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**PRÓTESES TOTAIS POR ENGENHARIA COMPUTADORIZADA: UMA REVISÃO
SISTEMÁTICA DOS DESFECHOS CLÍNICOS E LABORATORIAIS**

Florianópolis
2020

Gabriela Panca Sabatini

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SISTEMÁTICA DOS DESFECHOS CLÍNICOS E LABORATORIAIS**

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Orientador: Prof. Dr. Luis André Mendonça Mezzomo

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SISTEMÁTICA DOS DESFECHOS CLÍNICOS E LABORATORIAIS**

O presente trabalho em nível de mestrado foi avaliado e aprovado por banca
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Dedico este trabalho aos meus pais,
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*“The capacity to learn is a gift; the ability to learn is a skill;
the willingness to learn is a choice”*

Brian Hernert

RESUMO

Objetivos: Responder às seguintes perguntas: "Quais são os resultados clínicos de Próteses Totais com Engenharia Computadorizada (PTECs) em comparação com Próteses Totais Convencionais (PTCs)", e 2. "Quais são os resultados mecânicos, ópticos e biológicos de Próteses Totais com Engenharia Computadorizada (PTECs) em comparação com Próteses Totais Convencionais (PTCs)?"

Materiais e Métodos: Uma busca eletrônica foi realizada em nove bases de dados, acrescida por pesquisas manual e na literatura cinzenta. Dois revisores selecionaram estudos com base em critérios de elegibilidade. Dados clínicos e laboratoriais sobre as características do estudo, da amostra, da intervenção e dos desfechos foram extraídos. Um terceiro revisor avaliou o risco de viés e a qualidade cumulativa das evidências. Meta-análise foi conduzida usando o modelo de efeitos randômicos a um nível de significância de 5%.

Resultados: 197 pacientes com 164 PTECs e 124 PTCs, de sete estudos clínicos, e 1.327 amostras de PMMA fresados, 190 de resinas impressas, 908 de resinas convencionais (por compressão) e 242 de resinas convencionais (por injeção), de trinta e quatro estudos *in vitro*, estiveram disponíveis para as análises descritiva e estatística. As PTECs proporcionaram aos pacientes edêntulos os benefícios de um número reduzido de consultas e custos gerais reduzidos, bem como uma maior satisfação e conforto. A meta-análise de efeitos randômicos revelou resultados estatisticamente melhores para amostras de PMMA fresados com relação à resistência à flexão ($p = 0,004$), módulo de flexão ($p < 0,001$) e manchamento em água ($p = 0,02$) e café ($p = 0,02$). Ângulo de contato, módulo de elasticidade, rugosidade da superfície e tenacidade à fratura também mostraram resultados melhores para amostras de PMMA fresadas, porém não significativos ($p = 0,48$, $p = 0,36$, $p = 0,55$, $p = 0,43$, respectivamente).

Conclusões: As PTECs são uma solução eficiente para o tratamento de pacientes edêntulos totais. Amostras fresadas de PMMA de alto desempenho mostraram melhores propriedades mecânicas, ópticas e biológicas em geral.

Palavras-chave: prótese total, bases de dentadura, polimetil metacrilato, desenho assistido por computador, impressão tridimensional, revisão sistemática.

ABSTRACT

Objectives: To answer the following questions: 1. “*What are the clinical outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*”, and 2. “*What are the mechanical, optical and biological outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*”

Materials and Methods: An electronic search was performed in nine databases, added by hand- and gray literature searches. Two reviewers selected studies based on eligibility criteria. Clinical and laboratory data on *study-*, *sample-*, *intervention-* and *outcome* characteristics were extracted. A third reviewer assessed risk of bias and the cumulative quality of evidence. Meta-analysis was conducted using the random-effects model at a 5% significance level.

Results: 197 patients with 164 CECDs and 124 CCDs, from seven clinical studies, and 1,327 CECD milled, 190 CECD printed, 908 conventional (compression) and 242 conventional (injection) samples, from thirty-four *in vitro* studies, were available for descriptive and statistical analysis. CECDs provided edentulous patients the benefits of a reduced number of appointments and overall costs, as well as an increased satisfaction and comfort. Random-effects meta-analysis revealed statistically better results for CAD/CAM milled samples with regards to flexural strength ($p = 0.004$), flexural modulus ($p < 0.001$) and stainability in water ($p = 0.02$) and coffee ($p = 0.02$). Contact angle, elastic modulus, surface roughness and fracture toughness showed non-significant better results for CAD/CAM milled samples ($p = 0.48$, $p = 0.36$, $p = 0.55$, $p = 0.43$, respectively).

Conclusions: CECDs are an efficient solution for the treatment of edentulous patients. High-performance PMMA CAD/CAM milled samples showed overall better mechanical, optical and biological properties.

Keywords: complete denture, denture bases, polymethyl methacrylate, computer-aided design, three-dimensional printing, systematic review

LISTA DE FIGURAS

Da Dissertação:

Figura 1. A) Escâner intraoral portátil Trios TC® (3Shape, Dinamarca). B) Escâner de bancada 7Series® (Dental Wings®, Canadá).....	25
Figura 2. Fresadora Programill® (Ivoclar Vivadent®, Lichtenstein).....	27
Figura 3. Método aditivo de prototipagem rápida (impressão 3D). Impressora NextDent 5100 (NextDent®, Holanda).....	28
Figura 4. A) Sistema Dentca® (Dentca Inc, EUA); B) Sistema AvaDent® (Global Dental Science, EUA); C) Sistema Baltic (Merz Dental GmbH®, Alemanha); D) Sistema Ivotion® Ivoclar Digital Dentures (Ivoclar Vivadent AG®, Liechtenstein).....	35

Do Artigo em inglês:

Figure 1. Flowchart of the screening and selection processes of the study.	49
Figure 2. Forest plot of the flexural strength values of: (A) CAD/CAM milled x Conventional (Compression) groups, and (B) CAD/CAM milled x Conventional (Injection) groups.....	68
Figure 3. Forest plot of the flexural modulus values of CAD/CAM milled and Conventional (compression) groups.....	68
Figure 4. Forest plot of the elastic modulus values of CAD/CAM milled and Conventional (compression) groups.....	69
Figure 5. Forest plot of the surface hardness values of: (A) CAD/CAM milled x Conventional (Compression) groups, and (B) CAD/CAM milled x Conventional (Injection) groups.....	70
Figure 6. Forest plot of the surface roughness values of CAD/CAM milled and Conventional (compression) groups.....	71
Figure 7. Forest plot of the fracture toughness values of CAD/CAM milled and Conventional (compression) groups.....	71
Figure 8. Forest plots of the stainability values of CAD/CAM milled and Conventional (compression) groups: (A) Water. (B) Coffee. (C) Wine.....	78
Figure 9. Forest plot of the contact angle values of CAD/CAM milled and conventional (compression) groups.....	79

Figure 10. A) Risk of bias of the clinical studies according to the Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental (Non-Randomized Experimental Studies) tool. 82

Figure 11. Risk of bias of the in vitro studies according to the Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental (Non-Randomized Experimental Studies) tool. 83

LISTA DE TABELAS

Table 1. Summary of descriptive characteristics of included clinical studies.....	54
Table 2. Summary of descriptive characteristics of included <i>in vitro</i> studies - Mechanical outcomes.....	61
Table 3. Summary of descriptive characteristics of included <i>in vitro</i> studies - Optical outcomes.....	75
Table 4. Summary of descriptive characteristics of included <i>in vitro</i> studies - Biological outcomes.....	80
Table 5. GRADE summary findings.....	84

LISTA DE ABREVIATURAS E SIGLAS

CAI	<i>Computer Aided Imaging</i>
CAD	<i>Computer Aided Design</i>
CAM	<i>Computer Aided Manufacturing</i>
PTEC	Prótese Total Assistida por Engenharia Computadorizada
PTC	Prótese Total Convencional
PROSPERO	<i>Prospective Register of Systematic Reviews</i>
<i>et al.</i>	e outros
PMMA	Polimetil-metacrilato
N	Newton
mm	Milímetro
ISO	<i>International Organization for Standardization</i>
STL	<i>Standard Triangle Language</i>
C	<i>Celsius</i>
MPa	Mega Pascal
3D	<i>Three-Dimensional</i>
SLA	<i>StereoLithography</i>
DLP	<i>Direct Light Projection</i>
SML	<i>Metal Laser Sintering</i>
EUA	Estados Unidos da América
Do artigo:	
CECD	<i>Computer-Engineered Complete Dentures</i>
CCD	<i>Conventional Complete Dentures</i>
CI	<i>Confidence Interval</i>
	<i>Preferred Reporting Items for Systematic Reviews and Meta-</i>
PRISMA-P	<i>Analysis Protocols</i>
LILACS	<i>Latin America and Caribbean Health Sciences</i>
PROMS	<i>Patient-Reported Outcome Measures</i>

RoB	<i>Risk of Bias</i>
GRADE	<i>Grading of Recommendations Assessments, Development and Evaluation</i>
WM	<i>Weighted Mean</i>
I ²	<i>Heterogeneity</i>
USA	<i>United States of America</i>
CFU	<i>Colony-Forming Units</i>

LISTA DE SÍMBOLOS

&	e
%	Por cento
-	Hífen
n	Número amostral
<	Menor que
>	Maior que
=	Igual
®	Marca registrada
±	Mais ou menos
™	TradeMark
ΔE	Varição de cor
°	graus
♂	Masculino
♀	Feminino

SUMÁRIO

1 INTRODUÇÃO	18
2 REVISÃO DE LITERATURA	21
2.1 Reabilitação em Edêntulos	21
2.1.1 Próteses Totais Mucossuportadas	21
2.1.2 Próteses Totais Implanto-suportadas	22
2.2 Método Convencional de Fabricação de Próteses Totais	23
2.3 Métodos Assistidos por Computador de Fabricação de Próteses Totais	24
2.3.1 Computer-Aided Imaging (CAI) – Obtenção de Imagem	25
2.3.2 Computer-Aided Design (CAD) – Desenho Virtual da Peça Protética	26
2.3.3 Computer-Aided Manufacturing (CAM) – Manufatura da Peça Protética .	26
2.4 Próteses Totais Assistidas por Engenharia Computadorizada (PTECs) .	29
2.4.1 Sistemas de Produção de PTECs.....	33
2.4.2 Propriedades mecânicas das PTECs	35
2.4.3 Propriedades ópticas das PTECs	36
2.4.4 Propriedades biológicas das PTECs.....	37
3 OBJETIVOS	39
3.1 Objetivo Geral	39
3.2 Objetivos Específicos	39
4 ARTIGO CIENTÍFICO	40
CONSIDERAÇÕES FINAIS	115
REFERÊNCIAS BIBLIOGRÁFICAS	116
ANEXO 1. Registro do protocolo no PROSPERO.	126
ANEXO 2. Normas da Revista <i>Dental Materials</i>.	127

1 INTRODUÇÃO

O edentulismo é uma doença oral que mostra uma alta prevalência na população de idosos no Brasil (SB BRASIL, 2010). As consequências mais comuns desta condição incluem a dificuldade na fala, deficiência mastigatória, baixa adesão social, deficiências nutricionais, insatisfação estética e pior qualidade de vida (GERRITSEN *et al.*, 2010). Para que estas consequências sejam amenizadas, tratamentos protéticos que recuperam o suporte de tecidos orais que frequentemente ocorre nestes pacientes são necessários, restabelecendo assim o equilíbrio do sistema estomatognático.

As soluções protéticas mais utilizadas para pacientes edêntulos totais são as próteses totais convencionais mucossuportadas, as quais se apresentam como uma opção que reconstitui a fonética, a estética oral e a função mastigatória ao paciente, e que por consequência melhora a sua qualidade de vida (VEYRUNE *et al.*, 2005). Apesar dos benefícios deste tipo de prótese, ainda existem limitações em sua utilização, sendo a retenção mecânica deficiente a principal delas. Por isso, os implantes dentários foram introduzidos por Brånemark *et al.* (1969) como pilares de ancoragem para as próteses totais, quer sejam elas removíveis (sobredentaduras) ou fixas. Ambos os tipos de próteses sobre implantes proporcionam melhora na estabilidade e retenção e, como consequência, um aprimoramento na qualidade da mastigação, da fonação e da satisfação do paciente em relação às próteses convencionais (DOUNDOULAKIS *et al.*, 2003; ATTARD; ZARB, 2004; WENNERBERG; ALBREKTSSON, 2011; COMPAGNONI *et al.*, 2014; MICHELON *et al.*, 2019).

A resina acrílica termicamente ativada tem-se mostrado como o material utilizado com mais frequência para a confecção de próteses totais em laboratório (ALI; YUNUS; ABU-HASSAN, 2008; ALLA; SWAMY; KONAKANCHI, 2015). Este material, também descrito como Polimetil-Metacrilato (PMMA), possui muitas vantagens em sua composição e comportamento físico, como a estética, estabilidade dimensional, adesão a dentes artificiais, biocompatibilidade e maior facilidade de processamento em laboratório (CO *et al.* 1975; CHOI *et al.* 2020). Apesar disso, algumas características físicas, como a resistência à fratura, não apresentam bons resultados (ALI; YUNUS; ABU-HASSAN, 2008). Assim, a busca por novos métodos e materiais

para a confecção de próteses totais com qualidades físicas, ópticas e biológicas mais favoráveis é de notável relevância.

A tecnologia CAD/CAM (*Computer Aided Design/Computer Aided Manufacturing*) tem como princípio a utilização de inteligência artificial de computadores para desenhar, analisar e posteriormente realizar a manufatura - aditiva ou subtrativa - de uma peça (GALHANO; PELLIZZER; MAZARO, 2012; LAURENT *et al.*, 2015). A manufatura subtrativa consiste no desgaste seletivo de blocos de materiais restauradores através de fresas, sendo esse processo assistido por computadores (DANKWORT *et al.* 2004; TINSCHERT *et al.*, 2004 BILGIN *et al.*, 2016). Por outro lado, a manufatura aditiva permite a obtenção de peças protéticas por meio da polimerização seletiva e gradual de resinas em estado líquido, caracterizando assim a impressão digital ou prototipagem rápida (KESSLER; HICKEL; REYMUS, 2020; BILGIN *et al.*, 2016; LIMA *et al.*, 2014). Ambos os métodos permitem a confecção de próteses totais de maneira mais previsível, especialmente quando se utilizam cirurgias guiadas para instalação de implantes, e posterior carregamento imediato com próteses provisórias desenhadas e manufaturadas de acordo com a posição planejada dos implantes (PAPASPYRIDAKOS *et al.*, 2018; LANIS *et al.*, 2019; OH *et al.*, 2019; ORENTLICHER; HOROWITZ; KOBREN, 2019).

Existem estudos que comparam o comportamento de diferentes materiais para confecção de bases de próteses totais, como as resinas de impressão e os blocos pré-polimerizados de PMMA para fresagem tipo CAD/CAM (LEE *et al.* 2019; HWANG *et al.* 2019; AL-QARNI *et al.* 2020; MASRI *et al.* 2020; PEREA-LOWERY *et al.* 2020). A aplicação do sistema CAD/CAM em prótese total foi relatada por recentes revisões sistemáticas da literatura, como a de Kattadiyil & Alhelal (2016) e a de Wang *et al.* (2020), que avaliaram os resultados clínicos e laboratoriais, respectivamente, associados às Próteses Totais por Engenharia Computadorizada (PTECs). Entretanto, ainda existe pouca evidência comprovando a eficácia dos métodos de fabricação de Próteses Totais por Engenharia Computadorizada. Assim, o objetivo deste estudo foi responder, por meio de uma revisão sistemática da literatura, às perguntas de pesquisa: 1. "Quais são os resultados clínicos de Próteses Totais com Engenharia Computadorizada (PTECs) em comparação com Próteses Totais Convencionais (PTCs)?", e 2. "Quais são os desfechos mecânicos, ópticos e

biológicos de Próteses Totais por Engenharia Computadorizada (PTECs) comparados às Próteses Totais Convencionais?”.

2 REVISÃO DE LITERATURA

2.1 Reabilitação em Edêntulos

O envelhecimento da população, associado a práticas pouco eficientes de saúde em Odontologia, possui como importante consequência o edentulismo, seja ele parcial ou total (PELTZER *et al.*, 2014). As consequências que o edentulismo ocasiona variam desde a deficiência nutricional por dificuldade mastigatória, até a dificuldade de inserção social, doenças cardiovasculares e alterações no sono, como a apneia obstrutiva do sono (ABNET *et al.* 2005; BUCCA *et al.*, 2006; ÖSTERBERG *et al.*, 2010). De acordo com a Pesquisa Nacional de Saúde Bucal (2010), na faixa etária de 64 a 75 anos, a porcentagem de brasileiros usuários de prótese total é de 63,1%, e sua utilização é necessária para que estes pacientes amenizem problemas sérios de saúde que possam surgir em decorrência do edentulismo.

2.1.1 Próteses Totais Mucossuportadas

Uma solução protética comumente utilizada para reabilitar pacientes edêntulos totais são as próteses totais mucossuportadas. Estas próteses possuem vantagens que proporcionam ao paciente edêntulo a recuperação de parâmetros ópticos, funcionais – mastigação, fonação –, sociais e nutricionais (BAJORIA; SALDANHA; SHENOY, 2012).

A qualidade de vida de pacientes edêntulos ao serem reabilitados com próteses totais convencionais mucossuportadas aumenta significativamente (REIS *et al.*, 2019). No estudo clínico de Ellis, Pelekis e Thomason (2007), foram avaliados 45 candidatos para receber próteses totais maxilares e mandibulares utilizando a técnica convencional ou a de duplicação de prótese, de acordo com as necessidades do paciente. Os pacientes avaliaram sua satisfação e qualidade de vida através de questionários (OHIP-20 e Escala Analógica Visual). Uma melhora estatisticamente significativa nos domínios relacionados à limitação funcional, inaptidão física e psicológica foi avaliada em ambos os tipos de próteses mucossuportadas. A qualidade de vida e satisfação dos pacientes foi aprimorada de maneira geral após a reabilitação com este tipo de prótese.

2.1.2 Próteses Totais Implanto-suportadas

Apesar dos benefícios oferecidos pelas próteses totais mucossuportadas, uma queixa frequente dos pacientes é relacionada à deficiência ou ausência de retenção e estabilidade deste tipo de prótese, principalmente a prótese inferior, podendo causar limitação na fonética e na função mastigatória (EL OSTA *et al.*, 2017). Assim, o tratamento de pacientes edêntulos através da colocação de implantes de titânio e posterior confecção de próteses implanto-suportadas tornou-se uma opção recorrente para restaurar função e estética, e assim melhorar a eficiência mastigatória e satisfação do paciente (DOUNDOULAKIS *et al.*, 2003; ATTARD; ZARB, 2004; WENNERBERG; ALBREKTSSON, 2011; COMPAGNONI *et al.*, 2014). O Consenso de McGill (FEINE *et al.*, 2002), e sua reafirmação pela Declaração de York (THOMASSON *et al.*, 2009), estabeleceu que a reabilitação de mandíbulas edêntulas com sobredentaduras retidas por 2 implantes passou a ser a abordagem terapêutica de primeira escolha.

Um estudo clínico avaliou o risco de má nutrição entre uma população idosa de edêntulos totais. Um total de quarenta pacientes, divididos em dois grupos: um grupo ($n = 23$) recebeu prótese total convencional dupla, e outro grupo ($n = 17$) recebeu prótese total convencional superior e prótese total inferior implanto-suportada, foram submetidos a testes nutricionais, assim como entrevista e exame clínico. Os pacientes que receberam próteses implanto-suportadas foram considerados bem nutridos (76,47%), quando comparados com os pacientes usuários de próteses totais convencionais duplas (43,48%), existindo uma diferença estatisticamente significativa entre os grupos ($\chi^2 = 4.35$). Os autores sugeriram que o risco de má nutrição foi maior nos pacientes que utilizam próteses totais convencionais (DE OLIVEIRA, FRIGERIO, 2004).

Van der Bilt *et al.* (2010), em um ensaio clínico randomizado com 10 anos de acompanhamento, avaliou a função oral – força de mordida e eficiência mastigatória – de 14 pacientes após instalação de implantes e reabilitação com sobredentaduras mandibulares implantorretidas. A força máxima de mordida após o tratamento com implantes foi significativamente maior do que o tratamento convencional sem apoio de implantes ($p < 0,001$). Além disso, como resultado da instalação da sobredentadura, a média de força máxima de mordida mais do que dobrou, aumentando de 162N para

341N. Esse resultado permaneceu inalterado durante os 10 anos de acompanhamento, comprovando que a instalação de implantes e próteses implanto-suportadas melhora sobremaneira a função oral dos pacientes edêntulos.

Sivaramakrishnan & Sridharan (2016), em uma revisão sistemática da literatura de estudos randomizados controlados, compararam sobredentaduras mandibulares implanto-retidas com próteses totais convencionais muco-suportadas em relação à qualidade de vida. Quatrocentas e quarenta e um (441) pacientes (228 com sobredentaduras mandibulares e 213 com próteses totais convencionais) foram analisados. Uma diferença estatisticamente favorável ao grupo de sobredentaduras foi encontrada em relação ao desconforto psicológico ($p = 0,05$), limitação funcional ($p = 0,002$), incapacidade física ($p < 0,00001$), psicológica ($p < 0,00001$) e social ($p = 0,05$), com exceção para a avaliação relacionada à dor física.

2.2 Método Convencional de Fabricação de Próteses Totais

Existem diferentes opções de materiais utilizados para confecção de próteses totais, como por exemplo as bases de poliamida e acrílicos de alta resistência (KANIE *et al.* 2004; VOJDANI; GITI, 2015). O Polimetil-Metacrilato termicamente ativado (PMMA) apresenta-se historicamente como o material mais utilizado, sendo possível receber reforços de fibra de vidro ou carbono em sua composição para melhora das suas propriedades físicas (ALI; YUNUS; ABU-HASSAN, 2008; ALLA; SWAMY; KONAKANCHI, 2015). Algumas das características essenciais de materiais para confecção de próteses totais para um bom comportamento na cavidade oral são: ótimas propriedades térmicas, durabilidade, biocompatibilidade e resistência mecânica (RICKMAN; PADIPATVUTHIKUL; SATTERTHWAITE, 2012). Assim, o PMMA possui atributos que estão de acordo para um bom desempenho de próteses em relação à sua composição e comportamento físico, como a baixa sorção à água, o fácil ajuste e reparo, e precisão na reprodução anatômica do modelo de gesso (CO *et al.* 1975; RICKMAN; PADIPATVUTHIKUL; SATTERTHWAITE, 2012). Apesar disso, estudos também relatam as limitações físicas, biológicas e ópticas que este material apresenta (GOODACRE *et al.* 2016; ARSLAN *et al.* 2018; DAYAN *et al.* 2019). Uma desvantagem do Polimetil-Metacrilato termicamente ativado é a liberação de monômeros residuais (monômero Metil Metacrilato – MMA), os quais afetam a

estabilidade dimensional da prótese e provocam maior aderência bacteriana (AWAD; JASSIM, 2012).

