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**Desarticulação interescapulotorácica em pacientes
com tumores mamários.
Revisão Sistemática da Literatura**

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

Orientador: Prof. Dr. René Aloísio da Costa Vieira

**Botucatu
2025**

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Aos meus pais, que fazem dos meus sonhos os sonhos deles, e aos meus irmãos, que me ensinam diariamente o significado de amizade e fraternidade

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RESUMO

INTRODUÇÃO: A desarticulação interescapulotorácica (DIET) em pacientes com carcinoma mamário invasivo (CMI) é considerada em casos selecionados: ressecção primária em tumor localmente avançado ou recorrente, Síndrome de Stewart & Treves (SST), ou sarcoma secundário a radiação pelo câncer de mama (SRI). No CMI, não há estudo que avalie através de casuística robusta indicações, resultados da DIET, complicações, recorrência e sobrevida global.

MATERIAL E MÉTODOS: Revisão sistemática da literatura em oito bases de dados até 31 de dezembro de 2022 segundo metodologia PRISMA. Os critérios de seleção foram publicações que incluíssem casuísticas, relatos ou série de casos de pacientes com CMI primário ou recorrente, SST ou SRI, com indicação ou submetidos a DIET. Dados das pacientes foram coletados em ficha padronizada, tabulados e analisados no programa IBM SPSS® for Mac®. Foram apresentadas estatísticas descritivas e avaliação da sobrevida pelo método Kaplan-Meier, sendo as diferenças avaliadas pelo método Log-rank.

RESULTADOS: Foram selecionados 54 artigos e coletados dados de 100 pacientes. A intenção e curativa em 48 casos (57,1%), paliativa em 32 (38,1%), realizada por SST (35%), disfunção de membro superior (18%), linfedema (10%), tumor axilar recorrente (10%) e SRI (9%). Descritas complicações em 10 casos, como necrose de pele e derrame pleural; havendo relatos de alívio de dor após a cirurgia, gratidão e bem-estar físico/emocional. A sobrevida atuarial global aos 12, 24, 36 e 60 meses foi 65.6%, 42.8%, 36.4% e 32.4%, respectivamente, e os principais fatores associados a sobrevida foram intenção curativa e SRI.

CONCLUSÃO: A DIET apresenta poucas complicações e atenua os sintomas, tanto nos casos com intenção curativa quanto paliativa. A cirurgia é justificada em casos selecionados como tumores localmente avançados, infiltração de estruturas axilares, linfedema de membro superior com perda de função, SST e SRI, e muitas vezes representando a principal chance de controle local da doença.

Palavras-chave: neoplasias de mama; desarticulação; desarticulação interescapulotorácica; amputação do quarto dianteiro; Síndrome de Stewart & Treves; Sarcoma radioinduzido.

ABSTRACT

INTRODUCTION: Forequarter amputation (FA) or Interscapulothoracic disarticulation is indicated in patients with invasive breast carcinoma (IBC) in selected cases: primary resection of a locally advanced or recurrent tumor, Stewart-Treves syndrome (STS), or sarcoma secondary to radiation due to breast cancer (radiation-induced sarcoma, RIS). However, no studies have robustly evaluated the indications, results, complications, recurrence and overall survival in the context of FA in patients with BC.

MATERIAL AND METHODS: We performed a systematic review of 8 databases according to the PICOS and PRISMA methodology through December 31, 2022. The selection criteria were publications that included case series, reports or case series of patients with primary or recurrent IBC, STS or RIS, with indication for or undergoing FA. Patient data were collected on a standardized form, tabulated and analyzed in the IBM SPSS® for Mac® program. Descriptive statistics are presented, and Kaplan–Meier survival curves were generated and compared with the log-rank method.

RESULTS: We identified 54 articles and collected data from 100 patients. The intention of FA was curative for 48 patients (57.1%) and palliative in 32 (38.1%). The procedure was performed due to STS (35%), upper limb dysfunction (18%), lymphedema (10%), recurrent axillary tumors (10%) and RIS (9%). Complications were described in 10 cases, such as skin necrosis and pleural effusion; there were reports of pain relief after surgery, gratitude and physical/emotional well-being. The overall actuarial global survival rates at 12, 24, 36 and 60 months were 65.6%, 42.8%, 36.4% and 32.4%, respectively. The main factors associated with survival were tumor's condition ($p=0.05$) and surgical intent ($p<0.001$; multivariate analysis).

CONCLUSIONS: FA has few complications and attenuates symptoms in patients treated with both curative and palliative intent. Surgery is justified in select cases, such as locally advanced tumors, infiltration of axillary structures, upper limb lymphedema with loss of function, and STS and RIS, and often represents the best chance for local disease control.

Key words: breast neoplasms; forequarter amputation; disarticulation; interscapulothoracic disarticulation; Stewart-Treves Syndrome; radiation-induced neoplasms

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LISTA DE SIGLAS E ABREVIATURAS

BC	Breast Cancer
CARE	Case Reporting
CEP	Comitê de Ética em Pesquisa
CONEP	Comissão Nacional de Ética em Pesquisa
DIET	Desarticulação interescapulotorácica
FA	Forequarter amputation
ISTD	Interscapulothoracic disarticulation
LABC	Locally advanced breast cancer
REC	Recurrence
RIS	Radiation-induced sarcoma
SRI	Sarcoma radio-induzido
SST	Síndrome de Stewart-Treves
STS	Stewart-Treves Syndrome

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INTRODUÇÃO

As cirurgias para ressecção de tumores localmente avançados com margens adequadas podem implicar em extensas ressecções de pele, músculos da parede torácica, entre outras estruturas, que origina grandes defeitos e necessidade de estratégias para fechamento (1, 2). As principais são as rotações de retalhos locais dermogordurosos, fasciocutâneos ou retalhos miocutâneos, a depender do tamanho do defeito, da experiência e preferência da equipe cirúrgica (1, 2). Uma das cirurgias realizadas em tumores avançados é a desarticulação interescapulotorácica (DIET) e consiste na ressecção do membro superior, clavícula e escápula, sendo indicada na ressecção de tumores primários ou metastáticos das cinturas escapulares que invadem o feixe neurovascular axilar.

A DIET é uma amputação descrita para tratamento, paliativo ou curativo, de tumores ósseos, sarcomas de partes moles, melanoma, como também para situações benignas, como osteomielites e grandes ferimentos. A cirurgia é indicada em casos de tumores que evoluem com ulceração, radionecrose, tumoração fixa em axila, com extensão para vasos sanguíneos e/ou plexo braquial, dor intratável, ou membro superior ipsilateral com linfedema e/ou sem função, geralmente aplicada a pacientes com razoável a bom status nutricional e como último recurso após tratamento padrão com cirurgia local, tratamento sistêmico e radioterapia (3, 4). Também é indicada para tratamento de sarcomas primários, na SST, em sarcomas pós mastectomia e linfedema.

