay grafts after Le Fort I osteotomy, both considered a predictable and suitable procedure. Naros et al[24] compared these two graft techniques in maxillary osteotomy gaps, and reported that Bio-Oss® block in onlay-position showed a weaker protecting effect on postoperative relapse, with a relapse rate of 30.3%, than the same bone substitute in inter-position, which showed 20.5% of postsurgical recurrence. However, the iliac crest graft, even inter-positioned, showed a recurrence rate of 33%, the highest

among groups. The authors[24] draw attention to the fact that the use of two-dimensional teleradiography restricts the accessibility of complex multidimensional postoperative changes. Therefore, according to this review, it seems that the interpositional graft is the most appropriate configuration for postoperative stability.

In fact, one limitation of the most articles included in this review was the use of 2D analysis rather than 3D. Essentially, the methods of stability analysis were performed by superimposition of 2D cephalometric radiographics (pre- and postoperative) based on skeletal and/or dental landmarks. Inaccuracies may occur due to measurement errors because, for example, the A point is unreliable in the vertical dimension, incisor tip can shift location because of postoperative orthodontics[96], PNS is difficult to locate, and ANS is often removed during Le Fort I procedures[14]. Only Lee et al.[51] used 3D analysis according to an x, y, z coordinate system to evaluate postsurgical stability. With the high level of technology present in several contemporary researches[97-99], stability analysis should be done by 3D images superimposition with surface-based registration or voxel-based registration to obtain greater accuracy of the results and to allow a better understanding of complex movements.

Conclusion

This current systematic review was able to analyze in detail the outcomes reported in the 23 included studies (Table 1 and 2) and provides improved effect estimates for surgical stability and postoperative complications of Le Fort I osteotomy with use of bone substitutes. There is an evidence that bone grafting reduces relapse

rate in large maxillary advancement and/or inferior repositioning, allowing greater stability in the long-term, especially if associated with rigid internal fixation.

Based on data obtained in this systematic review, the measure of stability was organized by stratifying surgical movement in the sagittal (minor, medium and major) and vertical (measures < 3 mm and ≥ 3 mm) planes. From this, it was verified that bone grafting can be designated for the following indications during one-piece Le Fort I surgery: maxillary advancement greater than 5 mm and inferior repositioning ≥ 3 mm.

The prevalence of postoperative complication with the use of bone graft substitutes in Le Fort I osteotomy is low, being considered a safe surgical technique when well indicated and planned. The most frequent complications were HA block displacement, scar spread of donor site and sinusitis. There is a weak evidence that allogeneic and alloplastic bone substitutes increase the rate of postoperative complications in maxillary osteotomy.

Long-term outcomes evaluation of a Le Fort I procedure with bone grafting should ideally include randomized controlled trials (test group x control group). Prospective studies need to be designed to evaluate postsurgical stability for at least 12 months, magnitude of movement, amount of relapse and incidence of complications. Further, uncontrollable clinical variables, such as age, sex, amount of mandibular movement, need to be documented and addressed.

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4 CONSIDERAÇÕES FINAIS

A técnica de enxertia óssea em gaps da OLFI para reposionamento maxilar em cirurgia ortognática é relativamente discutida na literatura, mas a sua decisão para uso de enxerto ósseo ou não ainda é um dilema clínico. Atraves da sumarização sistemática dos resultados presente na literatura, essa revisão elucida que essa técnica cirúrgica apresenta boa evidência na literatura para minimizar a taxa de recidiva, e consequentemente manter estabilidade esquelética a longo prazo.

A produção científica[7,30,36,40] sobre a magnitude e o tipo de movimento cirúrgico maxilar é irregular do ponto de vista dos resultados e conclusões quanto à indicação do emprego de substitutos ósseos em OLFI. Diante disso, essa revisão foi estratificada de acordo com os movimentos cirúrgicos maxilares: avanço – (1) menor: < 5mm, (2) médio: 5 – 8 mm e maior: > 8 mm; e para reposicionamento inferior – medida < 3 mm e medida > 3 mm, permitindo uma categorização dos movimentos cirúrgicos e um entendimento melhor dos resultados. Diante dos estudos controlados (grupo controle x grupo teste)[27-30], os dados coletados corroboram com a indicação de enxerro ósseo em casos de deslocamentos cirúrgicos de avanço maxilar maior que 5 mm e reposicionamento inferior ≥ 3 mm.

A qualidade metodológica dos artigos incluídos na revisão sistemática foi baixa para todos os artigos, apresentando, portanto, alto potencial de risco de viés. O estudo de Naros et al.[36] foi o único estudo prospectivo que apresentou randomização, mas mesmo assim teve alto risco de viés por não se

enquandrar nos demais critérios da qualidade metodológica (Tabela 3). Faz-se necessária a produção de ensaios clínicos randomizados bem delineados para a avaliação da estabilidade pós-cirúrgica e das complicações pós-operatóras, e isso somente é viável através do cegamento do avaliador, comparação entre grupo controle x grupo teste, follow-up ≥ 12 meses, validação das mensurações de preferência com a utilização de métodos de sobreposição 3D para maior precisão e confiabilidade.