Pfeiffer & Rosenbauer (2004) compararam em seu estudo laboratorial a quantidade de monômeros residuais, quantidade de sorção de água e a solubilidade de cinco materiais de bases de próteses, sendo um deles PMMA (Paladon[®] 65, metacrilato termoativado – grupo controle) e outros quatro hipoalergênicos: 1) Sinomer[®] (metacrilato modificado termoativado); 2) Polyan[®] (metacrilato modificado termoplástico); 3) Promysan[®] (à base de tereftalato termoplástico); e 4) Microbase[®] (à base de poliuretano polimerizado por microondas). Para isso, espécimes de cada material foram testados para avaliação de monômero residual (%wt, $n = 3$), quantidade de sorção de água (microg/mm³, $n = 5$) e a solubilidade em água (microg/mm³, $n = 5$), de acordo com as normas da ISO 1567:2000. Houve uma quantidade significativamente menor de monômeros residuais nas bases de Sinomer[®] e Polyan[®] quando comparadas com o PMMA do grupo controle (média: $0,90 \pm 0,20\%$ wt, $p < ,05$). A quantidade de sorção de água nas bases de Promysan[®] (média: $16,21 \pm 0,96$ microg/mm³) foi significativamente menor do que nas bases de PMMA do grupo controle (média: $23,04 \pm 3,13$ microg/mm³, $p < .0001$). Assim, para os autores, as bases hipoalergênicas de materiais de prótese exibiram menor quantidade de monômero residual quando comparadas com as de PMMA termoativado.

2.3 Métodos Assistidos por Computador de Fabricação de Próteses Totais

Devido a uma crescente demanda por reabilitações em edêntulos, quer sejam convencionais ou associadas com implantes dentários, o desenvolvimento de novos materiais e de novas técnicas de confecção de próteses totais tem sido estimulado. O sistema CAD/CAM tem modificado o protocolo de confecção de peças protéticas, que anteriormente eram confeccionadas apenas de maneira convencional, incluindo as próteses totais (INFANTE *et al.*, 2014).

Este novo fluxo de trabalho compreende as etapas de aquisição de imagem (*CAI – Computer-Aided Imaging*), desenho virtual (*CAD – Computer-Aided Design*) e manufatura assistida por computador da peça protética (*CAM – Computer-Aided Manufacturing*).

2.3.1 Computer-Aided Imaging (CAI) – Obtenção de Imagem

Para que um fluxo digital na Odontologia seja possível, é necessário que inicialmente sejam realizadas aquisições de imagens. Estas imagens virtuais são adquiridas por meio de escâners, de maneira direta ou indireta, tendo como resultado uma malha de triângulos que transformam um objeto físico em um objeto tridimensional virtual, representado por um arquivo em formato *Standard Triangle Language* (STL). O escaneamento realizado diretamente dos tecidos moles e duros do paciente em boca é denominado escaneamento intraoral (método direto) (Figura 1A), para o qual utilizam-se os escâners intraorais portáteis. Por outro lado, o escaneamento de um molde ou de um modelo de gesso obtido através de uma moldagem do paciente denomina-se escaneamento de bancada, ou método indireto (Figura 1B). Tanto o método direto quanto o indireto podem ser utilizados para capturas de elementos dentários unitários ou quadrantes, assim como para uma arcada edêntula que receberá uma prótese total (GALHANO; PELLIZZER; MAZARO, 2012).

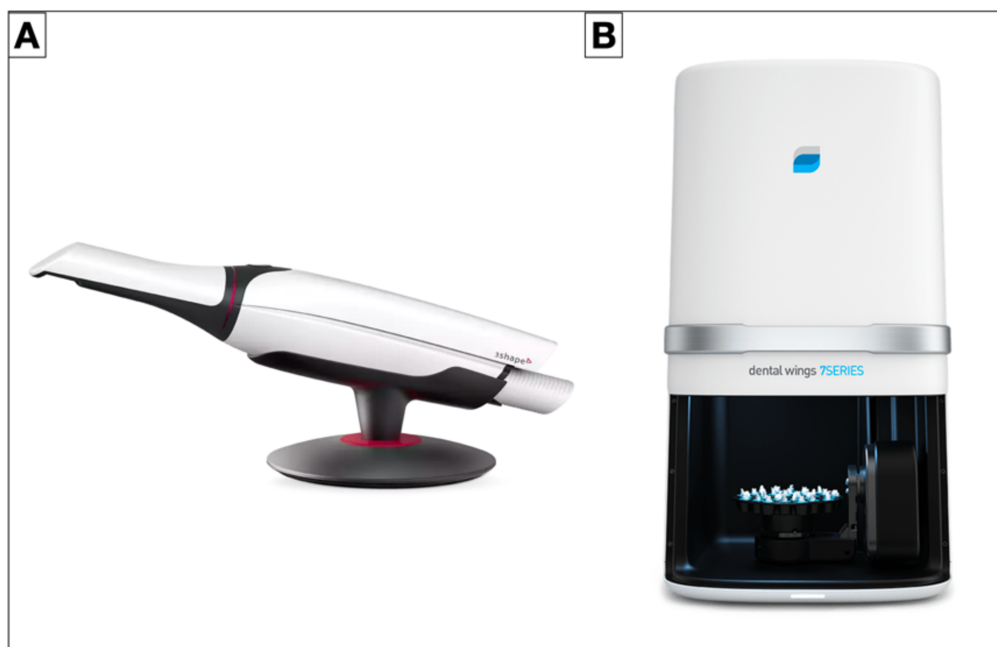


Figura 1. A) Escâner intraoral portátil Trios TC[®] (3Shape[®], Dinamarca). B) Escâner de bancada 7Series[®] (Dental Wings, Canadá).

Fonte: A) <https://www.3shape.com/pt/scanners/trios/>;
B) https://dentalwings.com/3dscanners/7series-faster-scanning_en/

Papaspyridakos *et al.* (2016) compararam, através de um estudo clínico, a acurácia das técnicas de moldagem convencional e escaneamento em pacientes edêntulos totais. Para isso, um modelo de gesso de mandíbula edêntula com cinco implantes serviu como modelo mestre (controle). Foram conectados pilares de escaneamento, ou *scanbodies*, sobre os implantes, e realizados 10 escaneamentos com escâner intraoral (TRIOS®, 3Shape, Dinamarca). Já as moldagens convencionais do modelo mestre foram realizadas com poliéster com e sem técnica de esplintagem dos transferentes de moldagem, tanto a nível do implante quanto a nível do pilar (4 grupos de modelos, $n = 10$ cada). Os modelos mestre e as moldagens convencionais foram digitalizados com um escâner de alta resolução (IScan® D103i, Imetric, Suíça). Os arquivos em formato STL dos cinco grupos – digital e convencionais – foram sobrepostos para avaliar os desvios tridimensionais. Os autores concluíram que os escaneamentos foram tão acurados quanto as moldagens convencionais, sendo as moldagens convencionais com esplintagem e à nível de implante as mais acuradas.

2.3.2 Computer-Aided Design (CAD) – Desenho Virtual da Peça Protética

Após a obtenção da imagem em formato de arquivo STL, seja uma imagem de preparo dental unitário ou de um rebordo edêntulo que receberá uma prótese total, desenhos e projetos das peças protéticas são realizados através de programas de computador específicos. Programas de diferentes fabricantes são capazes de realizar desenhos protéticos variados, desde restaurações parciais (*inlay/onlay*), copings, laminados, coroas unitárias, pilares protéticos para implantes, próteses telescópicas, até próteses totais e barras metálicas para instalação sobre implantes (ALGHAZZAWI, 2016).

2.3.3 Computer-Aided Manufacturing (CAM) – Manufatura da Peça Protética

Após a conclusão do desenho da peça, realiza-se o processo de *Computer-Aided Manufacturing*, que consiste em transformar o projeto virtual em um objeto físico através do processo da manufatura. Este processo introduziu mudanças fundamentais na obtenção desde componentes e peças protéticas, modelos, até guias cirúrgicas e estruturas metálicas para próteses (CIOCCA *et al.*, 2019).

A manufatura pode ser realizada através da fresagem assistida por computador de blocos de materiais restauradores, ou seja, através de desgastes seletivos, denominada *manufatura subtrativa* (NG; RUSE; WYATT, 2014; LEE *et al.*, 2019; WINTER *et al.*, 2020) (Figura 2). Muitas são as vantagens apresentadas pelo método de fresagem, como a precisão, acurácia e alta resistência à tração (LEE *et al.*, 2019; AL-DWAIRI *et al.*, 2020).



Figura 2. Bloco de PMMA sendo fresado pelo método subtrativo em uma Fresadora Programill® (Ivoclar Vivadent®, Lichtenstein).

Fonte: <https://www.ivoclardigital.com/en/laboratory/material/removable-prosthetics>

A fresagem de cromo-cobalto é considerada um dos melhores métodos de manufatura de estruturas metálicas para próteses fixas sobre implantes, obtendo peças precisas e resistentes (ORTORP *et al.*, 2003; SIERRAALTA *et al.*, 2012). Apesar disso, a técnica de fresagem de metais não se mostra eficiente em determinados aspectos, tendo em vista o alto desperdício de material, maior tempo de manufatura, e demanda de materiais de alto custo para fresagem (JODA *et al.*, 2017).

Murakami *et al.* (2013) avaliaram em um estudo *in vitro* os efeitos da polimerização sob alta pressão nas propriedades mecânicas de resinas de bases de próteses utilizadas no método CAD/CAM. Para isso, polimerizou-se resina PMMA termicamente ativada sob pressão de 500 MPa a 70°C durante 24 horas para

confeccionar espécimes de dimensões 30mm (comprimento) x 2mm (largura) x 2mm (espessura). Cada espécime foi defletido em uma máquina de teste de flexão de 3 pontos até a fratura ocorrer. Os espécimes expostos à alta pressão apresentaram ductilidade aumentada e sem fratura, enquanto espécimes sob condições normais de pressão e temperatura sofreram fratura. Os autores concluíram que uma aplicação potencial de polimerização sob alta pressão aprimora a resistência à fratura de resinas para próteses à base de PMMA.

A *manufatura aditiva* (ou impressão 3D ou prototipagem rápida), por sua vez, consiste na adição de materiais como resina em estado líquido em camadas até a formação final da peça. A estereolitografia (SLA – *StereoLithogrAphy*) e Projeção Direta de Luz (DLP – *PolyJet and Direct Light Projection*) são algumas das técnicas possíveis de serem empregadas na manufatura aditiva de resinas (VAN NOORT, 2012). Durante a utilização do método de impressão 3D, pouco material é desperdiçado, apresentando-se assim como uma grande vantagem da técnica. Além disso, os componentes da impressora sofrem pouco desgaste a longo prazo, diferente da manufatura subtrativa que demanda altos gastos com substituição de fresas. A impressão 3D ainda apresenta a grande utilidade de possibilitar a impressão de alguns objetos ao mesmo tempo, de acordo com o desenho planejado em programa de computador (REYMUS *et al.*, 2020) (Figura 3).



Figura 3. Método aditivo de prototipagem rápida (impressão 3D). Impressora NextDent® 5100 (NextDent®, Holanda). Fonte: <http://www.dentalasia.net/en/news-archive/dentures-at-unbeatable-speed-and-cost-effectiveness/2657>

Apesar de estudos relacionados à resistência de resinas de impressão 3D ainda serem escassos, as poucas evidências disponíveis mostram superioridade de peças fresadas quando comparadas com as impressas, como relatado por Prpić *et al.* (2020). Neste estudo, um total de 160 espécimes foram fabricados, divididos em 3 diferentes grupos: três tipos de resinas termicamente ativadas (ProBase Hot[®], Paladon 65[®], e Interacryl Hot[®]), três tipos de blocos de resinas para fresagem (IvoBase[®] CAD, discos de PMMA Interdent[®] CC, e discos Polident[®] CAD/CAM), um tipo de resina para impressão (NextDent Base[®]), e um material de poliamida para confecção de base de prótese (Vertex ThermoSens[®]). A força flexural dos espécimes foi avaliada através do teste de flexão de três pontos. Como resultados, as resinas fresadas (média = 109,95 MPa) e de poliamida (sem fratura) obtiveram os maiores valores de força flexural, enquanto a resina de impressão 3D apresentou os menores valores (71,70 MPa ± 7,38). Os autores concluíram que os materiais de fresagem apresentam características mecânicas superiores do que as resinas termicamente ativadas e as resinas de impressão 3D.

Mais recentemente, a tecnologia de sinterização direta de metal a laser (SML – *Direct Metal Laser Sintering*) tem sido utilizada para impressão de metais. Durante o processo de sinterização, um pó metálico passa por ciclos de fusão rápida, seguida de resfriamento e solidificação do metal. Este sistema busca contornar as desvantagens vinculadas à fresagem de metais, apresentando menor custo e menos desperdício de materiais, sem comprometer a qualidade final da peça (KOUTSOUKIS *et al.*, 2015; REVILLA LEÓN *et al.*, 2017). Assim, a tecnologia de impressão de metais tem se mostrado com grande potencial para substituir as técnicas convencionais de fundição e de fresagem de blocos metálicos.

2.4 Próteses Totais Assistidas por Engenharia Computadorizada (PTECs)

O método convencional de confecção de próteses totais apresenta vantagens inerentes como a customização da disposição de dentes artificiais no momento da consulta, e também a confirmação de etapas anteriores antes da continuação com as etapas seguintes da confecção (JACOB, 1998). Entretanto, o método convencional de fabricação apresenta desvantagens como a necessidade de, no mínimo, 5 etapas clínicas e 4 laboratoriais – além das consultas de preservação (o que aumenta o

tempo clínico necessário e por consequência os custos do tratamento) –, alta variação de custos laboratoriais e deficiência de contato íntimo com a mucosa devido à contração de polimerização do material de base (CHRISTENSEN, 2006).

O sistema CAD/CAM surgiu como uma nova abordagem para o desenho e fabricação de próteses totais convencionais mucossuportadas e próteses totais sobre implantes (INFANTE *et al.* 2014). Este método apresenta vantagens tanto para os pacientes edêntulos quanto para os dentistas, como redução do tempo clínico, redução do custo, além de reprodutibilidade (BIDRA; TAYLOR; AGAR, 2013).

Maeda *et al.* (1994) relataram pela primeira vez na literatura a utilização do sistema CAD/CAM para confecção de próteses totais, utilizando a tecnologia de prototipagem rápida com resinas polimerizadas por luz. A partir disso, diferentes metodologias de confecção de Próteses Totais Assistidas por Engenharia Computadorizada (PTECs) foram desenvolvidas (KAWAHATA *et al.*, 1997; SUN; LÜ; WANG, 2009). Assim, os sistemas digitais de fabricação de próteses totais começaram a ser desenvolvidos e comercializados, utilizando tanto o sistema de fresagem quanto o de prototipagem rápida, através de protocolos específicos de confecção de acordo com o fabricante (BIDRA; TAYLOR; AGAR, 2013).

Em 2014, Bidra descreveu pela primeira vez um relato de caso clínico de confecção de prótese total superior e sobredentadura mandibular por meio do sistema CAD/CAM, utilizando apenas duas visitas do paciente ao dentista. Na primeira consulta, foram realizadas as moldagens definitivas junto com o registro das relações maxilo-mandibulares (relação cêntrica e dimensão vertical de oclusão). Um *template* de plástico com a forma dos dentes anteriores foi adaptado sobre o leitor de plano de mordida para determinar a forma e o tamanho dos dentes anteriores. O conjunto obtido foi encaminhado ao fabricante (Avadent® Digital Dentures; Global Dental Sciences, EUA), que digitalizou o conjunto dando origem aos arquivos STLs. Os dentes artificiais foram dispostos digitalmente usando referências intraorais. A seguir, as bases das próteses foram fresadas e receberam dentes artificiais aderidos em locais definidos virtualmente. Na segunda consulta, as próteses foram instaladas, as quais adaptaram corretamente em boca, com mínimos ajustes necessários, simplificando o tratamento para apenas 2 etapas clínicas e 1 laboratorial.

Já em 2016, Bidra *et al.* realizaram um estudo clínico prospectivo para avaliar os desfechos clínicos e centrados no paciente durante a confecção de PTECs

monolíticas fresadas confeccionadas em 2 consultas. Vinte participantes com próteses totais superiores tendo como antagonistas próteses totais mandibulares ou sobredentaduras mandibulares já existentes foram selecionados. O protocolo de confecção de 2 próteses totais para cada paciente foi realizado, iniciando com a duplicação das próteses já existentes para servir de moldeira individual. A moldagem definitiva foi realizada com silicone de adição de consistência leve, seguida da colocação de cera sobre a duplicação da prótese na face vestibular e oclusal a fim de reestabelecer o suporte labial e concluir a reconstituição fisionômica. O registro das relações maxilomandibulares foi realizado, e um *template* de plástico com o formato de dentes para o paciente foi escolhido e adaptado sobre o plano de cera. O conjunto foi encaminhado ao laboratório do fabricante (AvaDent®, Global Dental Sciences, EUA). O conjunto foi escaneado e os dentes artificiais foram projetados virtualmente usando referências intraorais. As próteses totais monolíticas foram fresadas a partir de um bloco de PMMA pré-polimerizado. Na segunda consulta, os pacientes receberam as PTECs, e ajustes basais e oclusais foram realizados, sendo os casos com implantes mandibulares capturados no momento da instalação. Uma Escala Analógica Visual (VAS) foi utilizada para registrar 12 desfechos relacionados ao paciente no *baseline* e após um ano de acompanhamento, sendo considerados os valores acima de “70” favoráveis, com subdivisão entre excelente (90-100), bom (80 – 90) e razoável (70 – 80). Os desfechos clínicos foram avaliados por dois protesistas experientes no *baseline* e após 1 ano de acompanhamento. Os resultados mostraram diferença mínima entre o *baseline* e 1 ano de acompanhamento, sendo ambos avaliados favoravelmente. No entanto, a proporção de classificação de “excelente” e “boa” para satisfação geral e avaliação foi maior para pacientes do que para os cirurgiões-dentistas. Um tempo e esforço clínico considerável foram dedicados no processo de fabricação das PTECs. As próteses totais monolíticas CAD/CAM são uma opção clínica viável para pacientes edêntulos totais, porém os dentistas devem reconhecer a necessidade de uma cuidadosa seleção do paciente e de tempo adicional para o processo de fabricação. Assim, melhorias nos protocolos, experiência, e o uso de uma prótese de prova exigindo uma terceira consulta podem superar alguns dos desafios atuais.

A confecção de próteses totais utilizando métodos subtrativos tem se tornado mais comum, enquanto a técnica de manufatura aditiva de impressão 3D começou a

ser desenvolvida mais recentemente. Jurado *et al.* (2020) relataram um caso clínico em que se utilizou o sistema Dentca™ 3D (Dentca CAD/CAM Dentures, California, EUA) para confeccionar uma prótese total imediata. Uma paciente de 72 anos apresentou-se com a dentição da arcada superior comprometida periodontalmente. Na primeira consulta as moldagens das arcadas superior e inferior foram realizadas – ainda com a dentição remanescente em boca –, as relações intermaxilares foram registradas e por fim a montagem em articulador foi realizada. O articulador foi escaneado (D2000®, 3Shape, Dinamarca) e os arquivos STL foram enviados ao laboratório. Os elementos remanescentes foram removidos digitalmente, e os dentes digitais da prótese foram adaptados de acordo com a oclusão pré-estabelecida. A base da prótese total foi impressa, assim como todos os dentes (M2 SpeedCell Printer®, Carbon, EUA) e depois unidos por sistema adesivo. Por fim, a exodontia dos dentes foi realizada e a prótese instalada com sucesso, sem necessidade de reembasamento. Neste mesmo artigo (JURADO *et al.*, 2020), os autores relataram um outro caso clínico, e desta vez utilizando o sistema subtrativo AvaDent® (Global Dental Sciences, EUA) para confeccionar uma prótese total imediata fresada. Após escaneamento do conjunto e desenho virtual da prótese, o sistema de fresagem de blocos pré-polimerizados de PMMA resultou em uma prótese total imediata para a paciente, que foi instalada no dia da extração dos dentes e implantes dentários condenados, sem necessidade de realizar reembasamento clínico.

Kattadiyil e Al-Helal (2016), em uma revisão sistemática da literatura, buscaram responder às perguntas “*Quais são os desfechos clínicos associados às PTECs?*” e “*Quais as aplicações e vantagens significantes das PTECs?*”. Trinta e sete artigos revelaram uma melhora significativa da retenção das PTECs, além de significativa redução no tempo clínico para próteses fresadas, quando comparadas com as próteses totais convencionais. Além disso, uma grande vantagem encontrada a respeito as PTECs foi a possibilidade de armazenamento dos arquivos do paciente para posterior confecção de novas próteses totais.

Já a revisão sistemática da literatura realizada por Wang *et al.* (2020) avaliou os fatores que influenciam a acurácia das PTECs: a técnica de fabricação, o tipo de sistema CAD/CAM, o formato do modelo de referência, os serviços de longo prazo, método analítico e indicadores estatísticos. Quatorze (14) artigos reportaram valores clinicamente aceitáveis para a adaptação e veracidade das PTECs, apresentando

adaptação similar às próteses totais convencionais. A importância da técnica de fabricação, o sistema CAD/CAM escolhido e o serviço de longo prazo foram estatisticamente significativos em relação à precisão da prótese. Os autores afirmaram que não existem conclusões claras a respeito da superioridade das PTECs em relação às próteses convencionais.

2.4.1 Sistemas de Produção de PTECs

O processo de fabricação de Próteses Totais por Engenharia Computadorizada (PTEC) é exequível devido à uma coleta de dados realizada clinicamente por um cirurgião-dentista e processos de CAD/CAM realizados por um laboratório para confecção da prótese. Por ser uma área em crescimento exponencial, diversos sistemas de confecção de PTECs e marcas disponíveis no mercado surgiram, apresentando diferentes propostas e protocolos a serem seguidos (BABA *et al.*, 2016).

O primeiro relato de fabricante a desenvolver o sistema de PTECs e realizar a manufatura dessas peças foi a empresa norte-americana Dentca® (Denta Inc., EUA), a qual possui um protocolo clínico e laboratorial que utiliza materiais odontológicos específicos, técnicas de uso e suporte laboratorial (BIDRA; TAYLOR; AGAR, 2013; DENTCA - CAD/CAM DENTURE; DENTCA INC.). Este sistema utiliza a manufatura aditiva para confeccionar as bases das próteses totais, as quais possuem encaixes precisos para que posteriormente os dentes artificiais – também impressos (Dentca™ teeth) sejam aderidos (Figura 4A). Para seguir o protocolo do sistema, é necessário que o cirurgião-dentista realize moldagens definitivas e registro das relações maxilo-mandibulares utilizando moldeiras específicas do sistema. Estas moldeiras, além de receberem o material de moldagem, possuem encaixes que permitem determinar a dimensão vertical de oclusão do paciente, e posicioná-lo em posição de relação cêntrica. Utilizando um papilômetro, mensura-se a o comprimento do lábio em repouso a partir da papila incisiva. Assim, o material é enviado ao laboratório central da Dentca®, onde o desenho e impressão das próteses são realizados.

Um outro sistema de confecção de PTECs que com frequência é descrito na literatura é o sistema AvaDent® (Global Dental Science, EUA). Como opções de próteses oferecidas, apresentam-se as PTECs definitivas – confeccionadas através da manufatura subtrativa –, e próteses temporárias ou tipo “*try-in*”, que são próteses

feitas através da impressão 3D. Para as próteses definitivas fresadas, o sistema apresenta as possibilidades de fresagem apenas da base da prótese e posterior adesão de dentes à base (Figura 4B), como também a opção de fresagem de um bloco monolítico da cor dos dentes escolhidos para o paciente. Esta última opção recebe também a caracterização de gengiva, que pode ser feita através de pigmentos ou resinas com diferentes tons de gengiva. O sistema AvaDent® apresenta diferentes opções de sequências possíveis de procedimentos a serem realizados, permitindo a confecção de próteses em somente 2 consultas do paciente ao cirurgião-dentista (AVADENT DIGITAL DENTAL SOLUTIONS).