Desarticulação interescapulotorácica e câncer de mama

A primeira publicação encontrada na literatura inglesa sobre a DIET em pacientes com câncer de mama foi realizada 1956, apresentando duas pacientes portadoras de neoplasia recorrente após tratamento primário, com edema, dor, tumoração axilar e perda de funcionalidade do membro superior ipsilateral a cirurgia (5). No entanto, é possível encontrar relatos na literatura de que o primeiro autor a conceber a DIET para tratamento de alguns casos avançados de câncer de mama foi um brasileiro, Antonio Prudente de São Paulo, Brasil, que realizou a primeira cirurgia em 1933 (6, 7).

Prudente defendeu a DIET associada a mastectomia radical para o

tratamento de casos selecionados, como metástases fixas de linfonodos axilares, grande linfedema do membro superior ipsilateral ao câncer, membro superior disfuncional secundário a comprometimento local pelo câncer, e paciente com bom status nutricional e risco cirúrgico adequado (5). Segundo Prudente, pacientes com câncer de mama localmente avançados e metástases à distância disseminadas, envolvimento profundo de estruturas torácicas, como arcos costais, que impossibilitassem ressecção tumoral completa e adequada, e metástases fixas em linfonodos supraclaviculares com invasão do feixe neurovascular na base do pescoço eram contraindicadas à DIET (6, 7).

No câncer de mama, observa-se descrições associadas a ressecção primária em tumor localmente avançado (8), ressecção de doença recorrente (9-12), associada a plexopatia braquial (12), Síndrome de Stewart-Treves (SST) (13, 14), ou sarcoma secundário a radiação pelo câncer de mama (15, 16) e doença metastática óssea (17). Frente a histologia após ressecção tumoral pela DIET, observa-se a presença de carcinomas (12, 18), tumor filoides maligno (19), além de sarcomas radioinduzidos como o angiosarcoma (13), o fibrosarcoma e o condrossarcoma (16). Para casos de câncer de mama localmente avançado, a cirurgia pode ser curativa, porém é feita na maioria das vezes no contexto paliativo (6). Outras indicações descritas estariam associadas a tumores primários localmente avançados ou recorrentes, com invasão do plexo braquial, cavo axilar, ou braço, SST e sarcoma radioinduzido (SRI) (20).

Em séries de pacientes submetidos à DIET, a associação com o câncer de mama representa cerca de 8,7% (21) a 12,5% das causas (22), com maior representação (37,5%) ao se considerar a DIET em pacientes com doença metastática (23), sendo a doença recorrente sua principal indicação (9-11, 23)), e em caráter paliativo (10, 12). A literatura é limitada sobre o tema, observando apenas dois casos descritos na literatura latino-americana: uma paciente com câncer de mama que evoluiu com metástase óssea e necessidade de DIET para tratamento de fratura patológica ou para preveni-la (17), e uma paciente com câncer de mama localmente avançado com recorrência no cavo axilar ipsilateral, com comorbidades (19), necessitando a DIET visando controle locorregional. Outras descrições relacionadas ao câncer de mama são observadas quando são avaliados casos de reconstrução da parede torácica (19, 24).

Gentil F. C. (21), em Tese de Livre-Docência (1978) não publicada,

reportou 80 casos de DIET, onde 7 pacientes eram portadoras de neoplasia da mama, representando 8,7% de seus 80 casos submetidos a DIET entre 1953 e 1974 no Hospital Antonio Camargo da Fundação Antonio Prudente. Das 7 pacientes submetidas a DIET por neoplasia mamária, cinco foram devido a doença axilar localmente avançada e um devido a metástase óssea umeral, com uma sobrevida de 14,2% em três anos, sendo que 6 pacientes evoluíram com morte por doença ou condição associada.

Com a implementação das estratégias de rastreamento mamográfico implicando em diagnósticos mais precoces, mudanças na radioterapia, além de novos tratamentos sistêmicos possibilitando melhor controle local da doença, tem se observado uma diminuição dos casos com indicação para a DIET (20).

Técnica cirúrgica

Em relação à técnica, é feita uma incisão na inserção do músculo esternocleidomastóideo na clavícula, estendida lateralmente ao longo da sua superfície anterior, dividida em Y à altura do acrômio. A incisão continua anteriormente no sulco deltopeitoral, sobre o músculo peitoral até a axila, e posteriormente ao longo da porção medial da escápula até se juntar à incisão anterior no ângulo escapular. A clavícula é toda exposta para permitir a visualização do eixo neurovascular, é dividida lateralmente à inserção do músculo esternocleidomastóideo, e então desarticulada do acrômio e do esterno. O músculo peitoral maior é dividido ao nível do peitoral menor. Os músculos peitoral menor, coracobraquial e bíceps são liberados de suas inserções para completar a exposição do eixo neurovascular. A veia e artéria subclávia, e plexo braquial são isolados e ligados. Os músculos rombóides maior e menor são divididos das suas inserções escapulares, permitindo a elevação da escápula para dividir os músculos trapézio, elevador da escápula e latíssimo dorso. O músculo serrátil anterior é liberado de sua inserção escapular. O membro superior é então removido em bloco. Quando há suspeita de acometimento tumoral de arcos costais, é possível removê-los em bloco com a peça cirúrgica pela secção dos arcos costais acometidos. Drenos são posicionados e um retalho miocutâneo vascularizado é usado para fechamento (9).

Em pacientes portadoras do câncer de mama, Prudente descreveu a técnica para remoção do membro superior em bloco com a mama. A incisão começa na borda interna do músculo deltóide, passa pelo sulco deltopeitoral e se

estende pela clavícula até a sua articulação com o esterno. A partir deste ponto, ela circunda a mama descendo a partir da sua borda medial, passando pela borda inferior e ascendendo pela margem lateral da mama, cruzando a parede lateral torácica em direção à borda medial do músculo grande dorsal. A incisão continua superior e diagonalmente em direção a borda posterior do músculo deltóide, circundando-o até o seu início. A desarticulação da clavícula é realizada no esterno e na escápula, o músculo subclávio é seccionado, há a exposição do plexo braquial e da artéria e veia subclávias, que são ligados e seccionados. A mama é excisada em bloco em conjunto com os músculos peitoral maior e menor. Linfadenectomia dos níveis I, II e III é realizada, bem como a ressecção dos nervos torácico longo e subescapular. O membro superior é rotacionado anteriormente, os músculos posteriores do úmero e da escápula são seccionados da parede torácica, e um retalho cutâneo a partir da região deltoide é confeccionado para ser utilizado como fechamento. Após estas etapas, é realizada a desarticulação interescapulotorácica em continuidade com a dissecação da fossa supraclavicular (6).