A análise de qualidade dos estudos incluídos nesta revisão sistemática foi baseada na análise de Clementini et al.[41], a qual foram acrescidos critérios para avaliar o efeito de comparação entre o grupo controle e o tipo de intervenção a ser testada e a realização de cegamento do avaliador. O critério de comparação entre intervenções foi acrescido para que se pudesse fazer a distinção entre ensaio clínico não randomizado e série de casos, e o critério de cegamento do avaliador foi incluído para avaliar presença de viés de aferição. Esses critérios adicionados são indispensáveis na análise de qualidade de estudos de intervenção, principalmente se o objetivo for verificar se há benefícios de um tipo de tratamento em relação a outro.

No contexto da evidência científica atual sobre o uso de enxerto ósseo em OLFI para estabilidade e suas complicações pós-operatórias, a realização de metanálise fica impossibilitada, pois, como mencionado anteriormente, todos os estudos apresentaram alto potencial de viés e foram bastante heterogêneos quanto a metodologia e técnica cirúrgica empregada. A revisão sistemática dos ensaios clínicos e estudos de intervenção menores, entretanto, pode servir para gerar hipóteses e estimular a realização de estudos de

intervenção maiores randomizados e bem delineados. A presente revisão sistemática teve um caráter descritivo onde pôde-se avaliar o nível da evidência científica atual disponível e, de forma organizada e sistematizada, melhorar as estimativas de efeito quanto aos resultados do uso do enxerto ósseo na OLFI para estabilidade esquelética e as possíveis complicações pós-operatórias.

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6 APÊNDICE 1

Ficha de Elegibilidade

Elegibilidade

Estudo: número do estudo cegado **Revisor:** nome do revisor

O estudo é sobre estabilidade maxilar e/ou complicações cirúrgicas com uso de substitutos ósseos em osteotomia Le Fort I para cirurgia ortognática?

Sim	Duvidoso	Não
⇩	⇩	⇩
Siga	Siga	Excluir

O estudo é de intervenção?

⇩	⇩	⇩
Siga	Siga	Excluir

O estudo é original?

Sim	Duvidoso	Não
⇩	⇩	⇩
Siga	Siga	Excluir

O estudo avalia o desfecho do uso de substitutos ósseos em osteotomia Le Fort I para promover estabilidade óssea e/ou avaliar suas possíveis complicações pós-operatórias?

Sim	Duvidoso	Não
⇩	⇩	⇩
Siga	Siga	Excluir

DECISÃO FINAL

☐ **INCLUIR**

☐ **DUVIDOSO** (discutir com revisores)

☐ **EXCLUIR** (não completar as páginas seguintes)

7 APÊNCICE 2

Ficha de Extração de Dados

Extração de Dados

Estudo:número do estudo cegado **Revisor:**nome do revisor **Data:**

Nome do primeiro autor: **Ano de publicação:**
Tipo de estudo: **País de origem:**

Dados demográficos do estudo:

	Tamanho da amostra	Idade (média/DP)	Gênero (%)	Etnia (%)	Tipo de deformidade dentofacial	Intervalo de acomplanhamento pós-operatório (Média/DP)
Total do estudo						

Dados do Tipo do Procedimento Cirúrgico Ortognático

	Cirurgia bimaxilar ou monomaxilar	Tipo de deslocamento/ movimentação da maxila	Quantidade da movimentação cirúrgica da maxila	Tipo de fixação interna rígida
Total do estudo				

Dados do tipo de enxerto ósseo ou biomaterial:

	Tipo de biomaterial	Tipo de fixação ou aposição do enxerto
Total do estudo		

Complicações pós-operatórias

	Localização	Sinais e sintomas	Intervenção	Tempo de acompanhamento (média/DP)
Trans-cirúrgico				
Pós-operatório				

Resultado da estabilidade:

	Tipo de avaliação	Recidiva (milímetros)	Taxa de sucesso
Total do estudo			

8 ANEXO

S I P E S Q

Sistema de Pesquisas da PUCRS

Código SIPESQ: 8670 Porto Alegre, 11 de junho de 2018.

Prezado(a) Pesquisador(a),

A Comissão Científica da ESCOLA DE CIÊNCIAS DA SAÚDE da PUCRS apreciou e aprovou o Projeto de Pesquisa "Estabilidade e complicações pós-operatórias em osteotomia Le Fort I associada ao uso de substitutos ósseos - Revisão Sistemática.".

Atenciosamente,

Comissão Científica da ESCOLA DE CIÊNCIAS DA SAÚDE

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