Para confecção de PTECs em duas consultas apenas, através do método de fresagem, é possível adotar o protocolo oferecido pelo Sistema de Próteses da Baltic® (Merz Dental GmbH®, Alemanha). Para isso, utiliza-se um dispositivo (BD KEY – Lock, Merz Dental GmbH®, Alemanha) que permite realizar as moldagens definitivas nos pacientes, além de registrar as relações verticais e horizontais da mandíbula. Assim, o laboratório realiza o desenho da peça protética utilizando programas de computador (BD Creator, Merz Dental GmbH®, Alemanha) e a fresagem de um bloco de resina para manufatura da base da prótese, a qual posteriormente recebe dentes pré-fabricados (Figura 4C). O cirurgião-dentista, portanto, recebe as próteses no consultório, proporcionando mais agilidade e previsibilidade no tratamento (BABA *et al.*, 2020; BALTIC DENTURE SYSTEM).

Outro sistema utilizado para confecção de PTECs é o Sistema Ivoclar Digital Dentures (Ivoclar Vivadent AG®, Liechtenstein). Para a manufatura das próteses, são possíveis protocolos que permitem a confecção das próteses em três ou quatro consultas, dependendo da preferência do clínico e verificação de parâmetros clínicos. Na primeira consulta do paciente, a moldagem definitiva do rebordo edêntulo é realizada, sendo possível utilizar como moldeira a duplicação da prótese antiga do paciente, além de parâmetros para montagem de dentes. Na segunda consulta, uma prótese “*try in*” impressa é adaptada no paciente, e os parâmetros ópticos, biológicos e funcionais são conferidos se estão no padrão adequado. Uma vez que a prótese “*try in*” é aprovada, o laboratório realiza a fresagem da prótese definitiva. Esta fresagem pode ser realizada de duas maneiras: (1) fresagem da base da prótese separadamente da fresagem dos dentes artificiais, e depois unidos por adesão com materiais específicos, ou (2) fresagem de um bloco pré-polimerizado monolítico com

duas cores – uma branca referente aos dentes artificiais, e outra rosa referente à base da prótese (Ivotion®, Ivoclar Vivadent AG®, Liechtenstein) (Figura 4D).



Figura 4. **A)** Sistema Dentca® 3D (Dentca®; Dentca Inc., EUA); **B)** Sistema AvaDent® (Global Dental Science®, EUA); **C)** Sistema Baltic® Denture System (Merz Dental GmbH®, Alemanha); **D)** Sistema Ivotion® Ivoclar Digital Dentures (Ivoclar Vivadent AG®, Liechtenstein).

Fontes: A) <https://dentca.com/products/dentca-3d>

B) <https://www.avadent.com/avadent/materials/>

C) <https://www.baltic-denture-system.de/en/dental-lab/>

D) <https://www.ivoclardigital.com/en/laboratory/material/removable-prosthetics>

2.4.2 Propriedades mecânicas das PTECs

Para que as próteses totais possuam um bom desempenho, é necessário que as propriedades mecânicas sejam favoráveis, devendo o material suportar a carga existente no momento do processo mastigatório. Algumas são as propriedades que devem ser avaliadas na escolha do material para a base da prótese, como o módulo de flexão, a tenacidade à fratura, resistência à tração, resistência à fratura, dureza e também a acurácia do material (LEE; LEE; ASAOKA, 2012).

Lee *et al.* (2019) avaliaram a acurácia de bases de prova fabricadas por diferentes métodos: técnica de injeção ($n = 10$), fresagem ($n = 10$) e impressão 3D ($n = 10$). Para isso, 10 modelos mestre foram confeccionados e escaneados. Para a técnica de injeção, as bases de prova que foram desenhadas em programa de computador foram fresadas em cera e fabricadas utilizando o sistema de injeção SR

Ivocap® (Ivoclar Vivadent AG, Liechtenstein) com resina PMMA (SR-Ivocap® high impact, Ivoclar Vivadent AG, Liechtenstein). Para a técnica de fresagem, as bases de prótese foram feitas utilizando uma fresadora de 5 eixos (ARUM® 5X-200, Doowon, Coréia do Sul) e bloco de PMMA (Vipi block GUM®, Vipi, São Paulo, Brasil). Já para o método de impressão, utilizou-se resina líquida de impressão NextDent® Base (NextDent®, Holanda), e uma impressora 3D DLP (Bio3D®. W1, Bio3D Inc., Coréia do Sul). A superfície das bases de prótese foram escaneadas e um programa de sobreposição de imagens foi utilizado para aferir a acurácia das diferentes técnicas, além de medidas feitas entre pontos e superfícies de entalhe pré-determinados para comparação de imagens. Os autores observaram que a acurácia do método de injeção foi menor que os dois outros métodos de fabricação ($p < 0,05$). A acurácia das bases de próteses feitas através de fresagem e impressão foi maior do que no método de injeção.

Arslan *et al.* (2018), através de um estudo *in vitro*, avaliaram a resistência à flexão, rugosidade de superfície e a hidrofobicidade de polímeros CAD/CAM à base de polimetilmetacrilato, e comparou as propriedades de diferentes polímeros CAD/CAM com PMMA termopolimerizável. Para isso, os autores confeccionaram um total de 60 espécimes de polímeros para fresagem: disco M-PM (Merz® Dental GmbH), disco AvaDent® Puck (Global Dental Science LLC), e disco Polident® CAD/CAM rosa Polident (Polident®, Slovenia) ($n = 20$ cada); e um polímero convencional termopolimerizável Promolux® (Merz® Dental GmbH) ($n = 20$). A rugosidade de superfície foi avaliada por um rugosímetro, a hidrofobicidade da superfície foi avaliada pelo ângulo de contato por meio de uma gota séssil, e a resistência à flexão foi avaliada em uma máquina de testes universal. Os polímeros de PMMA CAD/CAM mostraram resistência à flexão maior do que o PMMA convencional ($p < 0,001$), além de maior hidrofobicidade ($p < 0,001$). A rugosidade de superfície apresentada pelos diferentes tipos de espécimes foi semelhante ($p > 0,05$).

2.4.3 Propriedades ópticas das PTECs

As propriedades ópticas e colorimétricas dos materiais também devem ser levadas em consideração. Al-Qarni *et al.* (2019) avaliaram através de um estudo *in vitro* o manchamento de resinas acrílicas CAD/CAM utilizadas em próteses totais, e

compararam com resinas acrílicas convencionais termicamente ativadas. Os espécimes de bases de prótese total foram confeccionados através de 3 métodos: compressão (Lucitone® 199, Dentsply Sirona) ($n = 15$), injeção (IvoBase®, Ivoclar Vivadent AG) ($n=15$), e fresagem CAD/CAM (AvaDent®, Global Dental Sciences, EUA) ($n = 15$). Todos os espécimes foram imersos em café, vinho tinto e água destilada (controle), e a diferença de cor antes e depois de imergir nas soluções foi determinada através do sistema de cor CIELab, utilizando um espectrofotômetro portátil (VITA Easyshade®). Os espécimes obtidos por injeção de resina apresentaram menor mudança de cor após exposição ao vinho tinto quando comparados aos fresados e obtidos por compressão ($p < 0,001$). Em relação ao manchamento relacionado à imersão em café, os espécimes fresados não apresentaram diferença estatística em comparação aos grupos de injeção ($p = 0,053$) e compressão ($p = 0,180$). Assim, os autores puderam afirmar que os resultados de manchamento de resina fresada não foram melhores do que os materiais convencionais.

Em um estudo semelhante, Dayan *et al.* (2019), avaliaram a estabilidade de cor de 60 espécimes de resinas termicamente ativadas (Paladent®, Kulzer Mitsui Chemicals Group), 60 espécimes de resinas de impressão 3D (Eclipse®, Dentsply) e 60 blocos de resina PMMA CAD/CAM fresadas (discos M-PM®, Merz Dental). Para isso, os espécimes de cada grupo foram randomizados e alocados em diferentes meios de armazenamento (café, coca, vinho tinto e água destilada), seguido de avaliação de cor em 7 e 30 dias, antes e depois do armazenamento, através de um espectrofotômetro. As variações de cor (ΔE) foram menores nas resinas de base de prótese fresada (média = 0.89 ΔE), em todos os tipos de armazenamento. Assim, o estudo concluiu que a estabilidade de cor das bases de prótese fresadas é melhor do que outros tipos de resina investigados.

2.4.4 Propriedades biológicas das PTECs

A liberação de monômero residual e a aderência microbiana são parâmetros biológicos importantes para o sucesso em longo prazo dos materiais utilizados para confecção de base de prótese total. Ayman (2017) avaliaram *in vitro* a quantidade de monômero residual em resinas para bases de prótese do tipo CAD/CAM. Para isso, um total de 70 espécimes foram fabricados e divididos em dois principais grupos: A)

PMMA termicamente ativado (Vertex RS[®], Dentimex) ($n = 35$) e B) Blocos de resina PMMA para fresagem (Polident[®]) ($n = 35$). A quantidade de monômero residual foi avaliada através de cromatografia por gás no *baseline*, após dois dias e após sete dias. Uma maior quantidade de monômero residual foi detectada no grupo das resinas termicamente ativadas, nos diferentes intervalos de tempo ($p < 0,001$). A redução do teor de monômero residual nas resinas do tipo CAD/CAM pode ser atribuída ao método de polimerização sob alta pressão, a qual proporciona benefícios biológicos e físicos. Os autores concluíram que o PMMA para fresagem é uma resina clinicamente adequada para a construção de bases de próteses.

Al-Fouzan, Al-Mejrad e Albarrag (2017) realizaram um estudo laboratorial que comparou a aderência de *Candida albicans* na superfície de resinas convencionais e CAD/CAM para bases de próteses totais. Dez discos de PMMA convencional termopolimerizável (Major Base[®] 20), e dez discos de PMMA CAD/CAM (Wieland Digital Denture[®], Ivoclar Vivadent) para fresagem foram confeccionados. A colonização de *Candida* foi realizada em todos os espécimes, e o número de células de leveduras aderidas foi calculado através das Unidades Formadoras de Colônia (UFCs) e por microscopia de fluorescência. Os resultados mostraram que as resinas de bases de prótese do tipo CAD/CAM exibiram menor aderência de *Candida albicans* do que as resinas convencionais ($p < 0,05$). Os autores sugerem, portanto, que o processo CAD/CAM de fabricação de próteses totais mostra grande potencial de redução de aderência de *Candida albicans* na superfície da base da prótese, e consequentemente diminuir a incidência de estomatite protética.

3 OBJETIVOS

3.1 Objetivo Geral

O objetivo deste estudo foi responder, por meio de uma revisão sistemática da literatura, às seguintes perguntas de pesquisa: 1. “Quais são os desfechos clínicos de Próteses Totais por Engenharia Computadorizada (PTECs) comparados às Próteses Totais Convencionais?”, e 2. “Quais são os desfechos mecânicos, ópticos e biológicos de Próteses Totais por Engenharia Computadorizada (PTECs) comparados às Próteses Totais Convencionais?”

3.2 Objetivos Específicos

- Comparar os desfechos clínicos de Próteses Totais confeccionadas por Engenharia Computadorizada (PTECs) com Próteses Totais Convencionais (PTCs);
- comparar *in vitro* os desfechos mecânicos de Próteses Totais confeccionadas por Engenharia Computadorizada (PTECs) com Próteses Totais Convencionais (PTCs);
- comparar *in vitro* os desfechos ópticos de Próteses Totais confeccionadas por Engenharia Computadorizada (PTECs) com Próteses Totais Convencionais (PTCs);
- comparar *in vitro* os desfechos biológicos de Próteses Totais confeccionadas por Engenharia Computadorizada (PTECs) com Próteses Totais Convencionais (PTCs).

4 ARTIGO CIENTÍFICO

Este trabalho foi escrito na forma de artigo científico e preparado de acordo com as normas para submissão ao periódico *Dental Materials* (Qualis A1, Fator de impacto 4.070).

COMPUTER-ENGINEERED COMPLETE DENTURES (CECDs): A SYSTEMATIC REVIEW OF THE CLINICAL AND LABORATORY OUTCOMES

Running title: *CAD/CAM Complete Dentures*

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Authors' Contributions:

Dr. Gabriela Sabatini worked on study conceptualization, design, data collection, data and statistical analysis, drafted the initial manuscript and approved the final manuscript as submitted.

Dr. Adriana Bezerra worked on data collection, data and statistical analysis, drafted the initial manuscript and approved the final manuscript as submitted.

Dr. Tarla Taynara Oliveira dos Santos worked on drafting the initial manuscript and approving the final manuscript as submitted.

Dr. Franciele Floriani worked on risk of bias assessment, drafted the initial manuscript and approved the final manuscript as submitted.

Dr. Analucia Philippi worked on drafting the initial manuscript and approving the final manuscript as submitted.

Dr. Thais Gonçalves worked on drafting the initial manuscript and approving the final manuscript as submitted.

Dr. Luis André Mezzomo worked on study conceptualization, design, data analysis, drafted the initial manuscript and approved the final manuscript as submitted.

Conflict of Interest

The authors declare that have no conflict of interest.

ABSTRACT

Objectives: To answer the following questions: 1. “*What are the clinical outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*”, and 2. “*What are the mechanical, biological and optical outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*”

Data: Clinical and laboratory data on *study-, sample-, intervention- and outcome* characteristics.

Sources: An electronic search was performed in nine databases, added by hand- and gray literature searches.

Study Selection: Two reviewers selected studies based on eligibility criteria. A blinded third reviewer assessed risk of bias and the cumulative quality of evidence. Meta-analysis was conducted using the random-effects model at a 5% significance level.

Results: 197 patients with 164 CECDs and 124 CCDs, and 1,327 CECD milled, 190 CECD printed, 908 compressed and 242 injected samples, were available for descriptive and statistical analysis. CECDs provided patients the benefits of a reduced

number of appointments and overall costs, as well as an increased satisfaction and comfort. Random-effects meta-analysis revealed better results for CAD/CAM milled samples with regards to flexural strength ($p = 0.004$), flexural modulus ($p < 0.001$) and stainability in water ($p = 0.02$) and coffee ($p = 0.02$). Contact angle, elastic modulus, surface roughness and fracture toughness showed non-significant better results for CAD/CAM milled samples ($p = 0.48$, $p = 0.36$, $p = 0.55$, $p = 0.43$, respectively).

Conclusions: CECDs are an efficient solution for the treatment of edentulous patients. High-performance PMMA CAD/CAM milled samples showed overall better mechanical, optical and biological properties.

Keywords: complete denture, denture bases, polymethyl methacrylate, computer-aided design, three-dimensional printing, systematic review

1. INTRODUCTION

Replacement of missing teeth with complete dentures has been reported to result in significant improvement in the quality of life of edentulous patients [1]. Conventional complete dentures (CCDs) are a type of prosthesis that present advantages such as the recovery of aesthetic parameters and chewing capacity [2]. Despite that, the deficiency in retention and stability is a recurrent complaint of patients rehabilitated with CCDs, in addition to the poor nutritional status and oral health perception [3]. Thus, implant-retained overdentures and fixed implant-supported prosthesis became the “*state-of-art*” option for edentulous patients to improve the masticatory efficiency and quality of life [4], [5], [6].

The digital workflow became a viable solution in Dentistry for planning and manufacturing prosthetic rehabilitations [7],[8]. The Computer-Aided Imaging/Design/Manufacturing (CAI/CAD/CAM) processes raised some advantages compared to the conventional workflow, including enhanced patient comfort, cost savings and elimination of time consuming steps [9]. CAI involves scanning data of patient’s intraoral hard and soft tissues that are converted to virtual impressions in a Standard Triangle Language (STL) format. This process can be made intraorally or indirectly from a desktop scanner by means of scanning either a conventional impression or a stone model. The CAD process involves de digital prosthetic design in

computer softwares, followed by the CAM manufacturing processes (milling or rapid prototyping).

CAD/CAM milling is a subtractive process that became popular in the manufacturing of inlays/onlays restorations, single crowns and complete dentures [10], [11], [12], [13]. Some advantages offered by the milling process include precision, accuracy and high flexural strength [13], [14]. On the other hand, the CAD/CAM printing, or rapid prototyping, is defined as an additive process that consists of polymerizing liquid acrylic resin layer by layer until yielding the final object [15]. Little material disposal and low maintenance cost are some of the advantages of this method [16].

There has been an increasing number of publications assessing clinical and *in vitro* outcomes of denture bases resins of Computer-Engineered Complete Dentures (CECDs), mainly focused on the comparison between milling PMMA blocks and printing resins [13], [17], [18], [19], [20]. Kattadiyil *et al.* (2015) [21], in a prospective clinical study, showed that the CAD/CAM denture treatment proved an equally effective and more time-efficient option when compared to the conventional process of complete denture fabrication.

Relevant outcomes related do CECDs have been assessed by previous systematic reviews. Kattadiyil & Al-Helal (2016) [22] revealed a significant improvement in retention of CECDs when compared to CCDs, besides the reduction in clinical time fabrication. Wang *et al.* (2020) [23] evaluated *in vitro* studies with details about the accuracy of CECDs. The majority of the studies have shown better adaptation and trueness of CECDs when compared to conventional CCDs, despite no clear conclusions can be drawn about the superiority of CAD/CAM milling and 3D printing regarding denture accuracy. Yet, an up-to-date, comprehensive and thorough systematic review that combined both clinical and *in vitro* outcomes associated with materials used for the fabrication of CECDs and fixed provisional full-arch implant-supported prosthesis is lacking. Therefore, this systematic review aimed at answering the following two focused questions: 1. “*What are the clinical outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*” and 2. “*What are the mechanical, biological and optical outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*”

2. MATERIALS AND METHODS

2.1. Protocol and Registration

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement ^[24]. A study protocol was elaborated and registered at the International Prospective Register of Systematic Reviews (PROSPERO) under number CRD42020180318.

2.2. Eligibility Criteria

Two focused questions were formulated based on the PICOS acronym (Population, Intervention, Comparison, Outcomes, Studies). The first one, where *P*: Edentulous patients, *I*: Computer-assisted (either milling or printing) manufacturing (CAM) methods, *C*: Conventional manufacturing method, *O*: primary (prosthesis-centered-outcomes, patient-centered outcomes, service-centered) and secondary outcomes, and *S*: Clinical (prospective experimental and observational) studies with a sample size of at least 10 dentures/specimens per group that assessed the clinical outcomes of computer-engineered complete dentures (CECDs) compared to those of conventionally-manufactured complete dentures (CCDs, control) were included. The second focused formulated question included *P*: Materials used for complete dentures, *I*: Computer-assisted (either milling or printing) manufacturing (CAM) methods, *C*: Conventional manufacturing method, *O*: primary (*in vitro* outcomes) and secondary outcomes, and *S*: *in vitro* studies with a sample size of at least 10 dentures/specimens per group that assessed the clinical, mechanical, biological and optical outcomes of computer-engineered complete dentures (CECDs) compared to those of conventionally-manufactured complete dentures (CCDs, control) were included. No restrictions of language or time of publication were applied. The following exclusion criteria were applied: 1) Studies with less than 10 samples (dentures or specimens) per group; 2) absence of comparative group; 3) studies that employed either self-curing acrylic resin or provisional materials as control group; 4) Retrospective studies; 5) Studies with missing data and/or not provided by the author after contact; 6) Studies not focused in denture bases outcomes; 7) Duplicated publication from the same study;

8) Reviews, letters, conference abstract, personal opinions, technique articles and clinical trials registrations.

2.3. Information Sources and Search Strategy

A comprehensive literature search was conducted applying individual search strategies for each of the following databases: PubMed/Medline, Embase, Latin American and Caribbean Health Sciences (LILACS), Scopus, Web of Science, and The Cochrane Library (CENTRAL). A grey literature search on Google Scholar, Proquest and Open Grey databases as well as hand-search of the references of the included studies were also performed. Additionally, experts were consulted in order to improve search findings. References were collected, and the duplicates were removed by using an appropriate software (EndNote® X9, Thomson Reuters, USA). Thereafter, references were organized and screened using Rayyan QCRI (Qatar Computing Research Institute, Qatar)^[25].

2.4. Study Selection

Study selection was performed by two independent reviewers (G.P.S. and A.P.B.) in a two-phase process. In phase one, titles and abstracts were screened and studies that did not fulfill eligibility criteria were excluded. In phase two, eligibility criteria were applied to the full texts of the studies. Any disagreement was resolved by discussion until mutual agreement between the two reviewers. If necessary, the third reviewer (L.A.M.M.) was involved to solve disagreements.

2.5. Data Collection Process

Two reviewers (G.P.S. and A.P.B.) independently collected data from included studies. Any controversies were discussed with a third reviewer (L.A.M.M.). Data collected according to the design of the study (clinical or laboratory) consisted of: 1) *Clinical studies* - study characteristics (author, year of publication, study design, country), population characteristics (sample size, gender distribution, age (mean and range), jaw location, and brands of CAD/CAM and conventional groups), intervention

characteristics (fabrication protocol of CAD/CAM and Conventional groups, clinical outcomes assessed, unit of measurement and test device) and outcome characteristics (retention of denture base, nonscheduled-postinsertion adjustment visits, prosthesis biofilm, PROMs, masticatory efficiency, clinical time spent, costs) and 2) *Laboratory studies* - study characteristics (author, year of publication, country), sample characteristics (sample size, material characteristics – type and brands of resins), intervention characteristics (storage parameters, assessments) and outcome characteristics (mean and standard deviations of mechanical, optical and biological outcomes). To retrieve any pertinent unreported information up to three attempts on a weekly basis were made to contact corresponding authors.

2.6. Risk of Bias in Individual Studies

Methodological quality and risk of bias were independently assessed by a blinded examiner (F.F.) using different critical appraisal tools, according to each study design. Cochrane Collaboration's Tool (Risk of Bias 2, Rob 2) [26] was used to analyze the randomized clinical trials, whereas the non-randomized clinical trials as well as the laboratory (*in vitro*) studies were assessed by means of The Joanna Briggs Institute Critical Appraisal Checklist For Quasi-Experimental (Non-Randomized Experimental Studies) [27] tool. Decisions about scoring were agreed upon by all reviewers before critical appraisal assessments, and studies were characterized according to the following: risk of bias was categorized as "high" when the study reached up to 49% score "yes"; "moderate" when the study reached 50% to 69% score "yes"; and "low" when the study reached more than 70% score "yes". Figures were made using the software RevMan® 5.3 (Review Manager 5.3, The Cochrane Collaboration) [28].

2.7. Confidence in Cumulative Evidence

A summary of the overall strength of evidence available was presented and analyzed using "Grading of Recommendations Assessment, Development and Evaluation" (GRADE) based on the rating of risk of bias, consistency, directness, precision, and

publication bias. A summary of findings table was generated using the online software GRADEpro[®] GDT (The GRADE Working Group, BMC Health Services Research).

2.8. Statistical Analysis

The means, standard deviations and confidence intervals from the original articles were extracted. Whenever possible, meta-analysis was performed. When not possible, a detailed descriptive analysis was performed. The data extracted from the original studies were considered as continuous. When more than one resin brand was investigated in either test or control group, the weighted average and standard deviation mean were performed according to Cochrane instructions (The Cochrane Collaboration) [28]. The weighted mean (WM) and its respective 95% confidence intervals (95% CI) were used as a measure of effect size (deviation). The meta-analysis was conducted using the random-effects model. Statistical heterogeneity was assessed using I^2 (95% CI) [28]. The I^2 was interpreted according to the general rule as low (25%), moderate (50%) and high (75%) (Higgins *et al.* 2003). All analyzes were conducted using the software RevMan[®] 5.3 (Review Manager 5.3, The Cochrane Collaboration) [28].

3. RESULTS

3.1 Study selection

Final electronic search was conducted on the 19th of August 2020. From main electronic database searches, a total of 2,710 references were identified (details of the search strategy as well as the results for each database are given in Appendix 1). A total of 1,315 articles remained for phase one after duplicated studies had been removed. Among the titles and abstracts read in phase one, 59 articles were selected for phase two (full-text reading) (Kappa score = 0.81). Thirty-eight (38) articles met all the inclusion criteria and were considered for qualitative synthesis. In addition, 4 articles were manually selected for qualitative synthesis. Twenty-one references were excluded and the reasons for exclusion are listed in Appendix 2. The complete process of identification and selection of studies is provided in the flowchart in Figure 1.