Resultados pós-operatórios da desarticulação interescapulotorácica

Na DIET clássica, a taxa de complicação é relativamente baixa, sendo geralmente associada a necrose de pele, deiscência local e derrame pleural (9-12). Elas são limitadas e não impactam negativamente no resultado pós-operatório (10). No entanto, por se tratar de uma cirurgia grande, a possibilidade de grande perda sanguínea, complicações locais como infecções, e tromboembolismo pulmonar devem ser considerados e incluídos na comunicação com o paciente e no seu manejo no perioperatório (12).

Um dos principais pontos a se considerar na DIET é o fechamento da área ressecada, o qual pode ser realizado por enxertos cutâneos, aproveitamento de parte da pele do membro, e rotação de retalhos miocutâneos (8-10, 12). Dentre as complicações relatadas, estão necrose de retalho ou da sua borda e cicatrização demorada.

Algumas complicações tardias são inerentes às amputações e são relatadas nas descrições de casos de pacientes com câncer de mama submetidas a DIET, por exemplo, a dor fantasma e a necessidade reabilitação das pacientes devido a ausência do membro. No entanto, com auxílio de uma equipe multidisciplinar, elas podem ser manejadas adequadamente, de forma a

contribuir com melhora da qualidade de vida dessas pacientes (12).

Intenção cirúrgica

Apesar do seu aspecto radical, a cirurgia permite controle locorregional, melhora dos sintomas, aumento do intervalo livre de doença e melhora da qualidade de vida, fato que justifica a sua realização em casos selecionados, podendo ser utilizado com intenção curativa ou paliativa (9, 10, 12). Da mesma forma, em pacientes com plexopatia braquial, envolvimento neurovascular da axila e disfunção do membro superior, este é um procedimento a ser considerado (12).

Série de casos mostraram que a sobrevida é melhor quando a intenção da DIET é curativa, sendo a média de 23 meses, diminuindo para 13 meses nos casos paliativos, tanto para controle de sintomas quanto para pacientes com doença sistêmica (10). A maioria das desarticulações interescapulotorácicas descritas para tratamento do câncer de mama são indicadas na recorrência local e/ou locorregional, principalmente axilares (9, 10, 12). No câncer de mama recorrente, a DIET pode ser curativa, na ausência de metástases à distância, ou paliativa e indicada para alívio dos sintomas locais, como dor não controlada, ulceração, odor fétido, infecções recorrentes, ulceração com necessidade de troca de curativos, sangramento, edema em membro superior, paralisia e/ou perda de funcionalidade do membro superior ipsilateral (24), ou para evitar estes desconfortos, visando controle local e sobrevida livre de doença (10).

Pundi e colaboradores, em uma série de casos levantados na literatura, relatam a média sobrevida de $23,4 \pm 14,6$ meses em pacientes com câncer de mama recorrente que foram submetidas à DIET com intenção curativa (10), e os casos levantados por Goodman apresentaram sobrevida de 22 a 48 meses (9). As pacientes com recorrência axilar de câncer de mama que evoluíram com plexopatia braquial por extensão local da doença, sem evidência de doença à distância, apresentam sobrevida global de 13 a 22 meses e sobrevida livre de progressão de 2 a 9 meses (12). No contexto paliativo, a sobrevida varia de 4 a 22 meses na doença recorrente e 4 a 60 meses na doença metastática (9), com sobrevida média é de aproximadamente 13 meses (10). São encontradas sobrevida livre de progressão de seis semanas e sobrevida global, de 4, 5, 6 a 17 meses devido a evolução da doença (10, 23, 24).

Desarticação interescapulotorácica e tumores consequentes ao tratamento do câncer de mama

Em 1948, Stewart e Treves publicaram seis casos de linfangiossarcoma em pacientes que evoluíram com linfedema de membro superior ipsilateral a mastectomia radical modificada secundária a câncer de mama, e dois foram submetidos a DIET (25). Posteriormente em 1952, foi denominada SST e sugerido que amputação radical precoce deveria ser indicada, por exemplo a DIET, assim que feito o diagnóstico (26). Desde então, são encontradas várias descrições de casos de SST que foram submetidos a DIET, tanto no contexto paliativo quanto no curativo, com sobrevida global e sobrevida livre de doença variáveis (13).

Em uma série de oito casos de pacientes com SST submetidas a DIET, a sobrevida livre de progressão local variou de 1 a 27 meses, sendo que duas pacientes não apresentaram recorrência local, e a sobrevida global variou de 2 meses a 72 meses, com relato de uma paciente viva sem evidência de doença por 6 anos (27). Quatro casos de SST tratados com DIET vivas e sem evidência de doença sobreviveram por 3, 16, 23 e 135 meses (13). Definir a extensão do linfangiossarcoma pode ser difícil, desta forma a DIET pode ser uma opção para ressecção cirúrgica completa, com margens negativas (27).

Em pacientes com câncer de mama, a radioterapia encontra-se associada a uma elevação do risco de desenvolvimento de uma segunda neoplasia não mamária, como o sarcoma radio-induzido (28), ou sarcoma ósseo. Apesar de histologia agressiva, a DIET permite controle locorregional, sendo descrito caso de paciente com sobrevida de 4 anos, evidenciando que esta cirurgia pode ser útil no contexto de neoplasias radio-induzidas após tratamento de câncer de mama (15, 16), apesar de ser um evento raro. A cirurgia é indicada de acordo com a extensão da doença e a possibilidade de ressecção completa, sendo que a escolha pela amputação pode proporcionar a cura. A cirurgia também possibilita diminuir os desconfortos da invasão local do SRI, geralmente localizados em ombro, região supra e infraclaviculares, e escápula (29).

A sobrevida global de pacientes com SRI após tratamento de câncer de mama submetidas a DIET descrita é de 12 a 24 meses, com óbito por metástases pulmonares (30, 31). Em uma série de sete casos de SRI após radioterapia por câncer de mama tratados com DIET, todos ressecados com margens

macroscopicamente livres, cinco pacientes estavam vivas com sobrevida de 18 a 60 meses após o diagnóstico do segundo tumor primário, e duas evoluíram para óbito por metástases após 6 e 17 meses do diagnóstico. Nenhuma paciente viva evoluiu com recorrência local, porém uma apresentou metástases pulmonares (29). Portanto, a DIET é uma opção para paliar sintomas e, em casos específicos, até curar pacientes com SRI selecionadas (30).

JUSTIFICATIVA

Apesar da cirurgia extensa e da sobrevida livre de doença e global variáveis, a DIET apresenta poucas complicações, que são pouco mórbidas e com pouco impacto na condução subsequente da neoplasia, e elevado sucesso na atenuação dos sintomas, tanto nos casos com intenção curativa quanto paliativa (9, 12, 23), elevando a qualidade de vida (18). Logo, a cirurgia é plenamente justificada em casos selecionados como tumores localmente avançados, infiltração de estruturas axilares, linfedema de membro superior importante com perda de função, na síndrome de Stewart-Treves e no sarcoma radio-induzido, e, muitas vezes representando a principal chance de controle local da doença e melhora na sobrevida destas pacientes (32).

A DIET, mesmo se tratando de uma amputação e, consequentemente, uma cirurgia desfigurante, possui valor no arsenal cirúrgico para manejo da paciente com câncer de mama. Observam-se descrições (relatos de caso) ou série de casos de pacientes com câncer de mama submetidas a DIET na literatura, apresentando resultados parciais, a partir de discussão de casos e cirurgia, faltando estudos que avaliem todos os aspectos multidimensionais relacionados à cirurgia.

Os relatos de casos encontrados na literatura nem sempre seguem os protocolos já existentes para a condução deste tipo de estudo e, consequentemente, apresentam dificuldade em avaliá-los pela falta de padronização das informações ali constantes (33). Existe também a dificuldade em agrupá-los em uma revisão sistemática pela ausência de metodologia para revisão sistemática de relatos e/ou série de casos. Além disso, os relatos de caso inerentemente possuem viéses de publicação, como a presença apenas de casos com desfechos positivos, inusitados ou surpreendentes, que atraiam a atenção, selecionados pelos próprios autores que os relatam, negligenciando os casos com negativos, sem resposta ou com desfechos desfavoráveis.

Até o presente momento, não se encontra descrito na literatura revisão sistemática sobre o tema. Uma revisão sistemática permite agrupar estes casos já descritos, avaliar as características dessas pacientes, o impacto da DIET no controle local, sobrevida global e recorrência das pacientes submetidas a esta opção cirúrgica, e traçar um padrão de evolução da doença (34-36) e dos

resultados do tratamento cirurgico (6, 19, 35).

OBJETIVOS

OBJETIVO GERAL

Realizar revisão sistemática de literatura de todos os casos publicados em base de dados de pacientes com câncer de mama ou com tumores consequentes ao tratamento do câncer de mama com indicação ou submetidas a desarticulação interescapulotorácica (DIET).

OBJETIVOS ESPECÍFICOS

- Descrever as características clínicas dos casos publicados;
- Avaliar quais são as indicações cirúrgicas, o caráter da cirurgia;
- Quantificar as complicações pós-operatórias;
- Avaliar recorrência local, locorregional e à distância, e sobrevida global das pacientes submetidas à DIET.

RESULTADOS

Esta revisão sistemática foi registrada no PROSPERO - International Prospective Register of systematic Reviews sob o número: PROSPERO 2025 RD420251118259 (37).

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FOREQUARTER AMPUTATION FOR BREAST CANCER. SYSTEMATIC REVIEW AND SURVIVAL ANALYSIS

ABSTRACT

Introduction: Forequarter amputation (FA) or Interscapulothoracic disarticulation is indicated in patients with invasive breast carcinoma (BC) in selected cases: primary resection of a locally advanced or recurrent tumor, Stewart & Treves syndrome (STS), or sarcoma secondary to radiation due to breast cancer (radiation-induced sarcoma, RIS). However, no studies have robustly evaluated the indications, results, complications, recurrence and overall survival in the context of FA in patients with BC.

Material and Methods: We performed a systematic review of 8 databases according to the PICOS and PRISMA methodology through December 31, 2022. Descriptive statistics are presented, and Kaplan-Meier survival curves were generated and compared with the log-rank method.

Results: We identified 54 articles and collected data from 100 patients. The intention of FA was curative for 48 patients (57.1%) and palliative in 32 (38.1%). The procedure was performed due to STS (35%), upper limb dysfunction (18%), lymphedema (10%), recurrent axillary tumors (10%) and RIS (9%). Complications were low. The survival rates at 12, 24, 36 and 60 months were 65.6%, 42.8%, 36.4% and 32.4%, respectively. The main factors associated with survival were tumor's condition ($p=0.05$) and surgical intent ($p<0.001$; multivariate analysis).

Conclusions: FA has few complications and attenuates symptoms in patients treated with both curative and palliative intent. Surgery is justified in select cases, such as locally advanced tumors, infiltration of axillary structures, upper limb lymphedema with loss of function, and STS and RIS, and often represents the best chance for local disease control and improvement in quality of life.

Key words: breast neoplasms; forequarter amputation; disarticulation; interscapulothoracic disarticulation; Stewart Treves Syndrome; radiation-induced neoplasms

INTRODUCTION

The first publication in the English literature on forequarter amputation (FA) or interscapulothoracic disarticulation (ISTD) in breast cancer patients dates back to 1956, describing the case of two patients with recurrent neoplasia following primary treatment presenting with edema, pain, axillary tumors and loss of functionality of the upper limb ipsilateral to the site of surgery¹. However, over time, the use of this procedure in the context of locally advanced tumor resection² (curative or palliative^{3,4}), recurrent disease⁵⁻⁹, brachial plexopathy⁸, Stewart & Treves syndrome (STS)¹⁰⁻¹², sarcoma secondary to radiation due to breast cancer (radiation-induced sarcoma, RIS)^{13,14} and metastatic bone disease¹⁵ has been reported. Histological types associated with the use of FA include carcinoma^{8,9}, malignant phyllodes tumors¹⁶, and RISs such as angiosarcoma¹⁰, fibrosarcoma and chondrosarcoma¹⁴.

Owing to its morbidity and case selection criteria, this surgery is not frequently indicated. In breast cancer, due to the multiple associated conditions, the use of FA is usually described in the form of case reports or case series^{4,8,17-21}. However, no studies have evaluated the indications, surgical results, complications, recurrence and overall survival associated with the use of this procedure. Thus, to better understand the multiple factors associated with FA in the context of breast cancer, a systematic review of the literature is necessary to understand the benefits of this procedure.

MATERIALS AND METHODS

This was a systematic review of the literature conducted in eight databases () through December 31, 2022, according to the PRISMA methodology²² (Figure 1). Two searches were conducted with the PICOS methodology, the first including the keywords ("Breast neoplasm") AND ((amputation) OR amputations) OR (disarticulation OR disarticulations) OR (forequarter) OR (periscapular) OR (interscapulothoracic)). The second search included ("Breast Neoplasm") AND ((amputation) OR amputations) OR (disarticulation OR disarticulations) OR (forequarter) OR (periscapular) OR (interscapulothoracic)) AND ((Sarcoma) OR (Lymphangiosarcoma)). Other equivalent controlled terms were employed depending on the database. In addition to those studies retrieved from the database search, four studies were identified from a search of the citations of the retrieved studies.