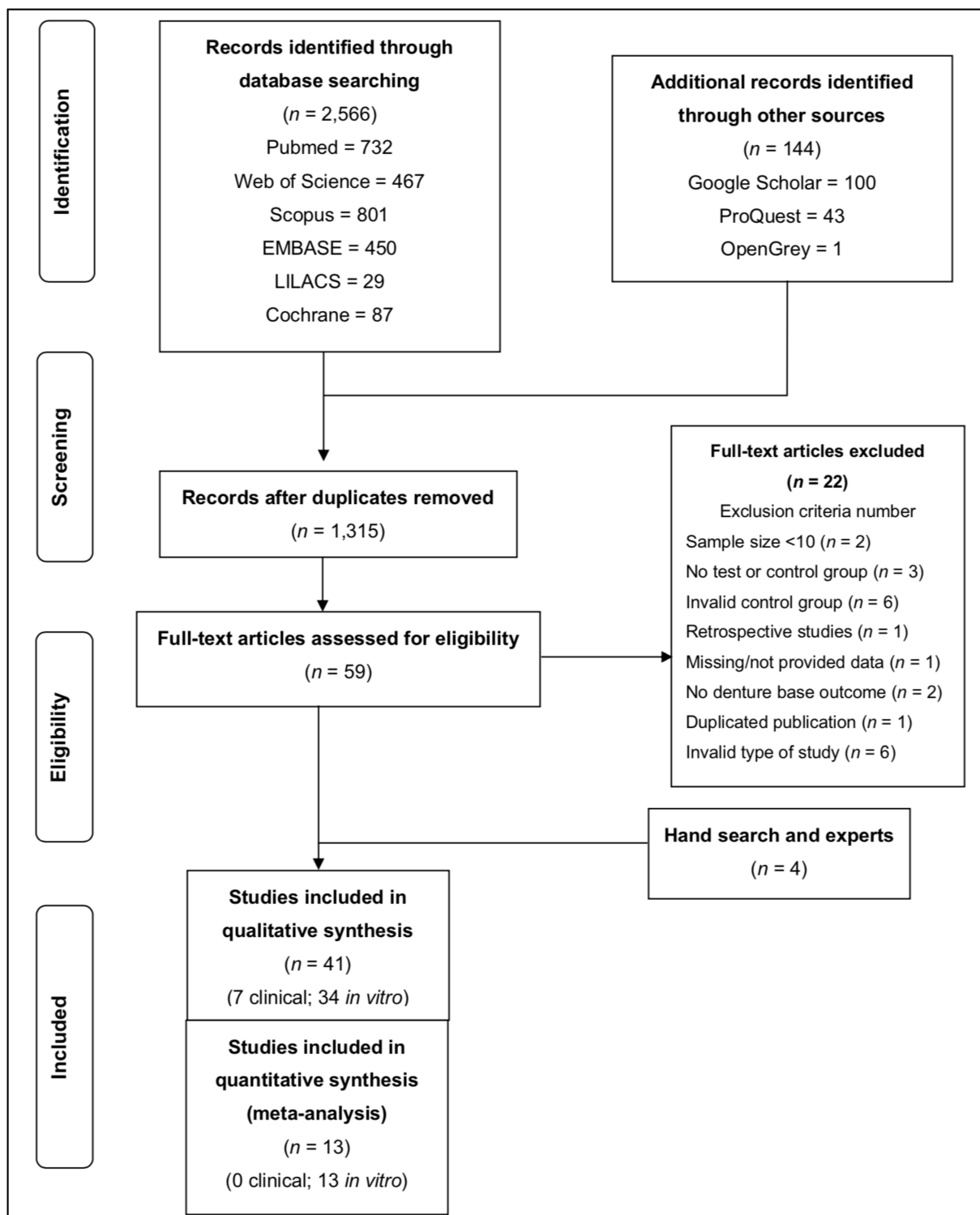


Figure 1. Flowchart of the screening and selection processes of the study.

3.2. Study Characteristics

3.2.1. Clinical studies

Seven (7) clinical studies met the eligibility criteria and were included for data extraction. They came from USA [21], [29], [30], [31], Saudi Arabia [32], China [33] and Switzerland [34]. The publication year ranged between 2015 and 2020. The study by Ling *et al.* (2020) [33] was originally published in Chinese, but authors kindly managed to provide an English version of the manuscript after contact by e-mail. The total population sample size was 197 patients receiving 164 CECDs and 124 CCDs, who were assessed before and after prosthetic treatment. A summary of the characteristics of included clinical studies is given in Table 1.

3.2.1.1. Service-Oriented Outcomes

3.2.1.1.1. Number of appointments

Drago & Borgert (2019) [30] compared in a one-year clinical study the number of nonscheduled postinsertion adjustment visits of patients rehabilitated with CECDs and CCDs. One hundred and six patients were included. Thirty-three patients received injection molded dentures, and the other 73 were milled using a CAD/CAM system. All the patients were scheduled for 1- or 2-week postinsertion office visits. The additional visits were assessed by a dental assistant that reviewed the charts and recorded the requisite data up to 1 year after insertion of the new dentures. The authors observed that approximately one half ($n = 56$) of all participants returned for scheduled postinsertion visits approximately 1 to 2 weeks after insertion of the dentures, and that return visits for unscheduled adjustments were not associated with the method of denture fabrication or any other demographic features ($p = 0.55$).

3.2.1.1.2. Clinical chairside spent and overall costs

Srinivasan *et al.* (2018) [34] evaluated the clinical time spent and the costs (in CHF – Swiss francs) incurred whilst constructing eighteen CAD/CAM complete dentures (two-

visit digital-denture protocol) compared to the conventional protocol for constructing the same amount of complete dentures, dividing into two groups of participants: 1. only upper denture; and 2. both the upper and lower denture. The costs involved with clinical procedures, materials, and laboratory were calculated, and cost minimization analysis was performed to compare the economic costs of the two protocols. The authors observed that conventional complete denture protocol required significantly longer clinical time than digital complete dentures in both groups (1. $p = 0.02$; 2. $p = 0.002$), but clinical materials costs were significantly higher for the digital complete dentures in both groups (1. $p < 0.0001$; 2. $p = 0.0002$). However, after evaluating the overall costs (clinical materials + laboratory fees), the conventional complete denture protocol showed significantly higher costs than digital denture protocol (1. $p = 0.0032$; 2. $p = 0.008$). Therefore, the authors concluded that the digital denture protocol is less costly (clinical + laboratory expenses) when compared with the conventional complete denture protocol.

3.2.1.1.3. Faculty and Predoctoral Preferences

In Kattadiyil *et al.* (2015) ^[21] study, fifteen predoctoral dental students fabricated 2 sets of maxillary and mandibular complete dentures for each patient: one of them CECD, and the other one a CCD. Then, the students were questioned which type of denture they preferred. The digital was the students' preferred method for fabricating complete dentures, and their considerations were especially related to “*no required laboratory work*” for fabricating 3D dentures, and “*improved festooning and denture base finish*”.

3.2.1.2. Prosthesis-Oriented Outcomes

3.2.1.2.1. Retention of denture base

AlHelal *et al.* (2017) ^[32] evaluated the retention of twenty CAD/CAM maxillary denture bases and twenty conventional maxillary denture bases installed in a total of twenty patients with a history of edentulism in the maxilla for a minimum period of 1 year. For conventional denture base, a heat-polymerized resin was applied (Lucitone 199; Dentsply Intl.), while for CAD/CAM denture base, the AvaDent® System (Global Dental Sciences, USA) was employed. To evaluate the retention, the authors used a test

device system that included: (1) a digitally advanced force gauge (Series 5 force gauges; Mark-10 Corp., USA) to read the force required to dislodge each denture base; (2) a motorized test stand (ESM301L[®], Mark-10 Corp., USA) to standardize the pulling rate; (3) a force transmission device made of a hollow aluminum rod with a pulley at each end; and (4) a Panadent[®] facebow (Panadent[®] Corp., USA). After three retention assessments of each denture base, the mean value of milled group was 74.14 ± 32.56 N, while compression group was 54.23 ± 27.36 N. The authors suggest that the retention offered by CAD/CAM milled pre-polymerized PMMA complete denture bases was significantly higher ($p < .001$) than that of conventional heat-polymerized denture bases, and that a milled denture base might be an appropriate choice when increased retention is required.

3.2.1.2.2. Masticatory efficiency

Ling *et al.* (2020)^[33], after evaluation of twenty edentulous patients that received two pairs of complete dentures (one CAD/CAM and one conventional), tested the masticatory efficiency of each pair of dentures after a 3- months adaptation period for each type of dentures. The masticatory performance of the CAD/CAM denture (1.20 ± 0.54 absorbance value) was slightly higher than that for the conventional denture (1.16 ± 0.53), but the difference did not reach statistical significance ($p = 0.691$).

3.2.1.2.3. Level of prosthesis biofilm

In the study by Jia-Mahasap (2017)^[31], where fourteen patients received conventional dentures and 14 patients received CAD/CAM dentures (AvaDent[®], Global Dental Science, USA), the level of prosthesis biofilm was assessed. After 1 month of usage, plaque samples were collected from the intaglio surfaces of maxillary complete dentures at 1 month post-delivery to culture for any colonization of bacteria and/or yeasts. The author concluded that there was no significant difference in microbial counts between two treatment groups (Total Aerobic microbials – $p = 0.4622$; Total Anaerobic microbials – $p = 0.2507$).

3.2.1.3. Patient-Reported Outcome Measures (PROMs)

Coffey (2018) ^[29] evaluated patient perception as it relates to (1) denture fabrication process; (2) extra-oral esthetics; (3) intra-oral esthetics; (4) patient phonetic satisfaction; (5) denture choice within different classes of edentulism; (6) patient functional satisfaction. Two sets of dentures were fabricated for each of 10 selected patients: 1 set of conventional and 1 set of CAD/CAM dentures. An intra-individual comparison was made regarding the clinical fabrication appointments, at prosthesis delivery appointment and after a 3 months usage of each type of denture. The responses were categorized and compared to determine any differences in patient satisfaction with esthetics, phonetics, and function. Due to the small number of participants, analysis for statistical significance was limited. However, based on descriptive observations both types of prostheses had positive attributes related to patient perceptions. At the end of the study, three patients would keep the 3D dentures, while 6 patients would keep the conventional one.

Jia-Mahasap (2017) ^[31] evaluated in a randomized clinical trial the satisfaction and quality of life of twenty-eight patients using OHIP-EDENT and patient satisfaction questionnaires. Fourteen patients received conventional dentures and wore for 1 month, and another 14 patients received CAD/CAM dentures (AvaDent[®], Global Dental Science, USA) and wore for 1 month. The questionnaires were applied at baseline and at 1 month of usage. There was a significant reduction in almost all OHIP-EDENT domains scores within both treatment groups at the 1 month follow-up ($p < 0.05$). The authors suggest there was no significant difference in patient satisfaction between CAD/CAM and conventional dentures groups both at baseline and at the 1 month visit for almost all aspects of satisfaction ($p > 0.05$).

Kattadiyil *et al.* (2015) ^[21] clinically compared CECDs with CCDs clinical treatment outcomes, patient satisfaction, and dental student preferences for digitally and conventionally processed in a predoctoral setting. Each of fifteen patients received one conventional set and one digital (AvaDent[®]) set of complete denture. The students' preferences and perceptions (CAD/CAM x conventional prosthesis) were recorded and analyzed. The authors suggest that significantly higher average scores were observed for digital dentures than for conventional dentures according to criteria evaluated by faculties ($p = 0.007$). Patients reported significantly higher overall average satisfaction

scores with digital dentures ($p = 0.001$), and related their preference to the digital dentures ($p < 0.01$).

Ling *et al.* (2020)^[33], in a prospective clinical trial, evaluated twenty edentulous patients that received two pairs of complete dentures: one CAD/CAM and one conventional fabrication workflow. The patients wore the conventional dentures for 3 months, and then swapped to wear digital dentures. Visual Analogue Scale (VAS) and Oral Health Impact Profile (OHIP-20) were applied to evaluate patients' satisfaction and Oral Health Related Quality of Life (OHRQoL) at baseline, 2 weeks, 1 month, 2 months, and 3 months following denture delivery. The authors concluded that there were no significant differences between the CAD/CAM group and conventional dentures group in VAS scores, and some of the OHIP-20E scores three months following denture delivery. Thus, the clinical efficacy of the CAD/CAM complete denture is not inferior to the conventional complete denture.

Table 1. Summary of descriptive characteristics of included clinical studies.

Study Charac.	Population Characteristics	Intervention Characteristics			Outcome Characteristics			
		Systems	Fabrication Protocol		Assessments	CAD/CAM	Conventional	Main Conclusions
First Author, Year Study Design Country	Participants 1. <i>n</i> of participants 2. <i>n</i> of CAD/CAM dentures 3. <i>n</i> of conventional dentures 4. Gender (♂; ♀) 5. Age (mean;range) 6. Jaw location (Maxilla/ Mandible/ Both) 7. Confounding Factors (YES/NO)	1. CAD/CAM Milled 2. CAD/CAM printed 3. Conventional (compression) 4. Conventional (injection)	CAD/CAM	Conventional	1. Clinical Outcome 2. Unit of Measurement 3. Assessment Tool(s)	1. Milled 2. Printed	1. Compression 2. Injection	
Al-Helal 2017 CCT Saudi Arabi	1. <i>n</i> = 20 2. <i>n</i> = 20 3. <i>n</i> = 20 4. 11♂; 9♀ 5. 68.2 yrs 6. Maxilla 7. NO	1. AvaDent [®] 2. - 3. Lucitone 199 [®] 4. -	Preliminary impression; Definitive impression; molding scanning; CAD/CAM denture base fabrication	Preliminary impression; Definitive impression; pouring; thermo-polymerization denture base fabrication	1. Retention of denture base 2. Newton (N) 3. Force gauge/ motorized test stand/ force transmission device/Panadent facebow	1. 74.14 ± 32.56 N 2. -	1. 54.23 ± 27.36 N 2. -	Retention of Milled pre-polymerized PMMA bases was significantly higher than conventional heat-polymerized bases and, thus, might be considered the first option when a higher retention is required.
Coffey 2018 CCT	1. <i>n</i> = 10 2. <i>n</i> = 10 3. <i>n</i> = 10 4. 10♂; 8♀ 5. 59.1 yrs (50-72)	1. Unclear 2. - 3. Lucitone [®] 199 [®] 4. -	Final impressions and joint relation record; CAD CAM denture try-in; Insertion of CAD CAM dentures and surveys	Initial impressions; Border molding of custom tray; Final impressions; Joint relation record; Tooth	1. Patient perception 2. Points in Likert scale, and categorized responses	1. Functional limitation: 80% Physical Pain: 67%	1. Functional limitation: 82% Physical Pain: 70%	More participants preferred the conventionally fabricated dentures over the digitally fabricated dentures. The digital denture fabrication process

USA	6. Both 7. NO		try-in; Insertion of conventional fabricated dentures and survey	3. OHIP questionnaire	Psychological discomfort: 71% Physical disability: 83% Psychological disability: 86% Social disability: 89%	Psychological discomfort: 80% Physical disability: 79% Psychological disability: 78% Social disability: 84%	2. -	2. -	results in more discomfort when compared to conventional means of fabrication.
Drago 2019	1. n = 106 2. n = 73 3. n = 33 4. 40♂; 66♀ 5. 56 (29-83) 6. Both = 65 participants 7. NO	1. AvaDent ^f 2. - 3. - 4. Ivocap [☆]	Preliminary scanning and impression; Definitive scan and impression/custom trays and jaw-relation records; Biofunctional (Ava- Dent CORE [®] ; Global Dental Sciences) evaluation (white milled dentures); Insertion	Preliminary impressions; Definitive impressions / custom trays; Jaw-relation records/tooth selection; Wax evaluation; Insertion.	1. Comparison of nonscheduled, postinsertion adjustment visits 2. (A) Number of patients for unscheduled denture adjustments e appointments; (B) Average time (wk) for first, second, third and fourth unscheduled visit after insertion 3. Review of the charts and record the requisite data up to 1 year after insertion of the new dentures	1. (A) 16 patients (22%) (B) First: 8.6, 10 patients Second: 6.3, 4 patients Third: 6.8, 4 patients Fourth: 11.8, 4 patients	1. - 2. (A) 7 patients (21%) (B) First: 4.8, 14 patients Second: 12.4, 9 patients Third: 9, 3 patients Fourth: 6.5, 2 patients	2. -	No differences in the number of unscheduled, postinsertion visits for participants treated with dentures made following either a CAD-CAM or conventional (injection) molding protocol were detected.
CCT									
USA									
Jia-Mahasap 2017	1. n = 28 2. n = 14 3. n = 14	1. AvaDent ^f 2. - 3. -	Preliminary impressions (obtain OHIP-EDENT form); Final impression,	Preliminary impressions (OHIP-EDENT form; Border	1. Patient satisfaction, quality	1. (A) Baseline: 31.56 (19.63)	1. (A) Baseline: 33.69 (19.66)		1. There was no significant difference on oral health-related to quality of life

Digital dentures
placement

Ling <i>et al.</i> 2020	1. <i>n</i> = 20 2. <i>n</i> = 20 3. <i>n</i> = 20 4. 8♂; 12♀ 5. 71.45 yrs 6. Both 7. NO	1. Unclear 2. - 3. Unclear 4. -	Unclear	Unclear	1. Patient satisfaction and oral health-related quality of life at (A) baseline, (B) 2 weeks, (C) 1 month, (D) 2 months, (E) 3 months and Masticatory efficiency 2. Score 3. Visual Analogue Scale/Score (VAS) and the Oral Health Impact Profile (OHIP-20E)	1. VAS: (A) 61.64 (22.35) (B) 85.95 (24.40) (C) 88.00 (12.39) (D) 92.00 (7.21) (E) 92.80 (7.12) OHIP: (A) 15.84 (6.15) (B) 11.78 (5.45) (C) 11.94 (4.88) (D) 11.25 (4.30) (E) 10.31 (3.55) Masticatory efficiency 1.20 ± 0.54 2. -	1. OHIP: (A) 15.84 (6.15) (B) 9.45 (3.00) (C) 8.78 (1.45) (D) 9.33 (4.48) (E) 8.25 (1.55) VAS: (A) 61.64 (22.35) (B) 86.70 (13.69) (C) 88.85 (14.13) (D) 87.55 (15.89) (E) 92.20 (10.74) Masticatory efficiency 1.16 ± 0.53 2. -	Clinical outcomes for CAD/CAM dentures fabricated using FSD were compared with conventional complete denture favorably at a 3-month follow-up. There is no significant difference after patient had worn dentures for three months at score of VAS, masticatory efficiency, and part score of OHIP-20E.
Srinivasan <i>et al.</i> 2018	1. <i>n</i> = 18 2. <i>n</i> = 18 3. <i>n</i> = 18 4. Unclear 5. Unclear 6. Maxillary = 12 Maxillary and mandible = 24 7. NO	1. AvaDent [®] 2. - 3. Unclear 4. -	Capturing all the clinical records required for denture construction; Denture insertion	Preliminary impression; Custom tray was checked for fit and extension followed by border moulding; Master impression; Face bow transfer, recording of vertical and horizontal jaw relations, aesthetic parameters, and tooth selection; Verify the anterior tooth setup	1. (A) Clinical time spent and (B) the costs incurred 2. (A) Hours (B) Swiss francs 3. (A) Stopwatch (B) Math formula	1. (A) Upper CD: 5.5 ± 0.6 hours Upper & Lower CD: 6.9 ± 0.6 hours (B) Upper CD: 954.17 ± 110.45 - Upper & Lower CD: 1999.26 ± 505.39 2. -	1. (A) Upper CD: 7.3 ± 1.2 hours Upper & Lower CD: 10.7 ± 0.9 hours (B) Upper CD: 688.26 ± 16.88 Upper & Lower CD: 1022.70 ± 74.09 2. -	The digital denture protocol is less costly when compared with the conventional complete denture protocol. The costs for clinical chairside time, laboratory and the overall costs were significantly lower for the digital denture protocol, even though the materials costs for this protocol were higher.

intraorally; Final try-in
of the completed set-
up; Denture insertion

[£] AvaDent[®], Global Dental Science, USA. ^{**} Ivoclar Vivadent AG[®], Liechtenstein. [°]Dentsply Sirona[®], USA

3.2.2. Laboratory (*in vitro*) studies

3.2.2.1. Mechanical Outcomes

Twenty-nine (29) controlled *in vitro* studies assessing mechanical outcomes met the eligibility criteria and were included for data extraction. They came from USA [35], [36], [37], [38], [39], [40], [41], [42], Jordan [14], [43], Saudi Arabia [44], [45], Austria [46], [47], [48], [49], Switzerland [50], [51], New Zealand [52], [53], Korea [13], [17], Istanbul [54], China [55], Lebanon [20], Turkey [56], France [57], Finland [19] and Croatia [58]. The publication period ranged between from 2014 to 2020. The overall sample size was 1,182 CAD/CAM milled, 130 CAD/CAM printed, 763 Conventional (Compression) and 227 Conventional (Injection) samples. A summary of the mechanical outcomes of the *in vitro* studies is given in Table 2.

Table 2. Summary of descriptive characteristics of included in vitro studies - Mechanical outcomes.

Study Charac.	Sample Characteristics					Interventions Characteristics	Outcomes Characteristics				
First Author, Year, Country	Features: 1. Shape 2. Dimensions 3. <i>n</i> total	CAD/CAM Group		Conventional Group		1. Storage Parameters 2. Assessments	Flexural Strength (Mpa) – Mean (\pm SD)		Surface Roughness (Ra) – Mean (\pm SD)		Main Conclusions
		Milled	Printed	Compression	Injection		CAD/CAM	Conventional	CAD/CAM	Conventional	
Aguirre <i>et al.</i> 2019 USA	1. Rectangle 2. 64x10x3.3mm 3. <i>n</i> = 30	1. <i>n</i> = 10 2. Vertex PMMA [£] (<i>n</i> = 10)	1. - 2. - 3. -	1. <i>n</i> = 10 2. Lucitone 199 [°] (<i>n</i> = 10)	1. <i>n</i> = 10 2. SR Ivocap High Impact * (<i>n</i> = 10)	1. Distilled water at 37°C for 1 week before testing 2. 3-point bend test	1. 146.6(6.6) 2. -	1. 116.6 (3.1) 2. 86.7 (7.1)	1. - 2. -	1. - 2. -	CAD-CAM milled denture resin exhibited higher flexural strength than the two conventional processing methods. The injection molded resin displayed pronounced deformation before fracture with a lower flexural modulus, whereas the CAD-CAM milled and compression molded resin fractured with minimal to no plastic deformation.
Al-Dwairi <i>et al.</i> 2018 Jordan	1. Rectangle 2. 65x10x3mm 3. <i>n</i> = 45	1. <i>n</i> = 30 2. AvaDent PMMA [£] (<i>n</i> = 15) 3. Tizian PMMA [€] (<i>n</i> = 15)	1. - 2. - 3. -	1. <i>n</i> = 15 2. Meliodent [∞] (<i>n</i> = 15)	1. - 2. - 3. -	1. Distilled water at 37°C for 1 week before testing 2. 3-point bend test	1.1. AvaDent: 123.1 (9.4) 1.2. Tizian: 130.6 (10.4) 2. -	1. 93.33 (8.6) 2. -	1. - 2. -	1. - 2. -	CAD/CAM PMMA groups exhibited significant improvement in flexural strength, impact strength, and flexural modulus when compared to the conventional heat-cured group. No significant difference was found between the two CAD/CAM materials tested.