The literature review was performed by two independent reviewers who, after excluding duplicates, selected articles on the basis of the title and abstract. The reviewers' databases were pooled and compared, and in cases of disagreement, the full

texts of the articles were evaluated. The selection criteria were publications including case studies, case series or reports of patients with primary or recurrent invasive breast carcinoma, lymphangiosarcoma or RIS following primary treatment for breast cancer with indications for or undergoing FA, with no restrictions on the period or type of treatment and written in English, Portuguese, Spanish, French or German. The exclusion criteria were as follows: a) older articles lacking abstracts, abstracts only, or articles published in journals unavailable on the internet or that cannot be retrieved from the Regional Library of Medicine (BIREME/Brazil); b) patients who underwent FA for other causes, such as other neoplasms, or who underwent other surgeries; and c) publications that did not allow the individualization of patients treated with FA. The full texts of the articles that met these criteria were subsequently evaluated.

Patient data, including age; characteristics of the neoplasm at the time of diagnosis and its primary treatment; characteristics of the tumor at the time of indication for FA, such as local, locoregional and systemic recurrence, and clinical presentation of the disease; FA indications; nature of surgery and its characteristics; specific information related to STS and RIS; complications; quality of life; recurrence; and survival were collected in a standardized form from the articles. The intention of the surgery was recorded as that reported by the author; if it was not defined, this information was considered ignored data. These data were then tabulated and analyzed with the IBM SPSS software□ for Mac□. Descriptive statistics are presented, and the Kaplan-Meier method was used to assess survival, with differences between survival curves assessed with the log-rank method. Univariate and multivariate analysis (conditional forward) was performed.

As this is a review of the literature, the present study fits Resolution 510/2016 of the National Health Council, which waives the need for registration and evaluation through the Research Ethics Committee (Comitê de Ética em Pesquisa, CEP)/National Research Ethics Commission (Comissão Nacional de Ética em Pesquisa, CONEP) system. This systematic review was not registered.

RESULTS

A total of 1327 articles were identified, among which 417 duplicates were excluded, resulting in 910 articles whose titles and abstracts were evaluated by two independent reviewers. Of these, 106 articles were selected for a full text reading. After applying the inclusion and exclusion criteria, 54 articles encompassing 100 patients with indications or who underwent FA due to BC (primary or recurrent), lymphangiosarcoma (STS) or RIS after primary treatment for BC (Figure 1) were selected for data collection.

These data came from single-case reports^{2,5-7,9,13,16,23-50}, two-case reports^{1,42,51-55}, and case series^{8,10,17-21,56,57} whose median and mean number of cases per article were 1 and 1.8 (range 1 to 9 cases), respectively.

The articles were published from 1955 to 2022 and consisted 69% of case reports and 29% of case series; 62% of cases reported in the literature of patients indicated for or undergoing FA were published from the 1990s onwards. Table 1 shows the main clinical characteristics of the published cases. The mean age at diagnosis of the primary neoplasm was 52.95 ± 9.56 years; 96% of the patients were female, and 78% were diagnosed with primary BC.

Information on the pretreatment clinical stage, histological type and histological grade, and immunohistochemical classification was not provided in most case reports (Supplementary Tables 1 and 2). Mastectomy (78%) and axillary lymphadenectomy (67%) were the most commonly performed surgeries for the treatment of primary breast cancer, and FA was performed as the first surgical treatment in 5% of cases. Among studies that reported adjuvant treatment, adjuvant radiotherapy was the most commonly described and performed (92.8%).

Regarding the tumor conditions at the time of FA indication, 47% of the cases had STS, 23% had recurrent BC, and 15% had RIS (Table 1 and Supplementary Table 3). The most commonly reported symptoms were edema (88.5%), pain (89.1%), and upper limb dysfunction (82.5%). In terms of recurrence, 31% reported local recurrence, and 16% described distant metastases, with the most common site being the lung (Supplementary Table 4).

In the 100 patients evaluated, FA was indicated with curative intent in 48 patients (57.1%) and palliative intent in 32 patients (38.1%); It was not possible to judge the intention of surgery for the remaining 20 patients. Four patients did not undergo FA despite presenting with indications for the procedure due to refusal, comorbidities or presence of distant metastases. Among the 96 patients who underwent the surgery, the main indications were STS (35%), upper limb dysfunction (18%), lymphedema (10%), recurrent and uncontrollable axillary tumors (10%) and RIS (9%). A total of 44 patients (60.3%) underwent surgery as the first treatment for the condition that indicated the need for FA, 14 (19.2%) underwent the procedure after adjuvant treatment, and 13 (17.8%) were treated after tumor resection surgery.

The chest wall was partial resected at the time of FA in 14 cases (60.9%), among whom primary closure was possible in 9 cases, and 16 cases required some type of flap or graft, such as myocutaneous flaps (2 Requiring latissimus dorsi myocutaneous flaps)

or extremity free flaps (Table 2). Complications after FA were reported in 10 cases, the most common of which were skin necrosis (22.6%), pleural effusion (17.25%) and delayed healing (11.1%). Thirteen reports described pain alleviation after surgery, six each described complete pain relief and phantom pain, and 10 (90.9%) and 14 (100%) reports described a sense of gratitude and physical/emotional well-being, respectively (Table 3).

After surgery, recurrence was present in 62.6% of cases, with distant recurrence being the most common (50%), followed by local recurrence (33.3%) (Supplementary Table 5, 6). Local recurrence was reported in 22/66 patients, occurring mainly when FA was used for STS (13/30), symptom control (10/30), and recurrent disease (7/15), irrespective of treatment intention [curative (7/35) or palliative (8/20)], tumor status or time of surgery.

The overall mean time from primary diagnosis to death or loss to follow-up was 128.7 ± 82.0 months; for patients treated with curative intent, the mean time was 149.8 ± 92.7 months, and for those treated palliative intent, the mean time was 99.3 ± 66.3 months. At the time of the last follow-up, 45.3% of the patients had died due to cancer, and 34.7% were alive without disease. The overall follow-up time after FA was 23.9 ± 30.8 months; 29.6 ± 36.6 months for curative intention; 18.5 ± 27.4 months for palliative intention and 3.3 ± 3.0 months for patients no submitted to FA.

The survival rates at 12, 24, 36 and 60 months were 65.6%, 42.8%, 36.4% and 32.4%, respectively. Evaluating factors associated to survival (Table 4, Figure 2), main indication ($p=0.194$), moment of surgery ($p=0.579$), surgical condition ($p=0.048$) and factors intention of surgery ($p<0.001$), two factors were observed. Multivariate analysis showed that treatment intention was the main factor associated to survival, since the inclusion ($p=0.003$) or not-inclusion ($p=0.001$) of missing data, and patients who underwent curative surgery had better survival.