Al-Dwairi <i>et al.</i> 2019 Jordan	1. Rectangle 2. 25x25x3mm 3. <i>n</i> = 45	1. <i>n</i> = 30 2. AvaDent® PMMA [£] (<i>n</i> = 15) 3. Tizian® PMMA [€] (<i>n</i> = 15)	1. - 2. - 3. -	1. <i>n</i> = 15 2. Meliodent [∞] (<i>n</i> = 15)	1. - 2. - 3. -	1. Distilled water for 48 hours 2. Sessile drop method and Vickers hardness	1.1. - 1.2. - 2. -	1. - 2. -	1.1.. 0.16 (0.03) 1.2. 0.12 (0.02) 2. -	1. 0.22 (0.07) 2. -	CAD/CAM PMMA groups exhibited significantly higher surface hardness and hydrophobicity in comparison to the heat-polymerized group. The AvaDent CAD/CAM PMMA group demonstrated the highest surface hardness (VHN), while the Tizian Schutz group registered the lowest Ra value for surface roughness.
Al-Fouzan <i>et al.</i> 2017 Saudi Arabia	1. Disk-shaped 2. 10x3mm 3. <i>n</i> = 20	1. <i>n</i> = 10 2. Wieland PMMA [★] (<i>n</i> = 10)	1. - 2. - 3. -	1. <i>n</i> = 10 2. MajorBase20 [†] (<i>n</i> = 10)	1. - 2. - 3. -	1. The discs were cleaned with water and soap using a regular toothbrush followed by a steam jet. 2. Polishing compact unit	1. - 2. -	1. - 2. -	1. 0.037 (0.001) (Sa) 2. -	1. 0.073 (0.015) (Sa) 2. -	The surface characteristics of complete dentures fabricated with the CAD/CAM procedure exhibited promising potential for reducing the adherence of <i>Candida</i> to the denture base surface.
Alp <i>et al.</i> 2018 USA	1. Rectangle 2. 25x2x2mm 3. <i>n</i> = 45	1. <i>n</i> = 30 2. M-PM- Disc* (<i>n</i> =15) 3. Polident PMMA ^Σ (<i>n</i> = 15)	1. - 2. - 3. -	1. <i>n</i> =15 2. Art Concept ArtDentine* (<i>n</i> = 15)	1. - 2. - 3. -	1. Distilled water at 37°C for 24h before testing 2. After Thermocycling	1.1. 131.9 (19.8) 1.2. 113.0 (16.9) 2. -	1. 66.1 (13.1) 2. -	1. - 2. -	1. - 2. -	The flexural strength of CAD/CAM PMMA-based polymers was greater than the flexural strength of bis-acrylate composite resin, which had greater flexural strength compared to conventional PMMA interim resin material.
Arslan et al. 2019	1. Rectangle 2. 64x10x3.3mm 3. <i>n</i> = 80	1. <i>n</i> = 60 2. M-PM- Disc*	1. - 2. - 3. -	1. <i>n</i> = 20 2. Promolux* (<i>n</i> = 20)	1. - 2. - 3. -	1. Humid incubator at 37°C for 24 hours before baseline	1.1. 122.4 (5.5) [†] 114.5 (5.8) [*]	1.1. 108.9 (5.3) [†] 1.2. 98.8 (6.3) [*]	1.1. 0.21 (0.07) [†]	1.1. 0.22 (0.07) [†] 1.2. 0.29 (0.09) [*]	CAD/CAM PMMA-based polymers showed significantly higher flexural strength than that

Turkey	(n = 20) 3. AvaDent PMMA [£] (n = 20) 4. Polident PMMA ^Σ (n = 20)					color measurements. 2. Three-point bending test, profilometric contact surface measurement device	1.2.118.3 (4.6) ⁺ 106.7 (3.3) [*] 1.3.133.4 (5.9) ⁺ 125.8 (3.9) [*] 2. -	2. - 2. -	0.18 (0.04) [*] 1.2. 0.22 (0.06) ⁺ 0.24 (0.04) [*] 1.3. 0.26 (0.09) ⁺ 0.32 (0.08) [*] 2. -	2. - 2. -	of conventional resin before and after thermal cycling. Thermal cycling resulted in decreased flexural strength for all denture base polymers. There were no significant differences among the surface roughness of tested denture base polymers before thermal cycling. Thermal cycling did not have a significant effect on the surface roughness of denture base polymers.
Murat <i>et al.</i> 2019 Turkey	1. Disk-Shaped 2. 10x2mm 3. n = 160	1. n = 120 2. M-PM-Disc* (n = 40) 3. AvaDent PMMA [£] (n = 40) 4. Polident PMMA ^Σ (n = 40)	1. - 2. - 3. -	1. n = 40 2. Promolux* (n = 40)	1. - 2. - 3. -	1. All specimens were subjected to 10,000 thermal cycling processes (5-55°C; 30-second dwell times) 2. Profilometric contact surface measurement device	1. - 2. -	1. - 2. -	1.1. 0.18 (0.04) 1.2. 0.20 (0.05) 1.3. 0.21 (0.04) 2. -	1. 0.34 (0.06) 2. -	CAD/CAM PMMA-based polymers showed less surface roughness, hydrophobicity, and Candida adhesion when compared to conventional heat-polymerized PMMA in uncoated groups.
Pacquet <i>et al.</i> 2019 France	1. Rectangle 2. 65x10x2.5mm 40x4x2 mm 3. n = 75	1. n = 25 2. IvoBase CAD [☆] (n = 25)	1. - 2. - 3. -	1. n = 25 2. Probase Hot [☆] (n = 25)	1. n = 25 2. Ivocap High Impact [☆] (n = 25)	1. Distilled water at 37°C for 24 hours 2. 3-point bend test, binocular microscope	1. 87.9 (7.3) 2. -	1. 97.3 (4.9) 2. -	1. 79.3 (10.0) 2. -	1. - 2. -	CAD mechanical properties result from the evolution of denture base materials, combining high-impact fracture toughness and improved flexural strength and hardness.
Patel <i>et al.</i> 2014	1. Rectangle 2. 64x10x2-, 3- or 5-mm	1. n = 15 2. Lucitone 199 [£]	1. - 2. - 3. -	1. n = 15 2. Lucitone 199 [°] (n = 15)	1. n = 15	1. Injection - flask was submerged in	1.1. 2mm: 75.9 1.2. 3mm:	1.1. 2mm: (no fracture) 1.2. 3mm:	1. - 2. -	1. - 2. -	Statistically significant difference was found between flexural strength of acrylic processed by

USA	40x4x2 mm 3. <i>n</i> = 45	(<i>n</i> = 15)			2. SR Ivocap High Impact * (<i>n</i> = 15)	water at 165°F for 9 hours 2. 3-point bend test	72.8 1.3. 5mm: 90.8 2. -	65.3 1.3. 5mm: 77.4 2.1 2mm: 77.3 2.2. 3mm: 88.8 2.3. 5mm: 103.2			CAD/CAM and Injection Mold with Injection Mold technique being superior.
Perea-Lowery <i>et al.</i> 2020 Finland	1. Rectangle and square 2. 65×3.2×10 mm 2×10×10 mm 3. <i>n</i> = 128	1. <i>n</i> = 96 2. L-Temp [§] (<i>n</i> = 32) 3. IvoBase CAD* (<i>n</i> =32) 4. Temp Basic Tissue* (<i>n</i> = 32)	1. - 2. - 3. -	1. <i>n</i> = 32 2. Paladon 65 [∞] (<i>n</i> = 32)	1. - 2. - 3. -	1. Half of the specimens were stored in water at 37 C for 30 days. The other half were dry stored for an equal number of days under ambient laboratory conditions (23 ±1 C) 2. Unclear	1.1. Water: 145.7 (12.68) Dry: 119.8 (5.6) 1.2. Water: 116.1 (4.23) Dry: 88.4 (9.1) 1.3. Water: 79.1 (3.43) Dry: 62.9 (3.2) 2. -	1.1. Water: 122.2 (13.0) 1.2. Dry: 143.9 (5.8) 2. -	1. - 2. -	1. - 2. -	The tested materials showed variation in their mechanical properties with satisfactory behavior of the CAD-CAM materials. The use of materials used for the conventional fabrication of complete dentures might still be advisable.
Prpic' <i>et al.</i> 2020 Croatia	1. Rectangle and square 2. 64 × 10 × 3.3 3. <i>n</i> = 80 [†]	1. <i>n</i> = 30 2. IvoBase CAD* (<i>n</i> = 10) 3. Interdent CC disc PMMA* (<i>n</i> = 10)	1. <i>n</i> = 10 2. NextDent Base* (<i>n</i> = 10)	1. <i>n</i> = 30 2. Probase Hot* (<i>n</i> = 10) 3. Paladon 65 [∞] (<i>n</i> = 10) 4. Interacryl Hot* (<i>n</i> = 10)	1. <i>n</i> = 10 2. Vertex ThermoSens [◇] (<i>n</i> = 10)	1. Water bath for 50 ±1 hour at 37°C. 2. Three-point flexure test; Zwick apparatus	1.1. (no fracture) 1.2. 111.9 (4.29) 1.3. 108.0 (6.88)	1. 71.70 (7.38) 2. -	1.1. 88.0 (8.9) 1.2. 76.2 (7.8) 1.3. 93.8 (8.3)	1. - 2. -	Polyamide and CAD/CAM materials exhibited higher flexural strength than heat-polymerized and 3D-printed acrylics. Materials with the same polymerization type can have different mechanical properties

		(n = 10) 4. Polident PMMA Σ (n = 10)				2. -		2. -		and 3D-printed acrylics have lower mechanical properties than most other denture base materials.	
Srinivasan <i>et al.</i> 2018 Switzer- land	1. Square, Square and rectangle 2. 11x11x2 mm; 20x20x1.5mm; 65x10x3mm 3. n = 60	1. n = 30 2. AvaDent PMMA ξ (n = 30)	-	1. n = 30 2. Aesthetic Red* (n = 30)	-	1. The specimens were placed in 70% ethanol solution for 5 min, and subsequently dried with sterile cotton. They were sterilized for 60 min under ultra-violet light with a wavelength of 254 nm emitted by a 15 watt UV lamp 2. Biocompatibility assays, Nanoindentation test; Three-point bending test and Laser profilometry	1. 71 (6) 2. -	1. 54 (11) 2. -	1. 0.37 (0.03) 2. -	1. 0.12 (0.29) 2. -	The tested CAD/CAM PMMA resin is equally biocompatible and presented with improved mechanical properties than the traditional heat-polymerized PMMA resin used in the fabrication of CRDPs. With its improved mechanical properties, the CAD/CAM resin may be suitable for a wider range of prosthetic designs specifically in special clinical indications.
Steinmass <i>l et al.</i> 2018c Austria	1. Complete Dentures 2. - 3. n = 50	1. n = 40 2. AvaDent PMMA ξ (n = 10) 3. Baltic PMMA* (n = 10) 4. Whole You	-	1. n = 10 2. Aesthetic Red* (n = 10)	-	1. The resin specimens were stored in 100 mL of deionized water for 7 days at a temperature of 21°C in darkness to simulate the intraoral situation	1. - 2. -	1. - 2. -	1.1. 0.28 (0.16) 1.2. 0.44 (0.13) 1.3. 0.04 (0.01) 1.4. 0.30 (0.10)	1. 0.55 (0.14) 2. -	Although most CAD/CAM dentures have smoother and more hydrophilic surfaces than conventional dentures, there is no difference regarding the free surface energy, except for coated dentures. These surface properties might make CAD/CAM denture surfaces less

Nexteeth PMMA coated ^Δ (<i>n</i> = 10) 5. Wieland PMMA [★] (<i>n</i> = 10)	2. Unclear	2. -	attractive for microbial colonization.
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[†] No Thermocycling* After Thermocycling. ^{**} After Thermocycling 1.200 cycles. [†] *n* total = 160; *n* = 80 for evaluation of flexural strength, and *n* = 80 for evaluation of surface hardness. [£] AvaDent[®], Global Dental Science, USA. [€] Shutz Dental[®], Germany. [★] Ivoclar Vivadent AG[®], Liechtenstein. ^{*} Merz Dental GmbH[®], Germany. ^Σ Polident[®], Slovenia. [§] Degos Dental GmbH[®], Germany. ^{*} Zirkonzahn[®], Italy. ^{*} Interdent[®], Slovenia. ^Δ Whole You[®], USA. [°] Dentsply Sirona[®], USA. ^{*} NextDent[®], Netherlands. [∞] Haerus Kulzer[®], Germany. [°] Major Prodotti Dentare[®], Italy. ^{*} Candulor[®], Switzerland. [◊] Vertex Dental[®], Netherlands.

3.2.2.1.1. Flexural Strength

3.2.2.1.1.1. CAD/CAM x Conventional (Compression)

A total of 257 CAD/CAM milled samples and 168 conventional compressed samples from eight studies were available for statistical analysis. Details of the main findings of flexural strength from all eight studies are given in Table 1. None study provided CAD/CAM printed samples for this specific comparison. The study by Ayman *et al.* (2017) ^[45] was excluded from the analysis due to an outlier information, and the study by Patel *et al.* (2014) ^[35] was excluded due to a completely different methodology. In Bedrossian's *et al.* (2019) ^[40] study, values of control group were applied. CAD/CAM (milled) samples revealed significantly higher mean flexural strength values (110 MPa; 95% CI: 106.78 – 113.22) than conventional (compression) samples (93.55 MPa; 95% CI: 89.87– 97.23) ($p = 0.004$). The overall standard mean difference was 1.99 MPa (95%CI: 0.63 - 3.35) (Figure 2A). The heterogeneity (I^2) of the studies was 96% ($\text{Chi}^2 = 186.11$; $\text{df} = 7$; $p < 0.00001$).

3.2.2.1.1.2. CAD/CAM x Conventional (Injection)

A total of 35 CAD/CAM milled samples and 35 conventional compressed samples from two studies were available for comparison purposes. None study provided CAD/CAM printed samples for this specific comparison. CAD/CAM (milled) samples revealed higher mean flexural strength values (104.72 MPa; 95% CI: 95.52 – 113.92) than conventional (injection) samples (81.45 MPa; 95% CI: 78.21 – 84.69), but this difference was not statistically significant ($p = 0.22$). The overall standard mean difference was 4.51 MPa (95%CI: -2.74 – 11.76) (Figure 2B). The heterogeneity (I^2) of the studies was 95% ($\text{Chi}^2 = 22.18$; $\text{df} = 1$; $p < 0.00001$).

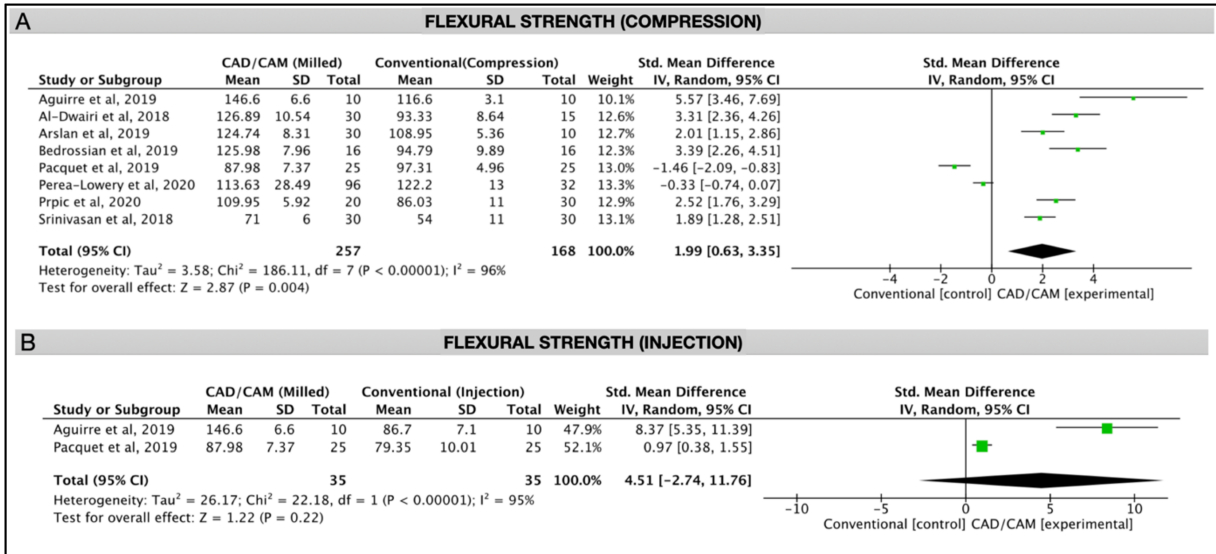


Figure 2. Forest plot of the flexural strength values of: (A) CAD/CAM milled x Conventional (Compression) groups, and (B) CAD/CAM milled x Conventional (Injection) groups.

3.2.2.1.2. Flexural Modulus

A total of 105 CAD/CAM milled samples and 90 conventional compressed samples from four studies were available for statistical analysis. None study provided neither CAD/CAM printed samples nor conventional (injection) samples for this specific comparison. CAD/CAM milled samples revealed significantly higher mean flexural modulus values (2.79 MPa; 95% CI: 2.71– 2.87) than conventional (compression) samples (2.17 MPa; 95% CI: 2.05– 2.29) ($p < 0.001$). The overall standard mean difference was 9.04 MPa (95%CI: 4.89 - 13.18) (Figure 3). The heterogeneity (I^2) of the studies was 98% (Chi² = 165.92; df = 3; $p < 0.001$).

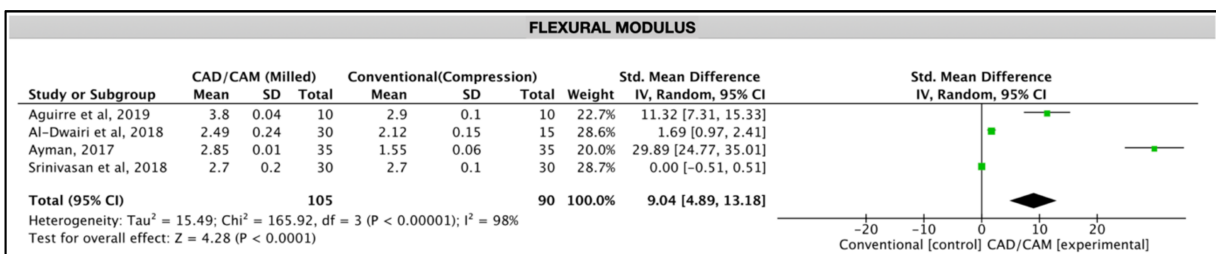


Figure 3. Forest plot of the flexural modulus values of CAD/CAM milled and Conventional (compression) groups.

3.2.2.1.3. Elastic Modulus

A total of 176 CAD/CAM milled samples and 72 conventional compressed samples from three studies were available for statistical analysis. None study provided neither CAD/CAM printed samples nor conventional (injection) samples for this specific comparison. CAD/CAM milled samples revealed higher mean elastic modulus values (5.00 GPa; 95% CI: 4.86 – 5.14) than conventional (compression) samples (4.74 GPa; 95% CI: 4.44– 5.04), without statistically significant difference ($p = 0.36$). The overall standard mean difference was 0.28 GPa (95%CI: -0.32 – 0.87) (Figure 4). The heterogeneity (I^2) of the studies was 93% ($\text{Chi}^2 = 28.30$; $\text{df} = 2$; $p < 0.00001$).

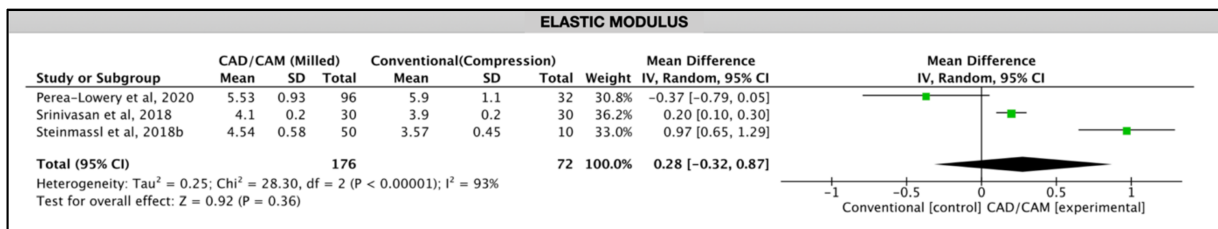


Figure 4. Forest plot of the elastic modulus values of CAD/CAM milled and Conventional (compression) groups.

3.2.2.1.4. Surface Hardness

3.2.2.1.4.1. CAD/CAM x Conventional (Compression)

A total of 246 CAD/CAM milled samples and 167 conventional compressed samples from six studies were available for statistical analysis. None study provided CAD/CAM printed samples for this specific comparison. Conventional (compression) samples revealed higher mean surface hardness values (17.49 VHN; 95% CI: 16.93 – 18.05) than CAD/CAM milled samples (17.43 VHN; 95% CI: 16.83 – 18.03), but this was not statistically different ($p = 0.13$). The overall standard mean difference was 1.20 VHN (95%CI: -0.37 - 2.77) (Figure 5A). The heterogeneity (I^2) of the studies was 98% ($\text{Chi}^2 = 204.57$; $\text{df} = 5$; $p < 0.00001$).

3.2.2.1.4.2. CAD/CAM x Conventional (Injection)

A total of 55 CAD/CAM milled samples and 35 conventional injected samples from two studies were available for statistical analysis. CAD/CAM printed samples were not retrieved from original studies for this specific comparison. CAD/CAM milled samples revealed significantly higher mean surface hardness values (15.91 VHN; 95% CI: 14.92 – 16.90) than conventional (injected) samples (13.99 VHN; 95% CI: 12.45–15.53) ($p < 0.00001$). The overall standard mean difference was 2.41 VHN (95%CI: 1.84 – 3.71) (Figure 5B). The heterogeneity (I^2) of the studies was 0% ($\text{Chi}^2 = 0.77$; $\text{df} = 1$; $p = 0.38$).

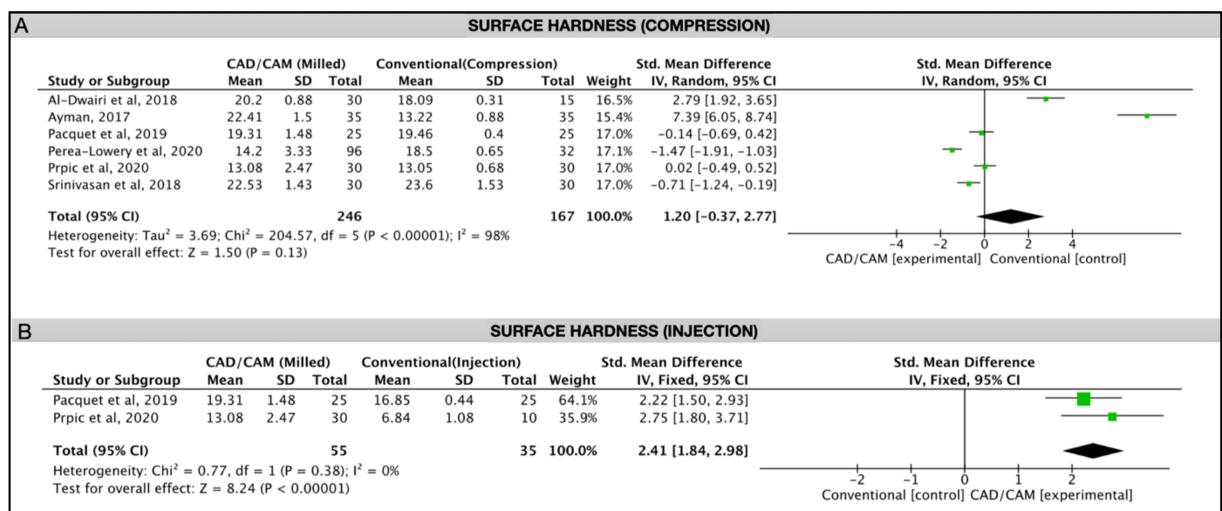


Figure 5 Forest plot of the surface hardness values of: (A) CAD/CAM milled x Conventional (Compression) groups, and (B) CAD/CAM milled x Conventional (Injection) groups.

3.2.2.1.5. Surface Roughness

A total of 120 CAD/CAM milled samples and 65 conventional compressed samples from four studies were available for statistical analysis. Details of the main findings of flexural strength from all four studies are given in Table 1. None study provided neither CAD/CAM printed samples nor conventional (injection) samples for this comparison. CAD/CAM milled samples revealed higher mean surface roughness values (0.27 Ra; 95% CI: 0.25 – 0.29) than conventional (compression) samples (0.22 Ra; 95% CI: 0.16 – 0.28) ($p = 0.55$), but this difference was not statistically significant. The overall standard mean difference was -0.44 Ra (95%CI: -1.86 – 0.98) (Figure 6). The heterogeneity (I^2) of the studies was 94% ($\text{Chi}^2 = 51.47$; $\text{df} = 3$; $p < 0.00001$).

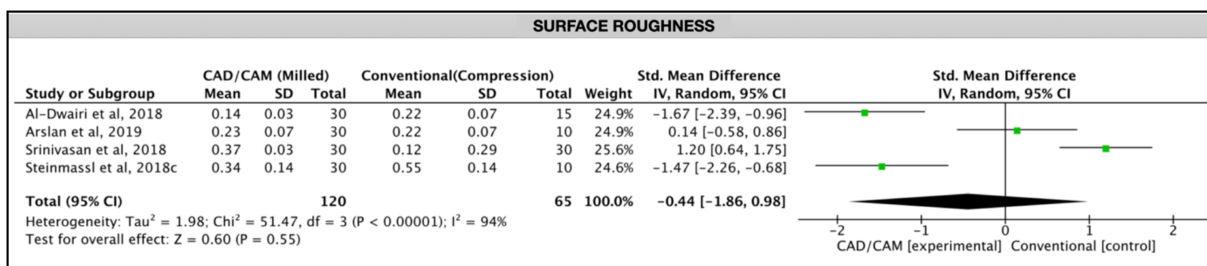


Figure 6. Forest plot of the surface roughness values of CAD/CAM milled and Conventional (compression) groups.

3.2.2.1.6. Fracture Toughness

A total of 85 CAD/CAM milled samples and 35 conventional compressed samples from two studies were available for statistical analysis. None study provided neither CAD/CAM printed samples nor conventional (injection) samples for this comparison. CAD/CAM milled samples revealed higher mean fracture toughness values (1.41 Mpa x m^{1/2}; 95% CI: 1.29 – 1.53) than conventional (compression) samples (1.36 Mpa x m^{1/2}; 95% CI: 1.31 – 1.41) ($p = 0.43$). The overall standard mean difference was 1.30 Mpa x m^{1/2} (95%CI: -1.90 – 4.50) (Figure 7). The heterogeneity (I²) of the studies was 97% (Chi² = 36.62; df = 1; $p < 0.00001$).

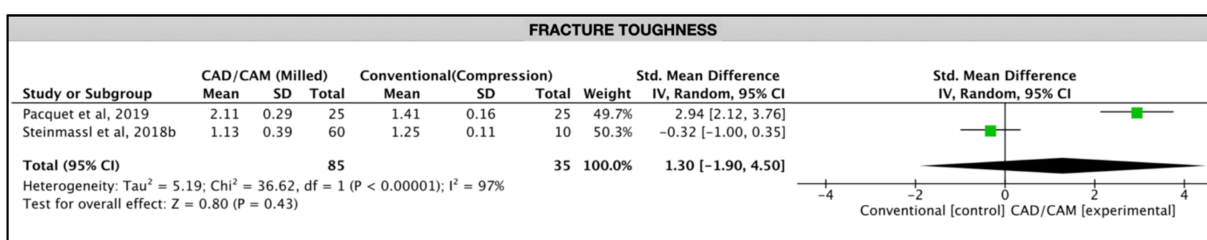


Figure 7. Forest plot of the fracture toughness values of CAD/CAM milled and Conventional (compression) groups.

3.2.2.1.7 Other mechanical outcomes

Al-Dwairi *et al.* (2018) ^[43] evaluated the *impact strength* of two commercial brands of CAD/CAM PMMA – AvaDent[®] PMMA (AvaDent[®], Global Dental Science, USA) and Tizian[®] PMMA (Shutz Dental[®], Germany) –, and a conventional heat-cured PMMA

Meliodont® (Haerus Kulzer®, Germany). The authors concluded that CAD/CAM PMMA specimens exhibited improved impact strength in comparison to the conventional heat-cured groups, expecting CAD/CAM dentures to be more durable.

Srinivasan *et al.* (2018) ^[51] assessed the *ultimate strength* and *young's modulus* of two types of resins: CAD/CAM milled AvaDent® PMMA (AvaDent®, Global Dental Science, USA) and conventional compression Aesthetic Red® (Candulor®, Switzerland). The groups presented different results, favoring the CAD/CAM milled group when both outcomes were evaluated (ultimate strength – $p = 0.0004$; young's modulus $p = 0.002$). Steinmassl *et al.* (2018b) ^[48] investigated the difference in *breaking load* and *fracture surface roughness* between a conventional compression resin – Aesthetic Red® (Candulor®, Switzerland) – and five CAD/CAM resins: AvaDent® PMMA (AvaDent®, Global Dental Science, USA); Baltic® PMMA (Merz Dental GmbH®, Germany); Vita Vionic® Base (Vita Zahnfabrik®, Germany); Wieland® PMMA (Ivoclar Vivadent AG®, Liechtenstein) and Whole You Nexteeth® PMMA (Whole You®, USA). Only Wieland® PMMA resin showed a significantly increased breaking load. Besides that, this resin showed the roughest fracture surface

The *nanohardness* of three CAD/CAM milled resins and one conventional compressing resin was assessed by Perea-Lowery *et al.* (2020) ^[19]. No difference in nanohardness was found when comparing IvoBase® CAD (Ivoclar Vivadent AG®, Liechtenstein) with Temp Basic Tissue® (Zirkonzahn®, Italy) ($p = 1.000$). Within other evaluated results, the authors concluded that the tested materials showed variation in their mechanical properties, with satisfactory behavior of the CAD/CAM materials.

Steinmassl *et al.* (2018c) ^[49] investigated the *hydrophilicity* and *free surface energy* of five CAD/CAM resins – AvaDent® PMMA (AvaDent®, Global Dental Science, USA); Baltic® PMMA (Merz Dental GmbH®, Germany); Vita Vionic Base (Vita Zahnfabrik®, Germany); Wieland® PMMA (Ivoclar Vivadent AG®, Liechtenstein) and Whole You Nexteeth® PMMA (Whole You®, USA) – besides one type of conventional compression resin Aesthetic Red® (Candulor®, Switzerland). The authors concluded that CAD/CAM dentures have smoother surfaces than conventional dentures, but there is no difference in their free surface energy.

Choi *et al.* (2018) ^[52] measured the *tensile bond strength* and *durability* of various combinations of 3 different *resilient denture liners* bonded to 3 different polymethyl-methacrylate denture base materials. The CAD/CAM resin IvoBase® CAD (Ivoclar

Vivadent AG[®], Liechtenstein) and the conventional thermo-curing resin Vertex[®] RS (Vertex Dental[®], Netherlands) were combined with 3 resilient denture liners (Ufi Gel[®] SC, Silagum-Comfort[®], and Vertex Soft[®]), and later the tensile bond strength between them was tested by a universal testing machine. The authors concluded that silicone-based resilient denture liners produced the highest tensile bond strength to all denture bases tested, whereas resilient denture liners bonded to CAD-CAM denture bases produced the weakest tensile bond strengths.

Choi *et al.* (2019) ^[53] evaluated the *denture teeth flexural bond strength* to heat-cured Vertex[®] RS (Vertex Dental[®], Netherlands), CAD/CAM milled IvoBase[®] CAD (Ivoclar Vivadent AG[®], Liechtenstein) and 3D printed denture resin Dima Print[®] Denture Base (Kulzer[®], USA). The authors observed that the bond strength decreased significantly with aging, and the teeth bonded to CAD/CAM milled and 3D printed denture base resins showed significantly lower bond strength, with no significant influence of aging.

McLaughlin, Ramos & Dickinson (2017) ^[38] compared the *shrinkage of denture bases* fabricated by three methods: CAD/CAM milled resin (AvaDent[®] PMMA, AvaDent[®], Global Dental Science, USA), conventional compression resin (Lucitone[®] 199, Dentsply Sirona[®], USA) and conventional injected IvoBase[®] Hybrid (Ivoclar Vivadent AG[®], Liechtenstein). The study showed that injection molding and CAD/CAM milled fabrication methods produced equally well-fitting dentures, with both having a better fit than compression molding.

Goodacre *et al.* (2016) ^[36] compared the *denture base adaptation by fit discrepancy* of three types of denture resin: 1. CAD/CAM milled AvaDent[®] PMMA (AvaDent[®], Global Dental Science, USA); 2. Compression resin Lucitone[®] 199 (Dentsply Sirona[®], USA); and 3. Injection resin IvoBase Hybrid (Ivoclar Vivadent AG[®], Liechtenstein). A sequence of superimposition images and measurements were made to evaluate the fit discrepancies at different areas. The authors observed that the CAD/CAM fabrication process was the most accurate and reproducible denture fabrication technique when compared with others denture base processing techniques.

Similar studies included in this systematic review evaluated the *fit discrepancy* of denture bases fabricated with different materials: Hwang *et al.* (2018) ^[17] showed that Digital Light Processing (3D printed) maxillary denture base showed better trueness and tissue surface adaptation than the milling process and conventional fabricating method for denture bases. In Masri *et al.* (2020) ^[20] *in vitro* study, the results revealed

that the CAD/CAM fabrication techniques seem to offer better adaptation of denture bases when compared to the conventional fabrication protocol, and that milled complete dentures presented the most homogeneous distribution of adaptation. Similar results were shown by Lee *et al.* (2019) ^[13], who proved that the overall accuracy of the denture base is higher in milling and 3D printing method than the injection molding method. The degree of fine reproducibility was higher in the injection molding method than the milling or 3D printing. Finally, Steinmassl *et al.* (2018a) ^[47] tested *in vitro* the improved fit of CAD/CAM denture bases compared to conventional ones, and the results revealed that CAD/CAM produces dentures with better fit than conventional dentures.

By evaluating the denture tooth movement between CAD/CAM and conventional fabrication techniques, Goodacre *et al.* (2017) ^[37] tested which denture base fabrication process produces the most accurate and reproducible prosthesis. After *in vitro* testing, the CAD/CAM monolithic dentures produced the best combination of accuracy and reproducibility, and varying amounts of tooth movement can be expected depending on the processing technique.

The *dimensional stability* of denture bases was investigated by Einarsdottir *et al.* (2019) ^[42]. Denture bases fabricated by a CAD/CAM methodology (AvaDent[®] PMMA – AvaDent[®], Global Dental Science, USA) exhibit fewer dimensional changes than either compression (Lucitone[®] 199 – Dentsply Sirona[®], USA) or injection molding (IvoBase[®] Hybrid – Ivoclar Vivadent AG[®], Liechtenstein). Distortion occurred during the fabrication of the denture base, and a second processing did not significantly affect the dimensional stability of the denture base.

3.2.2.2. Optical Outcomes

Only two (2) controlled *in vitro* studies assessing optical outcomes, both published in 2019, met the eligibility criteria and were included for data extraction. They came from Saudi Arabia (al-Qarni *et al.* 2019) ^[18] and Turkey (Dayan *et al.* 2019) ^[59]. The total sample size was 75 CAD/CAM milled-, 60 CAD/CAM printed-, 75 Conventional (Compression)- and 15 Conventional (Injection)- samples. A summary of the optical outcomes of the *in vitro* studies is given in Table 3.

Table 3. Summary of descriptive characteristics of included *in vitro* studies - Optical outcomes.

Study Charac.	Sample Characteristics					Interventions Characteristics	Outcomes Characteristics				Main Conclusions
	Features	CAD/CAM Group		Conventional Group			Stainability CIELab (ΔE_{ab})				
		Milled	Printed	Compression	Injection	Parameters	CAD CAM Milled	CAD CAM Printed	Compression	Injection	
First Author, Year, Country	1. Shape 2. Dimensions 3. <i>n</i> total	1. Brand 2. <i>n</i> total	1. Brand 2. <i>n</i> total	1. Brand 2. <i>n</i> total	1. Brand 2. <i>n</i> total	1. Storage Parameters 2. Assessments	1. Water 2. Coffee 3. Cola 4. Red Wine	1. Water 2. Coffee 3. Cola 4. Red Wine	1. Water 2. Coffee 3. Cola 4. Red Wine	1. Water 2. Coffee 3. Cola 4. Red Wine	
al-Qarni <i>et al.</i> 2019 Saudi Arabia	1. Square 2. 10x2mm 3. <i>n</i> = 45	1. Lucitone 199 ^f 2. <i>n</i> = 15	1. - 2. -	1. Lucitone 199 ^g 2. <i>n</i> = 15	1. IvoBase [®] Hybrid [☆] 2. <i>n</i> = 15	1. Humid incubator at 37°C for 24 hours before baseline color measurements 2. Intraoral Spectro-photometer	1. 0.3 (0.1)* 2. 2.1 (0.1)* 3. - 4. 3.0 (0.6)*	1. - 2. - 3. - 4. -	1. 1.4 (0.2)* 2. 2.3 (0.3)* 3. - 4. 3.2 (0.3)*	1. 0.4 (0.1)* 2. 1.8 (0.2)* 3. - 4. 2.1 (0.5)*	1. All evaluated acrylic resin specimens had significant color change when immersed in coffee or red wine. Coffee produced the greater color difference. 2. Monolithic teeth and base acrylic resin materials used in CAD-CAM dentures had similar color change to conventionally processed acrylic resin. 3. At the tooth-denture base interface, CAD-CAM milled specimens were less likely to harbor stains than compression- or injection-molded specimens.

Dayan <i>et al.</i> 2019	1. Disk- shaped	1. M-PM- Disc*	1. Eclipse ^o	1. Paladent 20 [∞]	1. - 2. -	1. Staining solutions	1. 0.44 (0.19)*	1. 0.96 (0.15)*	1. 1.06 (0.24)* 1.04 (0.14)**	1. - 2. -	The color stability of CAD/CAM denture base resins is better than that of some other kinds of denture base resins. All the changes in the color values of the groups, except those in Eclipse, which was stored in red wine, were under the clinically perceptible value. The color stability of the Eclipse denture base resin was lower compared to other denture base groups. All beverages used in the study had an effect on color change.
	2. 15x2mm	2. n = 60	2. n = 60	2. n = 60		2. Portable Spectro- photometer	0.43 (0.64)**	1.18 (0.96)**	2. 1.02 (0.06)*	3. -	
	3. n = 240						2. 0.76 (0.16)*	2. 1.08 (0.57)*	3. 1.02 (0.07)*	4. -	
Turkey							1.08 (0.27)**	3.02 (1.08)**	1.92 (0.44)**		
							3. 0.53 (0.13)*	3. 0.94 (0.15)*	4. 1.00 (0.08)* 2.17 (0.66)**		
							0.99 (0.29)**	2.90 (0.96)**			
						4. 0.90 (0.50)*	4. 1.04 (0.14)*				
						2.04 (1.03)**	3.59 (1.32)**				

Note: * 1 week | ** 30 days

£AvaDent®, Global Dental Science, USA. *Merz Dental GmbH®, Germany. °Dentsply Sirona®, USA. ☆ Ivoclar Vivadent AG®, Liechtenstein. ∞Haerus Kulzer®, Germany.

3.2.2.2.1. Stainability

A total of 30 CAD/CAM milled samples and 30 conventional compressed samples from two studies were available for statistical analysis of the comparison in different solutions (water, coffee and wine). None study provided neither CAD/CAM printed samples nor conventional (injection) samples for these comparisons.

3.2.2.2.1.1. Stainability on Water

CAD/CAM milled samples revealed significant better mean stainability values on water (0.16 ΔE_{ab} ; 95% CI: 0.10 – 0.22) than conventional (compression) samples (1.23 ΔE_{ab} ; 95% CI: 1.13 – 1.33) ($p = 0.02$). The overall standard mean difference of samples in water was -4.69 ΔE_{ab} (95%CI: -8.58 – 0.79) (Figure 8A). The heterogeneity (I^2) of the studies was 92% ($\text{Chi}^2 = 12.25$; $df = 1$; $p = 0.00005$).

3.2.2.2.1.2. Stainability on Coffee

CAD/CAM milled samples revealed significant better mean stainability values on coffee (1.43 ΔE_{ab} ; 95% CI: 1.18 – 1.68) than conventional (compression) samples (1.66 ΔE_{ab} ; 95% CI: 1.41 – 1.91) ($p = 0.02$). The overall standard mean difference was -1.45 ΔE_{ab} (95%CI: -2.65 – 0.26) (Figure 8B). The heterogeneity (I^2) of the studies was 76% ($\text{Chi}^2 = 4.10$; $df = 1$; $p = 0.04$).

3.2.2.2.1.3. Stainability on Wine

Conventional (compression) revealed better mean stainability values on wine (1.65 ΔE_{ab} ; 95% CI: 1.35 – 1.90) than CAD/CAM milled samples (1.95 ΔE_{ab} ; 95% CI: 1.52 – 2.2) ($p = 0.5$). The overall standard mean difference in wine group was 0.57 ΔE_{ab} (95%CI: -1.10 - 2.24) (Figure 8C). The heterogeneity (I^2) of the studies was 89% ($\text{Chi}^2 = 9.48$; $df = 1$; $p = 0.002$).

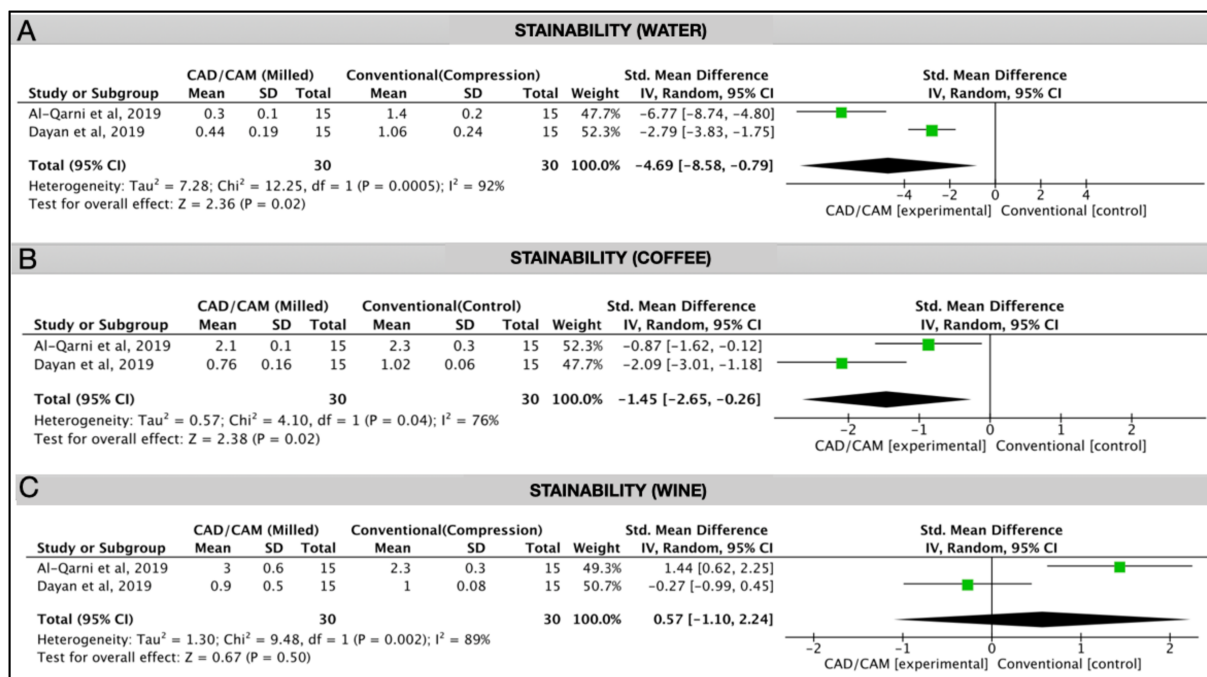


Figure 8. Forest plots of the stainability values of CAD/CAM milled and Conventional (compression) groups: (A) Water. (B) Coffee. (C) Wine.

3.2.2.3. Biological Outcomes

Only two (2) controlled *in vitro* studies assessing biological outcomes met the eligibility criteria and were included for data extraction. They came from Saudi Arabia [44] and USA (Alshehri, 2018) [60] and were published in 2017 [44] and 2018 (Alshehri, 2018) [60]. The total sample size was 20 CAD/CAM milled and 20 conventional (Compression) samples. A summary of the biological outcomes of the *in vitro* studies is given in Table 4.

Ayman et al. [45] evaluated the residual monomer 35 heat-cured PMMA and 35 CAD/CAM pre-polymerized acrylic resin blocks at baseline, two-day and seven-day intervals using gas chromatography (GC). The authors concluded that higher release of the monomer content was detected by GC in heat-cured PMMA group at different time intervals with a statistically significant difference ($p < 0.001$) in residual monomer content.

3.2.2.3.1 Contact Angle

A total of 110 CAD/CAM milled samples and 35 conventional compressed samples from three studies were available for statistical analysis. None study provided neither CAD/CAM printed samples nor conventional (injection) samples for this specific comparison. CAD/CAM milled samples revealed higher mean contact angle values (76.8°; 95% CI: 75,26 – 78.34) than conventional (compression) samples (72.97°; 95% CI: 70.32– 75.62), but this was not statistically significant ($p = 0.48$). The overall standard mean difference was 0.65° (95%CI: -1.15 - 2.44) (Figure 9). The heterogeneity (I^2) of the studies was 94% ($\text{Chi}^2 = 35.45$; $\text{df} = 2$; $p < 0.00001$).

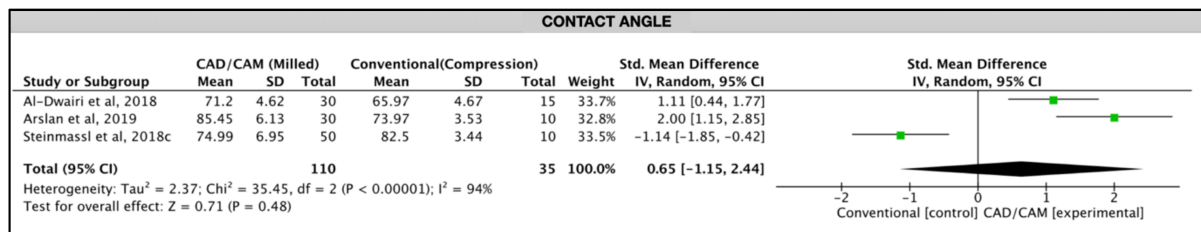


Figure 9. Forest plot of the contact angle values of CAD/CAM milled and conventional (compression) groups.

Table 4. Summary of descriptive characteristics of included *in vitro* studies - Biological outcomes.