DISCUSSION

In a series of patients who underwent FA, the indication for the procedure in approximately 12.5% of the patients was breast cancer⁵⁸. This procedure is usually performed for patients with metastatic disease²⁰ and recurrent disease^{5-7,20} and with palliative intent^{6,8}. In this review, the main indication for the procedure was STS^{12,59}, followed by breast cancer recurrence^{5,6,8}, RIS^{13,14}, and metastatic disease¹⁵.

In terms of metastasis, one patient with breast cancer who progressed to bone metastasis required FA to treat or prevent pathological fracture, and one patient with

locally advanced breast cancer experienced recurrence in the ipsilateral axillary cavus^{9,15}. Other descriptions related to breast cancer involved the evaluation of chest wall reconstruction^{16,24}. In patients with STS and RIS, surgery is usually intended to be curative (21/25 patients); in the presence of recurrent/unresectable axillary disease or to control symptoms, it tended to be palliative (28/54 patients). In this sample, potential bias should be considered in the selection of cases, as patients with better performance are usually selected for surgery. Among the four patients who did not undergo surgery, the mean survival time was 4.1 ± 3.2 months, indicating that even in unfavorable and palliative scenarios, surgery helps control symptoms, potentially improving quality of life.

The results of this review indicated that the interval between the initial treatment until the development of RIS and STS was 9.0 ± 4.1 years and 15.8 ± 18.9 years, respectively (Supplementary Table 3). Factors such as the type of radiotherapy may have affected these values, since STS has become less prevalent with new forms of energy associated to radiotherapy.

One of the main points to consider in FA is the closure of the resected area, which can be performed using part of the skin of the affected limb, skin grafts, and myocutaneous flaps^{2,5,6,8}. Few articles have reported surgical results, such as margins (free in 19/24 patients), chest wall resection (present in 14/23 patients) and the need for flaps to close the defect (9/25), usually with a primary or free graft (2/25).

In classical FA, the complication rate is relatively low and usually related to skin necrosis, local dehiscence and pleural effusion⁵⁻⁸. These complications can be considered limited and do not negatively impact the postoperative outcome⁶. Among the complications reported are necrosis of the flap or its edge and delayed healing. In this sample (Table 3), the complication rate was approximately 25% (10/40); the primary complications included necrosis (7/31 = 22.6%), pleural effusion (5/29 = 17.3%), dehiscence (3/29=10.4%), delayed healing (3/27=11.1%) and infection (1/24=4.2%), fully justifying the surgery.

The lack of standardization among the reports, as well as the wide range of indications and follow-up times, limits the evaluation of the immediate results of the procedures, especially when used for symptom control. According to this review, pain relief (13/25) or control (6/25), phantom pain (6/25), and senses of gratitude (10/11), and physical, social and/or emotional well-being (14/14) have been reported following FA.

A review of the literature on patients undergoing FA for recurrent disease (n = 28) revealed better survival with a curative intent, with a mean of 23 months, whereas palliative intent was associated with a mean survival of 13 months when used both for

symptom control and for patients with systemic disease⁶. In this review (n=100), we included patients in different situations who underwent FA, with mean survival times of 29.6□ 36.6 months and 18.5□ 27.5 months following treatment with curative and palliative intent, respectively. Given its systematic nature, this review includes the largest number of patients to date, which allows us to compare groups using survival estimation. The results indicated that patients undergoing curative surgery had significantly greater survival ($p<0.001$); nevertheless, of the patients who underwent palliative surgery, half were alive at 12 months, and a quarter were alive at 24 months, so it is important to evaluate indicators of quality of life in future studies.

Another factor associated with survival was the condition that led to surgical treatment. Survival was significantly associated with the surgical condition ($p= 0.048$); specifically, patients with RIS and those with metastatic disease had longer and shorter survival times, respectively. In RIS, surgery allows the degree of discomfort associated with local invasion, usually located in the shoulder, supraclavicular and infraclavicular regions, and scapula, to be reduced²¹. The overall survival of patients who developed RIS after treatment for breast cancer following FA was 12-24 months; in this group, death was mainly due to lung metastases^{23,25}. In a series of seven patients with RIS after radiotherapy for breast cancer treated with FA, all of which were resected with macroscopically free margins, five patients survived with survival of 18 to 60 months after the second primary diagnosis, and two died due to metastases at 6 and 17 months after the diagnosis. No patient who survived experienced local recurrence, but one patient developed lung metastases²¹. FA was chosen as an option for alleviating symptoms and curing patients with RIS²⁵. This series included 13 patients, with a mean follow-up of 35.6□ 47.1 months and RIS is associated with the best prognosis.

FA for the treatment of STSs has been described in the literature since 1948, in a six-case series published by Stewart and Treves, who gave the syndrome its name¹². In a series of eight patients with STS who underwent FA, local progression-free survival ranged from 1 to 27 months, with one patient surviving without evidence of disease for 6 years¹⁹. Four patients with STS treated with FA survived without evidence of disease for a mean time of 44.2 months⁴. STS patients have the highest local recurrence rate (10/23). In this study, in a group of 39 patients, the mean follow-up was 22.2□ 32.7 months, and the 24-month survival rate was 42.3%.

In the treatment of BC, FA is primarily indicated for local and/or locoregional recurrence, especially axillary recurrence^{5,6,8}. In a case series from the literature, Pundi et al. reported a mean survival of 23.4 ± 14.6 months in patients with recurrent breast

cancer who underwent FA with curative intent⁶, while Goodman presented a survival of 22 to 48 months in a separate case report⁵. Patients with axillary breast cancer recurrence who progressed to brachial plexopathy due to local extension of the disease without evidence of distant disease demonstrated an overall survival of 13-22 months and progression-free survival of 2-9 months⁸. Patients with locally advanced primary, recurrent and metastatic disease presented with follow-up times of 33.4 ± 30.7 months, 21.5 ± 15.5 months and 8.8 ± 5.3 months, respectively.

Palliative surgery is indicated for the partial or complete relief of local symptoms such as uncontrolled pain, ulceration, foul odors, recurrent infections, ulceration requiring dressing changes, bleeding, upper limb edema, and paralysis and/or loss of functionality of the ipsilateral upper limb²⁴, with the goal of local control and disease-free survival⁶. In the palliative setting, survival ranged from 4 to 22 months in patients with recurrent disease and from 4 to 60 months in patients with metastatic disease⁵, while a median survival of approximately 13 months has been reported⁶. Progression-free survival of six weeks and overall survival of 4, 5, 6 or 17 months have been reported in patients with disease progression^{6,20,24}. In this series, patients with recurrent disease had a better prognosis than did patients with metastatic disease, among whom only 16.7% were alive at 12 months.