Study Charac.	Sample Characteristics			Interventions Characteristics		Outcomes		
First Author, Year	Sample features: 1. Shape 2. Dimensions 3. N total	CAD/CAM Group	Conventional Group	Storage Parameters	Assessments	C. Albicans Adherence (CFUs/ml) - Mean (SD)		Main Conclusions
		Groups (Milled) 1. Brand 2. n total	Groups (Comp.) 1. Brand 2. n total			CAD CAM Milled	Compression	
Al-Fouzan <i>et al.</i> 2017 Saudi Arabia	1. Disk-shaped 2. 10x3mm 3. n = 20	1. Wieland® PMMA* 2. n = 10	1. MajorBase20® ^a 2. n = 10	Candida isolates were subcultured on Sabouraud dextrose agar for 24 hours at 37°C. The colony-forming unit (CFU) counts were determined after 24 hours of incubation at 37°C.	Fluorescent microscope	CA-1: 1.1 x 10 ³ (6.0 x 10 ²) CA-2: 2.1 x 10 ³ (8.7 x 10 ²) CA-3: 1.2 x 10 ³ (8.8 x 10 ²) CA-4: 1.5 x 10 ³ (7.2 x 10 ²)	CA-1: 2.3 x 10 ³ (8.4 x 10 ²) CA-2: 5.4 x 10 ³ (1.6 x 10 ²) CA-3: 2.0 x 10 ³ (9.7 x 10 ²) CA-4: 2.4 x 10 ³ 1.1 x 10 ³)	The CAD/CAM procedure for fabricating complete dentures showed promising potential for reducing the adherence of Candida to the denture base surface. Complete dentures made with the CAD/CAM procedure might decrease the incidence of denture stomatitis compared with conventional denture.
Alshehri 2018 USA	1. Square 2. 5x5x2.5mm 3. n = 20	1. AvaDent® PMMA [£] 2. n = 10	1. Lucitone® 199 [°] 2. n = 10	Specimens were stored in phosphate buffered saline and 10 mM was used to rinse samples prior to inoculation. Specimens will be then incubated for 3 hours on a shaker at 37°C.	Suspensions were dotted in 10µl aliquots on BHI agar in triplicate for colony forming units (CFU/ml) to assay microbial viability as a quantification of initial adherence of microbes.	6.22 x10 ⁷ (0.046 x10 ⁷) 6.47 x10 ⁷ (0.027 x10 ⁷)		For <i>C. Albicans</i> , heat polymerized PMMA and the CAD/CAM PMMA group showed significantly higher CFUs/ml than other studied groups. For <i>S. Aureus</i> , there was no statistically significant differences between the Heat polymerized PMMA and CAD/CAM PMMA groups.

* Ivoclar Vivadent AG®, Liechtenstein. ^aMajor Prodotti Dentare®, Italy. [°]Dentsply Sirona®, USA. [£]AvaDent®, Global Dental Science, USA.

3.3. Results of Risk of Bias of Individual Studies

3.3.1. Clinical Studies

The original design of the studies was considered for Risk of Bias assessments. Six Non-Randomized Controlled Clinical Trials [21], [29], [30], [32], [33], [34] were included, and The Joanna Briggs Institute Critical Appraisal Checklist For Quasi-Experimental (Non-Randomized Experimental Studies) [27] tool was applied. Questions number 1 “*Is it clear in the study what is the ‘cause’ and what is the ‘effect’?*”, number 4 “*Was there a control group?*”, number 6 “*Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?*”, number 7 “*Were the outcomes of participants included in any comparisons measured in the same way?*”, number 8 “*Were outcomes measured in a reliable way?*”, and number 9 “*Was appropriate statistical analysis used?*” were positively answered by all six non-randomized studies. Questions number 2 “*Were the participants included in any comparisons similar?*”, number 3 “*Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?*” and number 5 “*Were there multiple measurements of the outcome both pre and post the intervention/exposure?*” were answered as “yes” in 1 (16.66%), 1 (16.66%) and 2 (33.33%) out of six studies, respectively.

According to this, 2/6 (33.33%) studies [29], [33] were considered as “low risk of bias”, whereas 4/6 (66.66%) studies [21], [32], [30], [34] were considered as “moderate risk of bias”. No study was considered as of “high risk of bias (Figure 10A).

Only one Randomized Clinical Trial [31] was included, and the Rob 2 (Risk of bias 2, Cochrane Collaboration) tool was applied. Question number 2 “*Allocation concealment*”, number 3 “*Blinding of participants and personnel*” and number 4 “*Blinding of outcome assessment*” were answered as “unclear”. All other four questions were positively answered (57.14%), indicating a moderate risk of bias (Figure 10B).

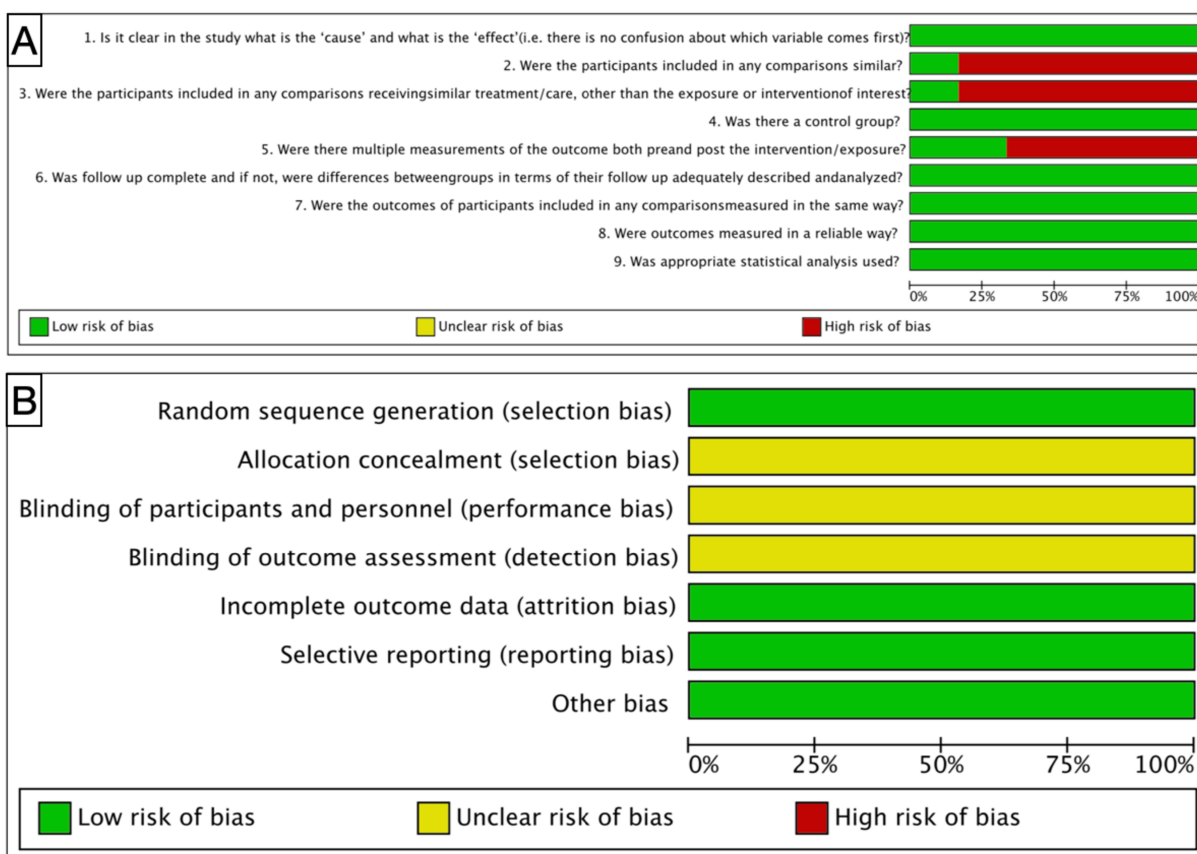


Figure 10. A) Risk of bias of the clinical studies according to the Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental (Non-Randomized Experimental Studies) tool. B) Risk of bias of the randomized clinical study according to the RoB 2 (Risk of Bias 2, The Cochrane Collaboration) tool.

3.3.2. Laboratory (*in vitro*) Studies

The Joanna Briggs Institute Critical Appraisal Checklist For Quasi-Experimental (Non-Randomized Experimental Studies) ^[27] tool was applied for the thirty-four *in vitro* studies. Questions number 4 “*Was there a control group?*”, number 6 “*Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?*”, number 7 “*Was the outcomes of participants included in any comparisons measured in the same way?*” and number 8 “*Were outcomes measured in a reliable way?*” were answered as “yes” in all thirty-four studies. Question number 1 “*Is it clear in the study what is the ‘cause’ and what is the ‘effect’?*” was answered as “yes” in 32 (94.11%) out of the thirty-four studies. Questions number 2 “*Were the participants included in any comparisons similar?*”, number 3 “*Were the participants included in any comparisons receiving similar treatment/care,*

other than the exposure or intervention of interest?” and number 5 “Were there multiple measurements of the outcome both pre and post the intervention/exposure?” were answered as “yes” in 5 (14.7%), 5 (17.7%) and 12 (35.29%) out of thirty-four studies, respectively. According to this, 15/34 (44.11%) studies were considered as “low risk of bias”, whereas 17/34 (50%) studies were considered as “moderate risk of bias” and 2/34 studies (5.88%) were considered as “high risk of bias” (Figure 11).

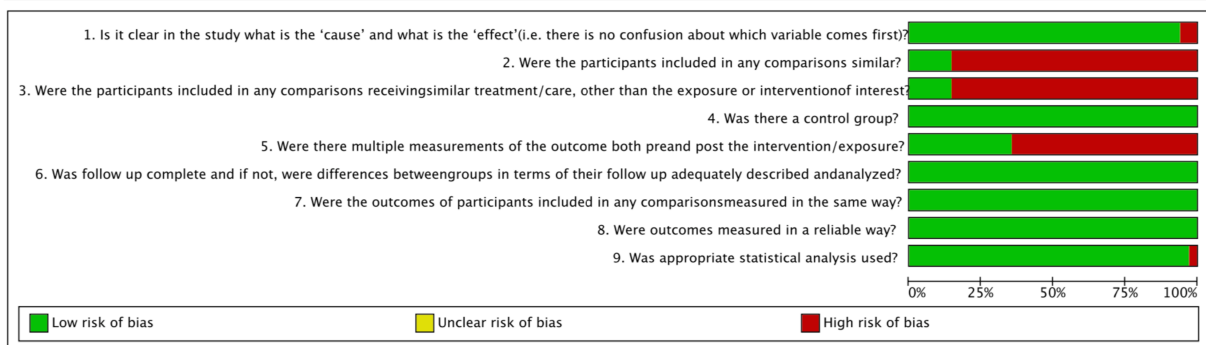


Figure 11. Risk of bias of the in vitro studies according to the Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental (Non-Randomized Experimental Studies) tool.

3.4. Results of Confidence in Cumulative Evidence

The GRADE evaluation was performed based on the clinical outcomes (retention of denture base, patient-reported outcome measures (PROMs), number of appointments, clinical chairside spent and overall costs, masticatory efficiency and level of prosthesis biofilm). The confidence in cumulative evidence was considered very low in all clinical studies included. The domains that downgraded the certainty were the results of risk of bias, the small sample size, the inconsistency between studies, the high statistical and methodological heterogeneity and the imprecision of the studies (Table 5).

Table 5. GRADE summary findings.

	Certainty assessment							№ of patients		Certainty
	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Complete Engineered Complete Dentures	Conventional Complete Dentures	
Retention of denture base	1	Controlled Clinical Trials	serious ^a	serious ^b	not serious	serious ^c	none	20	20	⊕○○○ VERY LOW
Patient-Reported Outcome Measures (PROMs)	4	Controlled Clinical Trials and Randomized Clinical Trials	serious ^a	serious ^d	not serious	serious ^c	none	73	73	⊕○○○ VERY LOW
Number of appointments	1	Controlled Clinical Trials	serious ^a	very serious ^e	not serious	serious ^e	none	73	33	⊕○○○ VERY LOW
Clinical chairside spent and overall costs	1	Controlled Clinical Trials	serious ^a	serious ^a	not serious	serious ^c	none	18	18	⊕○○○ VERY LOW
Masticatory efficiency	1	Controlled Clinical Trials	not serious ^a	serious ^c	not serious	serious ^c	none	20	20	⊕○○○ VERY LOW
Level of prosthesis biofilm	1	Controlled Clinical Trials	serious ^a	serious ^e	not serious	serious ^c	none	14	14	⊕○○○ VERY LOW

Explanations

- a. After risk of bias evaluation, at least one question regarding high risk
- b. Insufficient time between testings
- c. Small sample size
- d. Different study methodologies
- e. High methodological heterogeneity

DISCUSSION

The development of computer-assisted digital technologies has presented Dentistry with alternatives capable of offering predictable and minimally invasive restorative treatments [61], [62]. Digital imaging (CAI) with last generation scanners and CBCT units, virtual prosthetic and surgical planning (CAD) softwares, as well as milling and printing manufacturing units (CAM) are all tools that have added the artificial intelligence (A.I.) of computers to the arsenal available to the clinician. Particularly with the manufacturing processes, many have been the benefits attributed to both milling and 3D printing when compared to conventional fabrication of either mucosa- or implant-supported complete dentures. Materials' properties, reproducibility, increased patients' satisfaction and comfort, and the reduced number of appointments could thus be highlighted as potential advantages of the digital workflow [21], [34], [63]. This is noteworthy when dealing with (frail) elderly patients, since existing dentures in need of replacement are often reworked, repaired or relined, and the conventional fabrication of complete dentures is still time consuming. In these cases, computer-engineered complete dentures (CECDs) could reduce the number of necessary appointments and increase the treatment accuracy, better addressing the needs of totally edentulous patients [64].

The present systematic review aimed at answering the focused question: "*What are the clinical, mechanical, optical and biological outcomes of Computer Engineered Complete Dentures (CECDs) compared to Conventional Complete Dentures (CCDs)?*". CECDs proved in the present study to be a predictable and viable solution for the treatment of edentulous patients, and this is in agreement with the previous systematic review by Kattadiyil & AlHelal (2016) [22], that revealed significantly reduced clinical time, improved retention, and digital archivability as the main advantages associated with CECDs. Given the innovative and dynamic character of the digital method, it is acceptable that the clinical evidence is still insufficient. Thus, some parameters that cannot be answered clinically have led us to also include *in vitro* studies as well as to broaden the searches up to the gray literature level, since new clinical evidences were expected to have emerged since then. In this sense, even unpublished literature [29], [31], [35], [60] have added to our study significant information in terms of patient-centered outcomes as well as mechanical and biological properties.

Likewise, in Wang's *et al.* (2020) ^[23] systematic review, influencing factors on the accuracy of CECDs have been assessed in *in vitro* studies. The fabrication technique, the CAD/CAM system, and the long-term service were the only factors that have significantly influenced denture accuracy. However, no clear conclusions could be drawn about the superiority of CECDs regarding denture accuracy.

In the present study, a comprehensive search strategy has been run aiming at identifying all the available evidences with regards to the computer-assisted fabrication of complete dentures. Seven original clinical studies, accounting for 197 patients with 164 CECDs and 124 CCDs, and thirty-four *in vitro* studies, computing for 1,327 CAD/CAM milled, 190 CAD/CAM printed, 908 conventional (compression) and 242 conventional (injection) samples, were available for either descriptive or statistical analysis. The 2-visits digital protocol for the fabrication of complete dentures has been pointed out as a remarkable advance in the treatment of totally edentulous patients in terms of clinical time, costs and patient's and clinician's preference. In the study by Srinivasan *et al.* (2018) ^[34], the conventional protocol required significantly longer clinical time than digital complete dentures. Nevertheless, in despite of the supposed advantage of time efficiency associated with the clinical fabrication of CECDs, both types of complete dentures showed similarity in the number of unscheduled and postinsertion visits after a 1-year follow-up of patients treated in the study by Drago & Borgert (2019) ^[30].

From an economic point of view, the only study that evaluated the economic aspect for making CECDs was a study developed in Switzerland. The digital method granted lower overall costs (in Swiss francs) when a comparison with the conventional method was performed ^[34]. It is important to note that the costs involved in treatments in Switzerland are different from those in other countries, due to a very particular country in relation to laboratory and clinical costs. In addition, this study evaluated the economic viability of digital flow in complete dentures only in a university setting. Since economic aspects are a key element in clinical decision-making, this type of study is necessary to map the cost feasibility for different regions in different countries, with different economic realities. Studies that evaluate the economic aspect in a private setting are also necessary, in view of the high initial investments of the digital flow.

The increasing use of digital CAD/CAM technology on the fabrication of complete dentures, associated with the development of new materials, suggests that the costs involved in these procedures might decrease in the near future. This is particularly relevant when it comes to totally edentulous, since the majority of these patients still depend on dental care offered by hospitals, dental schools and insurance services. Therefore, further cost-benefit investigations are necessary in different social and economic scenarios to assess the efficiency of the digital method.

It is also important to emphasize that the use of digital equipment for fabricating CECDs in the public health system of different countries can be advantageous in a long-term, because despite the high initial cost for image acquisition and prosthesis manufacturing, over time it can be worthwhile both for the system and for the health of patients.

With that in mind and taking into account that the digital method is a promising field for use also in higher dental education, studies such as the prospective clinical study by Kattadiyil *et al.* (2015)^[21] are crucial for evaluating the relation between the complete denture teaching and the feedback from predoctoral students. The students preferred the digital method for fabricating complete dentures, and their considerations were especially related to “*no required laboratory work*” for fabricating 3D dentures, and “*improved festooning and denture base finish*”. In despite of the student’s preference, it should be kept in mind that both methods involve a learning curve, and that a consolidated knowlegment of the conventional fabrication method of complete dentures, with its principles, must be always respected.

High-performance PMMA blocks used for the subtractive manufacturing of complete denture bases demonstrated better clinical retention, as seen in the studies by Kattadiyil *et al.* (2015)^[21] and AlHelal *et al.* (2017)^[32]. This might be explained by the lack of polymerization shrinkage associated with the industrial pre-processing of polymethylmethacrylate. This finding corroborates the results obtained by Kattadiyil & AlHelal’s (2016)^[22] systematic review, which showed improved retention with CECDs. It is noteworthy that the denture retention studies included in the above-mentioned systematic review were all cross-sectional and pilot cohort studies, and thus might present some level of bias. Despite not being published in scientific literature, nowadays the milled monolithic PMMA can be considered as a definitive material for

implant-retained full-arch rehabilitation, once this material presents good mechanical, optical and biological proprieties.

In view of the clinical evidences available, the two methods of fabrication of complete dentures did not exhibit difference in the patient's masticatory performance up to three months after installation ^[33], and in the level of denture biofilm after one month of usage ^[31]. This last finding contradicts the *in vitro* findings of Al-Fouzan *et al.* (2017) ^[44], where CAD/CAM milled samples showed the capacity of reducing the adherence of microorganisms to the denture base surface, potentially decreasing the incidence of denture stomatitis. These contradictory findings might be explained by the short follow-up period of the clinical studies. Biofilm adherence to the denture's surface is dependent either on the patient's oral hygiene and dietary habits ^[65] and on the degree of deterioration presented by the material, which are parameters that might not be properly assessed in a short follow-up period.

Patient-Reported Outcome Measures (PROMs) revealed inconclusive results among studies. In a cross-sectional intra-individual comparison of ten patients, Coffey (2018) ^[29] assessed patient's preference with regards to the fabrication method of complete dentures. Patients related discomfort with the Anatomical Measurement Device (AMD) used in the digital method to simultaneously register the vertical dimension of occlusion, the centric relation position and the lip support. In the study of Jia-Mahasap (2017) ^[31], no difference was found in patient's satisfaction between CECD and CCD groups both at baseline and at the 1 month visit using the validated OHIP-EDENT questionnaire. In contrast, Kattadiyil *et al.* (2015) ^[21] observed cross-sectionally that patients reported greater satisfaction with digital dentures. This might be related to treatment time as the conventional fabrication process required significantly more visits than the 2- or 3-visits digital protocol. The three-months follow-up study by Ling *et al.* (2020) ^[33] revealed favorable results for CAD/CAM Functional Suitable Denture (FSD) system when patients' satisfaction and Oral Health Related Quality of Life (OHRQoL) were assessed. Although no differences were found in an intra-individual comparison, it is likely that the sequence of installation of the two types of dentures might have affected this subjective perception. Last but not least, it is well known that complications (artificial tooth wear, chipping of the veneering material and denture base fracture) associated with resins used in the conventional fabrication method of complete dentures that might affect patient's perception do not manifest in a short

period of time (one- to three months). Thus, it is suggested further studies to be carried out with larger samples and longer follow-up evaluation.

A recent application of CECD includes the Guided Prosthesis Concept (either milled or printed), which are full-arch provisional restorations aiming at immediately restoring dental implants placed by means of static computer-assisted guided surgery. This is a treatment modality where a combined surgical and prosthetic digital planning allows the clinician to manufacture the restoration based on the desired three-dimensional position of the implant prosthetic platforms [66], [67], [68], [69]. Thus, accuracy of dental implant placement plays a crucial role for the success of this concept. Nevertheless, recent evidences from systematic reviews [70], [71] have shown that a mean 1.0mm coronal horizontal linear deviation might be expected with this type of surgery in edentulous patients. In this sense, the digital design and manufacturing of an exact fitting of the prosthetic platforms on the prosthesis base is not recommended. On the contrary, a wider opening with a safety margin over the likely position of the prosthetic abutments should be designed in the software, allowing the prosthodontist to predictably install the prosthesis. In this systematic review, none of the clinical studies included assessed the outcomes of CAD/CAM Guided Prosthesis.

The International Organization for Standardization states that acrylic resins should have a flexural strength no less than 65 MPa [72] making it suitable for clinical use. The specimens were subjected to a 3-point bend test that simulates its ability to succeed intraorally under high functional loads during mastication and parafunction [73]. Although CAD/CAM milled samples showed higher flexural strength values in relation to either compressed- or injected thermo-polymerized samples, the overall means of all groups showed mean values higher than 65 MPa, justifying the safe application of PMMA for the fabrication of complete dentures, regardless of the method of fabrication (digital vs. conventional). Likewise, the flexural modulus reflects the material's stiffness and rigidity [74]. In our review, this parameter has been assessed in four *in vitro* studies [41], [43], [45], [51]. CAD/CAM milled samples achieved better results in comparison to conventional (compressed) ones. Since stiffness and rigidity of the denture are prerequisites for the ability of forces distribution by the denture base, CAD/CAM milled PMMA might present as a potential material for the fabrication of complete dentures. Fracture toughness has been defined as the critical stress intensity factor of a sharp crack where propagation of the crack suddenly becomes rapid and unlimited. In other

words, it is a quantitative way of expressing a material's resistance to crack propagation [75]. In this systematic review, two *in vitro* studies [48], [57] showed superior mean fracture toughness values for CAD/CAM milled samples when compared to conventional (compression) samples. This might be explained by the industrial pre-processing of PMMA blocks, that make them more resistant to fracture even when a crack is already present. The process of polymerization under high temperature and pressure of the high-performance PMMA blocks produces longer polymer chains, leading to a higher degree of monomer conversion and lower values of residual monomer [76].

In this review, CAD/CAM milled samples released significantly less residual monomer than conventional heat-cured PMMA samples *in vitro* [45], [46] and this is clinically relevant in terms of tissue irritation due to allergic reaction to methyl methacrylate. In addition, dental materials with lower surface free energy exhibit a higher water contact angle, and consequently a higher hydrophobicity. This, in turn, might interfere with the formation of the acquired film and adherence of microorganisms on the denture's surface [77]. In other words, the greater the contact angle, the lower the likelihood of bacterial and fungal adherence to the material's surface. In this study, CAD/CAM milled samples revealed higher mean contact angle values than conventional (compression) samples. This may recommend the CAD/CAM milled PMMA block as a more hygienic material and as a potential reducer of the incidence of stomatitis [44].