In this review, we sought to evaluate the main data associated with FA exclusively in the context of breast cancer through a rigorous analysis of the literature, extracting key conclusions that allowed us to evaluate the main groups treated with this procedure as well as their survival. Despite these strengths, a number of limitations should be noted, including the retrospective nature of the study, in which we observed a large variation in the quantity and quality of the information present in the studies, possibly due to the characteristics of the publications, which were typically case reports and small case series. Nevertheless, to the best of our knowledge, this is the first study to estimate the survival rates of these patients. Another major limitation was the lack of adequate evaluation of outcomes associated with improvements in symptoms and quality of life, which is necessary to better understand the benefits of this surgery in palliative contexts and especially metastatic patients. To address this issue, we present the main points to be addressed in future studies (Supplementary Table 7).

We suggest conducting systematic reviews of case reports or series. The standardization of data to be used to conduct case reports, CARE⁶⁰ (CAsEReporting), dates from 2013, but it is still not used frequently. We performed a systematic review according to the PRISMA methodology²² with the goal of identifying relevant articles and

extracting key data. We are aware of the need to standardize data to be used in future studies, so we suggest that review articles⁶¹ or systematic reviews, including case reports, consider the information in Supplementary Table 8.

Despite the extensiveness of the surgery and wide range of disease-free and overall survival, FA is associated with few complications and high success in relieving symptoms, both in curative and palliative contexts^{5,8,20}, leading to improvements in quality of life⁹. Surgery is fully justified in carefully selected cases, such as locally advanced tumors, infiltration of axillary structures, significant upper limb lymphedema with loss of function, and both STS and RIS, and often represents the best chance for local disease control, improvement in patient survival⁶², possibly contributing positively to quality of life.

CONCLUSIONS

Despite its nature as an amputative and, consequently, disfiguring surgery, FA has value as part of the surgical arsenal for managing patients with breast cancer. Better results are observed when employed in a curative context and for patients with RIS. It results in few complications, and those that occur are not very morbid and have little impact on the subsequent management of the primary tumor⁵. When used in palliative contexts, the goal is mainly to control symptoms. It allows the relief of pain and discomfort caused by swelling of the upper limbs and infiltration of axillary tumors into neurovascular bundles and/or ulcers, increasing patient quality of life⁹.

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Author contributions

Flavia Cardoso Franca: Conceptualization, Methodology, Investigation, Data curation, Visualization, Writing - original, Writing - review and editing; Idam de Oliveira-Junior: Data curation, Investigation, Visualization, Writing – original, Writing – review and editing; Rene Aloisio da Costa Vieira: Conceptualization, Supervision, Project administration, Methodology, Investigation, Data curation, Formal analysis, Resources, Visualization, Validation, Writing – original, Writing – review and editing.

Conflict of interest

The authors declared no conflict of interest.

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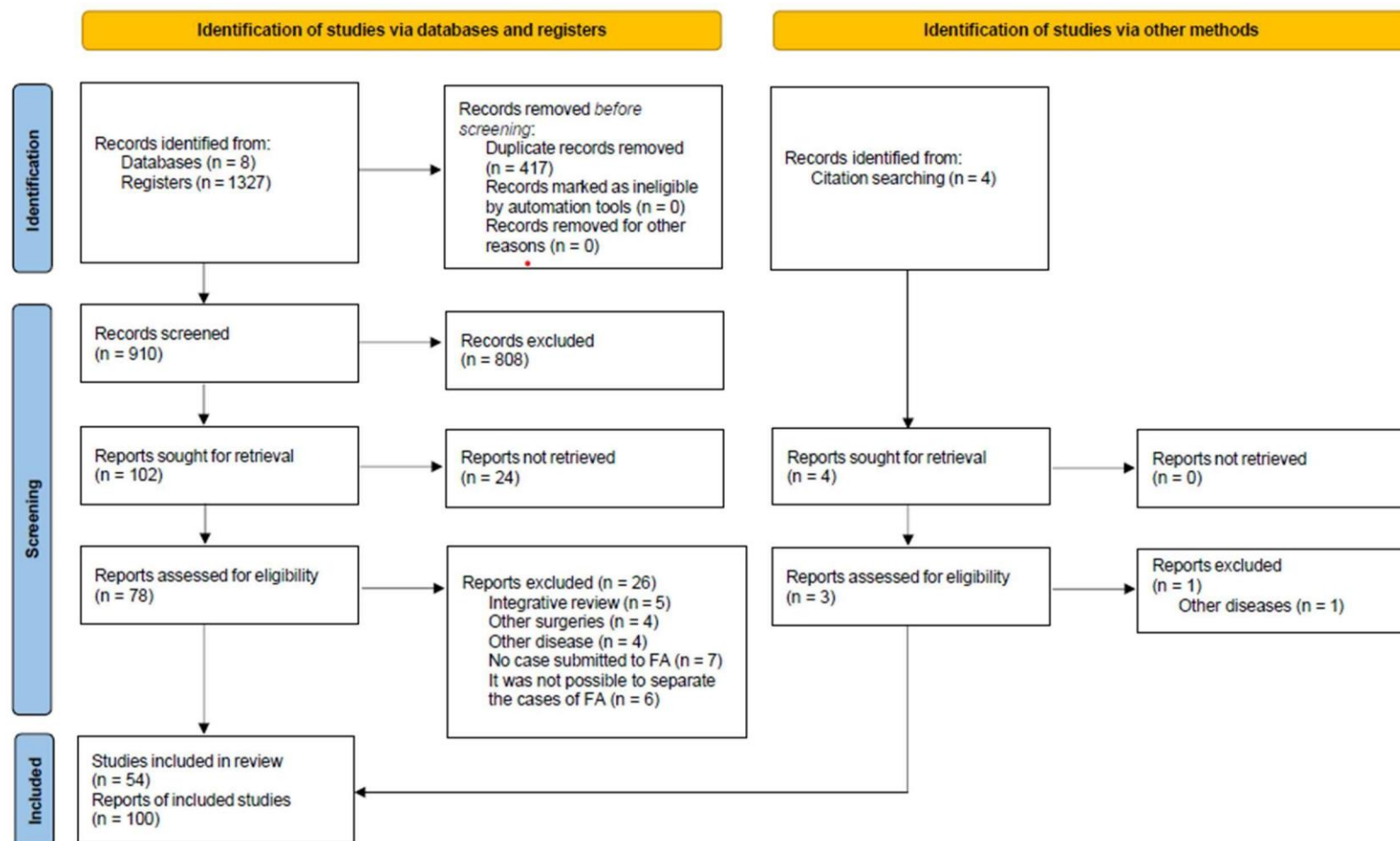
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LIST OF FIGURES

Figure 1. Prisma Flowchart

Figure 2. Actuarial survival according to conditions related to clinical indication



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>

Figure 1. Prisma flowchart. Fa: forequarter amputation.