Surface hardness is defined as "*the ability of a material's surface to resist permanent penetration or indentation*". There is a correlation between surface hardness and the material's mechanical properties. For instance, the amenability of acrylic-polymer to degradation makes it vulnerable to fracture and aggravates the chance of plaque, microorganism, and pigment retention, eventually jeopardizing the denture base longevity. In this review, conventional (injection) samples showed the lowest mean surface hardness values, and CAD/CAM milled samples showed intermediate results. The conventional (compression) denture resin showed the higher mean surface hardness values, affecting positively this material performance.

In parallel, surface roughness has been described as "*little indentations or irregularities that characterizes a surface and has its influence on wetting, quality of adhesion, and brightness of a surface*". Rough surfaces tend to induce halitosis and are considered more vulnerable to discoloration than smooth surfaces, thereby reducing patient

comfort. As microbial adhesion and colonization usually occur on rough surfaces, dental prostheses must have smooth surfaces to minimize the retention of plaque and microorganisms. The surface roughness of complete dentures should not exceed a threshold of 0.2 μm , which can be achieved by common laboratory and chairside finishing and polishing procedures. In this study, the CAD/CAM milled samples showed the lower mean surface roughness values, and this might explain the reduced *Candida albicans* adherence found in the study by Al-Fouzan *et al.* (2017) [44].

The longevity of a complete denture might also be related to its appearance. Edentulous patients usually seek for replacement of their existing old dentures when the aesthetic aspect causes them difficulties in social interaction. In this sense, the optical properties of the materials used for the fabrication of complete dentures play a decisive role. The stainability of acrylic resin specimens has been tested *in vitro* after immersion in different beverages (water, coffee and wine). In the present systematic review, two studies [18], [59] observed significant color changes in all specimens evaluated, regardless of the method of fabrication. However, this change was under the clinically perceptible value. Furthermore, the color stability of CAD/CAM denture base resins was better. At the tooth-denture base interface, CAD-CAM milled specimens were less likely to harbor stains than compression- or injection-molded specimens.

Ayman's study [45] drew attention about milled PMMA good results for the releasing of residual monomers. Since high monomer content has deleterious effects on the mechanical properties of the resin, rendering the resin softer affecting the prostheses clinical performance, in addition to possibly causing allergic processes in patients, the release of residual monomers must be taken into account when choosing which type of resin to use to manufacture complete dentures. The encouraging results for milled PMMA could be attributed due to the method of polymerization under high pressure to which the resin is submitted, providing good clinical results.

To the best of our knowledge, this is the first systematic review that evaluated the risk of bias and the confidence in cumulative evidence of the studies which assessed the clinical and laboratory outcomes of computer-engineered complete dentures. The lack of a baseline homogeneity was the most common shortcoming among the non-randomized clinical trials, yielding a moderate risk of bias in 2/3 of the studies. The RCT from Jia-Mahasap (2017) [31] did not report allocation concealment and blinding

of both participants and investigators. Furthermore, the small sample sizes, the inconsistency between studies, the high statistical and methodological heterogeneity and the imprecision of the studies were domains that downgraded the certainty to a very low level. These findings strongly recommend us to interpret the clinical evidences available with caution. On the other hand, the strong possibility of controlling biases in laboratory studies would lead us to a high expectation. However, there were still nineteen studies out of thirty-four that showed a moderate-to-high risk of bias. The most common issues raised were the uncertainty with regards to the similarity of the samples from both test and control groups at study initiation (baseline homogeneity). The 3D printed CECDs have the potential to be an economical and efficient method to provide a comfortable fitting removable prosthesis for the edentulous population. In despite of the advantages of this additive manufacturing process, rapid prototyping still has some limitations, especially with regards to the lack of scientific evidences to sustain its use. Few *in vitro* and none of the clinical studies included in this systematic review assessed the outcomes of 3D printing resins for the fabrication of complete dentures. Because it is a promising material, more studies should be carried out in order to evaluate their mechanical-, optical- and biological properties, as well as its long-term clinical behavior.

This systematic review showed remarkable advantages of CECDs and the related materials used for their fabrication. Nevertheless, more randomized clinical trials studies with CECDs, with larger sample sizes and longer follow-up periods, as well as *in vitro* studies, especially with rapid prototyping (3D printed) CECDs, are necessary to draw more robust evidences.

CONCLUSIONS

Within the limitations of the present systematic review, it can be concluded that Computer-Engineered Complete Dentures (CECDs) proved to be a predictable and viable solution for the treatment of edentulous patients, offering them the benefits of a reduced number of appointments, an improved retention, an increased satisfaction and comfort as well as a digital archivability (reproducibility).

Besides that, it can also be concluded that:

- High-performance PMMA CAD/CAM milled samples showed *in vitro* overall superior mechanical, optical and biological properties compared to resin samples fabricated by means of the conventional (either compressed or injected);
- CECDs are preferred by predoctoral dental students and consist in a relevant topic for use in Complete Denture teaching in a higher dental education;
- the digital manufacturing of complete dentures is inserted into a learning curve and the theoretical principles involved in the facially-oriented rehabilitation of the edentulous patients with complete dentures must always be respected;
- there is still not enough evidence to confirm the economic viability for making CECDs, since the only study carried out so far has been developed in Switzerland, which has a different economic reality.
- the level of clinical evidences of CECDs is still rather low.
- there is a lack of clinical and laboratory evidences to support the use of rapid prototyping (3D printing) resins on the fabrication of computer-engineered complete dentures;
- the clinical performance of CECDs supported by dental implants (Guided Prosthetics) still needs to be clarified.
- scientific evidence related to CECDs is still insufficient, and although promising, the results of CAD/CAM dentures still do not justify the total replacement of the conventional method.

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Appendix 1. Details of the search strategy as well as the results for each database.

SEARCH TERMS AND DATABASES	
DATABASE	SEARCH
PubMed (<i>n</i> = 732)	("Denture" OR "Dentures"[Mesh] OR "Dentures" OR "Denture, Complete, Upper"[Mesh] OR "Denture, Complete, Upper" OR "Denture, Complete, Lower"[Mesh] OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete"[Mesh] OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Bases"[Mesh] OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins"[Mesh] OR "Acrylic Resins" OR "Polymethyl Methacrylate"[Mesh] OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Computer-Aided Design"[Mesh] OR "Printing"[Mesh] OR "Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction"[Mesh] OR "Patient Satisfaction" OR "Prognosis"[Mesh] OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort"[Mesh] OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip support" OR "Esthetics"[Mesh] OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics"[Mesh] OR "Phonetics" OR "Speech"[Mesh] OR "Speech" OR "Public Speaking" OR "Visual analog scale"[Mesh] OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis Retention"[Mesh] OR "Prosthesis Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment"[Mesh] OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" [Mesh] OR "Centric Relation" OR "Vertical Dimension"[Mesh] OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR "Mandibular Rest Position" OR "Mandibular Rest

	<p>Positions" OR "Dental Occlusion"[Mesh] OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication"[Mesh] OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition"[MeSH Terms] OR "Deglutition" OR "Swallowing" OR "Bite force"[MeSH Terms] OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength"[Mesh] OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion"[Mesh] OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductivity" OR "Adhesion" OR "Adherence" OR "Thermal conductivity"[Mesh] OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic Modulus"[Mesh] OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement")</p>
<p>SCOPUS (<i>n</i> = 801)</p>	<p>TITLE-ABS-KEY (("Denture" OR "Dentures" OR "Denture, Complete, Upper" OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins" OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction" OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip</p>

	<p>support" OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics" OR "Speech" OR "Public Speaking" OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR "Mandibular Rest Position" OR "Mandibular Rest Positions" OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition" OR "Swallowing" OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductivity" OR "Adhesion" OR "Adherence" OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement")) AND (LIMIT-TO (DOCTYPE , "ar"))</p>
<p>Web of Science (<i>n</i> = 467)</p>	<p>("Denture" OR "Dentures" OR "Denture, Complete, Upper" OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins" OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-</p>

	<p>polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction" OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip support" OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics" OR "Speech" OR "Public Speaking" OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR "Mandibular Rest Position" OR "Mandibular Rest Positions" OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition" OR "Swallowing" OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductivity" OR "Adhesion" OR "Adherence" OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement")</p>
<p>Cochrane (n = 87)</p>	<p>("Denture" OR "Dentures" OR "Denture, Complete, Upper" OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins" OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR</p>

	<p>"CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction" OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip support" OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics" OR "Speech" OR "Public Speaking" OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR "Mandibular Rest Position" OR "Mandibular Rest Positions" OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition" OR "Swallowing" OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductivity" OR "Adhesion" OR "Adherence" OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement")</p>
<p>EMBASE (<i>n</i> = 450)</p>	<p>("Denture" OR "Dentures" OR "Denture, Complete, Upper" OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins" OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR</p>

	<p>"Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction" OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip support" OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics" OR "Speech" OR "Public Speaking" OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR "Mandibular Rest Position" OR "Mandibular Rest Positions" OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition" OR "Swallowing" OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductivity" OR "Adhesion" OR "Adherence" OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement")</p>
<p>LILACS (<i>n</i> = 29)</p>	<p>("Denture" OR "Dentadura" OR "Dentures" OR "Dentaduras" OR "Complete prosthesis" OR "Prótese completa" OR "Prótese Total" OR "Complete prostheses" OR "Próteses completas" OR "Próteses Totais" OR "Dental prosthesis" OR "Prótese dental" OR "Próteses dentais" OR "Complete Denture" OR "Complete Dentures" OR "Dentaduras completas" OR "Full arch denture" OR "Prótese arco total" OR "Full arch dentures" OR "Próteses arco total" OR "Denture Base" OR "Base de dentadura" OR "Bases de prótese" OR</p>

	<p>"Base de prótese" OR "Bases de prótese" OR "Acrylic Resin" OR "Resina acrílica" OR "Acrylic Resins" OR "Resinas acrílicas" OR "Polymethyl Methacrylate" OR "Polimetil Metacrilato" OR "Poly(methyl methacrylate)" OR "Poli(metal metacrilato)" OR "Polymethylmetacrylate" OR "Polimetilmetacrilato" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Impressão" OR "Impresión" OR "Diseño Asistido por Computador" OR "Projeto Auxiliado por Computador" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer-Assisted Design" OR "Computer Assisted Design" OR "Fabricação Assistida por Computador" OR "Fabricación asistida por computador" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Impresso" OR "Impresa" OR "Impreso" OR "Milled" OR "Fresado" OR "Fresada" OR "Molida" OR "Molido" OR "Milling" OR "Prototyping" OR "Creación de prototipos" OR "3D") AND ("Conventional" OR "Convencional" OR "Conventionally" OR "Convencionalmente" OR "Conventional dentures" OR "Dentadura convencional" OR "Dentaduras convencionais" OR "Dentaduras convencionales" OR "Prótese convencional" OR "Próteses convencionais" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Termopolimerizável" OR "Termopolimerizado" OR "Curado por calor" OR "Curável por calor" OR "Conventional curing" OR "Curado convencionalmente" OR "Thermo curing") AND ("Cost" OR "Custo" OR "Costo" OR "Patient Satisfaction" OR "Satisfação do Paciente" OR "Satisfacción del paciente" OR "Prognosis" OR "Prognoses" OR "Prognóstico" OR "Pronóstico" OR "Prognostic Factors" OR "Prognostic Factor" OR "Factores pronósticos" OR "Fatores prognósticos" OR "Overall result" OR "Resultados totales" OR "Total de Resultados" OR "Patient Comfort" OR "Comfort, Patient" OR "Conforto do paciente" OR "Comodidad del paciente" OR "Comfort Care" OR "Conforto" OR "Comodidad" OR "Time" OR "Tempo" OR "Tiempo" OR "Lip support" OR "Suporte labial" OR "soporte labial" OR "Esthetics" OR "Aesthetics" OR "Estética" OR "Tooth arrangement" OR "Arreglo dental" OR "Disposição dos dentes" OR "Phonetics" OR "Fonética" OR "Speech" OR "Habla" OR "Discurso" OR "Public Speaking" OR "Falar em público" OR "Hablar en público" OR "Visual analog scale" OR "Visual Analog Scales" OR "Escala visual analógica" OR "Escalas visuais analógicas" OR "Stability" OR "Estabilidade" OR "Estabilidad" OR "Retention" OR "Retenção" OR "Retencion" OR "Prosthesis Retention" OR "Retención de Prótesis" OR</p>
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	<p>"Retenção de Prótese" OR "Retenção de Próteses" OR "Prosthesis Fixation" OR "Fijación de Prótesis" OR "Fixação de Prótese" OR "Fixação de Próteses" OR "Extention" OR "Extensión" OR "Extensão" OR "Adaptation" OR "Adaptación" OR "Adaptação" OR "Occlusal Adjustment" OR "Ajuste Oclusal" OR "Base Adjustment" OR "Ajuste de la base" OR "Ajuste de base" OR "Ajuste da base" OR "Centric Relation" OR "Relación céntrica" OR "Relação Cêntrica" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Dimensão Vertical" OR "Dimensões Verticais" OR "Dimensión Vertical" OR "Dimensiones Verticales" OR "Rest Vertical Dimension" OR "Dimensión Vertical de Descanso" OR "Dimensão Vertical de Descanso" OR "Dimensão Vertical de Repouso" OR "Mandibular Rest Position" OR "Posición de descanso mandibular" OR "Posição de descanso mandibular" OR "Posição de repouso mandibular" OR "Mandibular Rest Positions" OR "Posiciones de descanso mandibular" OR "Posições de descanso mandibular" OR "Posições de repouso mandibular" OR "Dental Occlusion" OR "Oclusión dental" OR "Oclusão dental" OR "Dental Occlusions" OR "Oclusiones dentales" OR "Oclusões dentais" OR "chewing" OR "sieving method" OR "mixing ability test" OR "biting" OR "bite" OR degluti* OR "swallowing" OR "occlusal force" OR "occlusal forces" OR mastiga* OR "método de peneiramento" OR "teste de habilidade de mistura" OR mordida* OR "força oclusal" OR "método de cribado" OR "fuerza oclusal" OR "Vickers" OR "Dimensional stability" OR "Estabilidade Dimensional" OR "Estabilidad Dimencional" OR "Flexural Strength" OR "Força Flexural" OR "Fuerza flexible" OR "Modulus of Rupture" OR "Módulo de ruptura" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistência Flexural" OR "Resistencia a la flexion" OR "Resistance" OR "Resistência" OR "Resistencia" OR "Fracture" OR "Fratuza" OR "Fractura" OR "Bend Strength" OR "Bend Strengths" OR "Força de dobramento" OR "Flexural Properties" OR "Flexural Property" OR "Propriedades Flexurais" OR "Propriedade Flexural" OR "Propiedades de flexión" OR "Propiedade de flexión" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Adhesion bacteriana" OR "aderencia bacteriana" OR "Adesão bacteriana" OR "Color Stability" OR "estabilidade de cor" OR "Estabilidad de color" OR "Stainability" OR "Staining" OR "Manchamento" OR "Tinción" OR "Residual monomer" OR "Monômero residual" OR "Monómero residual" OR "Electrical conductivity" OR "condutividade elétrica" OR "conductividad electrica" OR "Adhesion" OR "Adherence" OR "Adesão" OR "Aderência" OR "Agarre" OR "Membresía" OR "Thermal conductivity" OR "Heat conductivity" OR "Conductividad Térmica" OR "Conductividade Térmica" OR "Coefficient of conductivity" OR "Coeficiente de condutividade" OR "Coeficiente de conductividad" OR "Convenience" OR</p>
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	<p>"Conveniencia" OR "Conveniência" "Efficiency" OR "Eficiência" OR "Eficiencia" OR "Clinical outcomes" OR "Resultados Clínicos" OR "Complications" OR "Complicações" OR "Complicaciones" OR "Monomer release" OR "liberación de monómero" OR "liberação de monômero" OR "Monomer elution" OR "Elución de monómero" OR "Eluição de monômeros" OR "Fit" OR "Adaptação" OR "Encaixe" OR "Adaptación" OR "Encajar" OR "Toughness" OR "Dureza" OR "Resin volume" OR "Volume de resina" OR "Volumen de resina" OR "Denture weight" OR "Peso de la dentadura" OR "Peso da dentadura" OR "Peso da prótese" OR "Archiving" OR "Arquivamento" OR "Archivo" OR "Elastic modulus" OR "Modulos elasticos" OR "Módulo de elasticidade" OR "Elasticity Modulus" OR "Tooth movement" OR "Movimento dentário" OR "Movimiento de diente")</p>
<p>ProQuest (n = 43)</p>	<p>NOFT (("Denture" OR "Dentures" OR "Denture, Complete, Upper" OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins" OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction" OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip support" OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics" OR "Speech" OR "Public Speaking" OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR</p>

	<p>"Mandibular Rest Position" OR "Mandibular Rest Positions" OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition" OR "Swallowing" OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductivity" OR "Adhesion" OR "Adherence" OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement"))</p>
<p>OpenGrey (<i>n</i> = 1)</p>	<p>("Denture" OR "Dentures" OR "Denture, Complete, Upper" OR "Denture, Complete, Lower" OR "Complete prosthesis" OR "Complete prostheses" OR "Dental prosthesis" OR "Denture, Complete" OR "Complete Denture" OR "Complete Dentures" OR "Full arch denture" OR "Full arch dentures" OR "Denture Base" OR "Acrylic Resin" OR "Acrylic Resins" OR "Polymethyl Methacrylate" OR "Poly(methyl methacrylate)" OR "Polymethylmetacrylate" OR "PMMA" OR "Polymethylmethacrylate") AND ("Printing" OR "Computer-Aided Design" OR "Computer Aided Design" OR "Computer Aided Designs" OR "Computer-Aided Designs" OR "Computer Assisted Design" OR "Computer Assisted Design" OR "Computer-Aided Manufacturing" OR "Computer Aided Manufacturing" OR "Computer-Assisted Manufacturing" OR "Computer Assisted Manufacturing" OR "Computer-Engineered" OR "Computer-engineered complete dentures" OR "CECD" OR "CAD-CAM" OR "CAD/CAM" OR "Digital" OR "Printed" OR "Milled" OR "Milling" OR "Prototyping" OR "3D") AND ("Conventional" OR "Conventionally" OR "Conventional dentures" OR "Heat-cured" OR "Heat-curing" OR "Heat-polymerized" OR "Conventional curing" OR "Thermo curing") AND ("Cost" OR "Patient Satisfaction" OR "Prognosis" OR "Prognoses" OR "Prognostic Factors" OR "Prognostic Factor" OR "Overall result" OR "Patient Comfort" OR "Comfort, Patient" OR "Comfort Care" OR "Time" OR "Care, Comfort" OR "Lip support" OR "Esthetics" OR "Aesthetics" OR "Tooth arrangement" OR "Phonetics" OR "Speech" OR "Public Speaking" OR "Visual analog scale" OR "Visual Analog Scales" OR "Stability" OR "Retention" OR "Prosthesis</p>

	<p>Retention" OR "Prosthesis Fixation" OR "Extention" OR "Adaptation" OR "Occlusal Adjustment" OR "Adjustment" OR "Centric Relation" OR "Vertical Dimension" OR "Vertical Dimensions" OR "Rest Vertical Dimension" OR "Mandibular Rest Position" OR "Mandibular Rest Positions" OR "Dental Occlusion" OR "Dental Occlusions" OR "Mastication" OR "Chewing" OR "Masticatory" OR "Sieving method" OR "Mixing ability test" OR "Biting ability" OR "Biting abilities" OR "Deglutition" OR "Swallowing" OR "Bite force" OR "Bite forces" OR "Maximum occlusal force" OR "Maximum occlusal forces" OR "Vickers" OR "Dimensional stability" OR "Flexural Strength" OR "Modulus of Rupture" OR "Rupture Modulus" OR "Flexural Resistance" OR "Resistance" OR "Fracture" OR "Bend Strength" OR "Bend Strengths" OR "Flexural Properties" OR "Flexural Property" OR "Bacterial adhesion" OR "Bacterial adhesions" OR "Color Stability" OR "Stainability" OR "Residual monomer" OR "Electrical conductibility" OR "Adhesion" OR "Adherence" OR "Thermal conductivity" OR "Heat conductivity" OR "Coefficient of conductivity" OR "Convenience" OR "Efficiency" OR "Clinical outcomes" OR "Complications" OR "Monomer release" OR "Monomer elution" OR "Fit" OR "Toughness" OR "Resin volume" OR "Denture weight" OR "Archiving" OR "Adjustments" OR "Elastic modulus" OR "Elasticity Modulus" OR "Tooth movement")</p>
<p>Google Scholar (<i>n</i> = 100)</p>	<p>("PMMA" OR "Complete Denture" OR "Denture Base") AND ("Printing" OR "Computer Aided Design" OR "Computer Assisted Manufacturing" OR "CAD/CAM") AND ("Conventional" OR "Heat-cured") AND ("Patient Satisfaction" OR "Esthetics" OR "Phonetics" OR "Visual analog scale" OR "Stability" OR "Adaptation" OR "Stainability" OR "residual monomer" OR "electrical conductibility" OR "Microbiological adhesion")</p>

APPENDIX 2. Excluded articles and reasons for exclusion ($n = 22$).

Author, year	Reasons for exclusion*
• Alaqeel, 2019	3
• AlHelal, 2016	7
• Alp, 2018	1
• Belety, 2019	8
• Bitencourt, 2019	3
• Digholkar, 2016	3
• dos Santos, 2020	2
• Heikal, 2018	8
• Ismail, 2018	8
• Isshiki, 2017	8
• Inokoshi, 2012	6
• Kawai, 2005	2
• Kawai, 2010	2
• Kuboki, 2015	8
• Meshni, 2018	3
• Mohmmed, 2020	5
• Park, 2018	3
• Saponaro, 2016	2; 4
• Shaker, 2018	8
• Stawarczyk, 2013	3
• Tasaka, 2019	1
• Wimmer, 2017	6

* 1) Studies with less than 10 samples (dentures or specimens) per group; 2) absence of either test or control group; 3) studies that employed either self-curing acrylic resin or provisional materials as control group; 4) Retrospective studies; 5) Studies with missing data and/or not provided by the author after contact; 6) Studies not focused in denture bases outcomes; 7) Duplicated publication from the same study; 8) Reviews, letters, conference abstract, personal opinions, technique articles and clinical trials registrations

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CONSIDERAÇÕES FINAIS

Dentro das limitações da presente revisão sistemática, pode-se concluir que as Próteses Totais por Engenharia Computadorizada (PTECs) se apresentam como uma solução previsível e viável para o tratamento de pacientes edêntulos totais, oferecendo-lhes os benefícios de um número reduzido de consultas e reduzidos custos globais, uma retenção melhorada, uma satisfação e conforto aumentados, bem como uma arquivabilidade digital (reprodutibilidade).

Além disso, é possível concluir também que:

- Amostras de PMMA de alta performance fabricados por manufatura subtrativa (fresagem) mostraram *in vitro* propriedades mecânicas, ópticas e biológicas gerais superiores quando comparadas com amostras de resina fabricadas pelo método convencional (tanto por compressão quanto por injeção);
- as PTECs são preferidas por estudantes de Odontologia e consistem em um tópico relevante para uso no ensino em Prótese Total na educação de nível superior em Odontologia;
- a manufatura digital de próteses totais está inserida em uma curva de aprendizado, e os princípios teóricos envolvidos na reabilitação orientada pela face de pacientes edêntulos totais devem sempre ser respeitados;
- o nível de evidências clínicas das PTECs ainda é muito baixo;
- há uma falta de evidências clínicas e laboratoriais para suportar o uso de resinas de prototipagem rápida (impressão 3D) na fabricação de próteses totais por engenharia computadorizada;
- o desempenho clínico de PTECs suportadas por implantes dentários (Prótese Guiada) ainda precisa ser esclarecido.

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ANEXO 1. Registro do protocolo no PROSPERO.



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