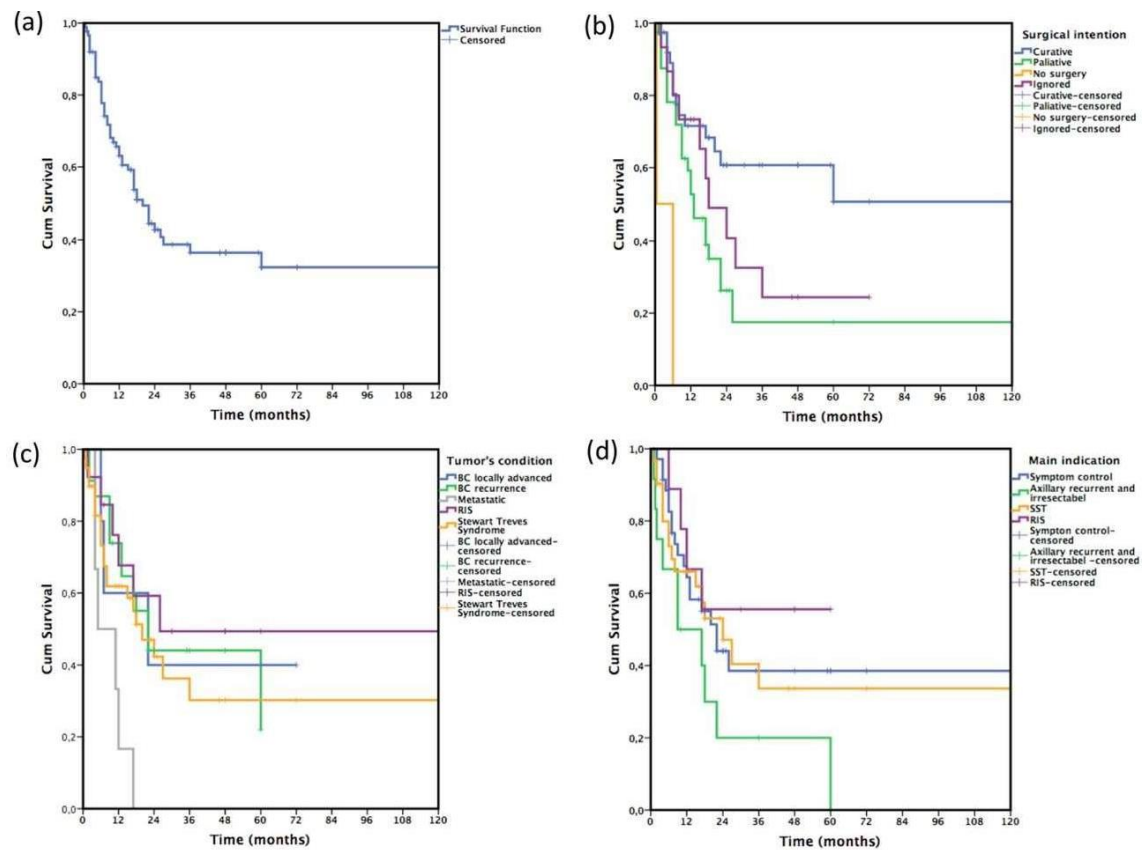


Figure 2. Actuarial survival according to conditions related to clinical indication. Cum. Survival: cumulative survival. Bc: breast cancer. Ris: radio-induced sarcoma

Table 1. Clinical characteristics of published cases (n = 100)

Category	Variables	N	Valid %
Gender (n = 98; 98%)	Feminine	96	97.9%
	Masculine	2	2.1%
	Ignored	2	
Age at diagnosis of primary neoplasia (n = 56; 56%)	Mean	52.95 ± 9.56	
Side of the neoplasia (n = 57; 57%)	Right	27	47.4%
	Left	30	52.6%
	Ignored	43	
Status at diagnosis of primary Neoplasm (n = 86; 86%)	Primary	78	90.7%
	Local recurrence with distant metastasis	5	5.8%
	Local recurrence without information on distant metastasis	2	2.3%
	Locally advanced primary neoplasm	1	1.2%
	Ignored	14	
Tumor conditions at the time of FA indication (n = 100; 100%)	STS	47	47%
	Breast cancer recurrence	23	23%
	RIS	15	15%
	Locally advanced primary neoplasm	6	6%
	Metastatic	5	5%
	Other	3	3%
	Bone metastasis in the shoulder joint	1	1%
Age at FA indication (n = 66; 66%)	Mean	60.8 ± 11.6	
Time from symptom onset to diagnosis (n = 11; 11%)	Mean	46.0 ± 64.3	
Larger clinical tumor size (n = 5; 5%)	Mean	10.4 ± 5.7 cm	
Time from treatment (primary surgery) to recurrence leading to FA (n = 49; 49%)	Mean	74.5 ± 49.4	
Time from treatment (primary surgery) to FA (n = 48; 48%)	Average	95.7 ± 79.9	
FA intent (n = 84; 84%)	Curative	48	57.1%
	Palliative	3)	38.1%
	Surgery indicated but not performed	4	4.8%
	Ignored	16	
FA performed (n = 100; 100%)	Yes	96	96%
	No	4	4%
Reasons for FA not indicated (n = 4)	Comorbidities	1	25%
	Refusal	2	50%
	Distant metastasis	1	25%
	Not applicable	96	
Patient status when FA not indicated (n = 4; 4%)	Death from neoplasia	1	25%
	Death from associated disease	2	50%
	Follow-up loss	1	25%

	Ignored	96	
Time from FA indication to outcome in a patient who did not undergo surgery (n = 3; 3%)	Mean	4.1 ± 3.2 months	
Main indication of FA (n = 100; 100%)	STS	35	35%
	Upper limb dysfunction	18	18%
	Lymphedema	10	10%
	Recurrent, unresectable axillary tumor	10	10%
	Pain	9	9%
	RIS	9	9%
	Ulceration	3	3%
	Locally advanced breast cancer	3	3%
	Bleeding	1	1%
	Paralysis	1	1%
	Other	1	1%
Timing of surgery (n = 73; 73%)	First surgical treatment for the reason for indication of FA	44	60.3%
	After adjuvant treatment	14	19.2%
	After tumor resection surgery	13	17.8%
	After limb-preserving adjuvant salvage treatment	2	2.7%
	Not applicable	4	
	Ignored	23	
Time from indication of FA to outcome in a patient undergoing surgery (n = 76; 76%)	Mean	24.1 ± 29.5 months	

STS: Stewart & Treves Syndrome; FA: forequarter amputation; RIS: radio-induced sarcoma.

Table 2. Aspects related to forequarter amputation (FA).

Category	Variable	N	Valid %
Size of the excised piece (n = 4; 4%)	Mean	32.7 ± 28.5 cm	
Pathological tumor size (n = 2; 2%)	Mean	12.5 ± 1.0 cm	
Type of resection (n = 7; 7%)	R0	5	71.4%
	R1	0	0
	R2	2	28.6%
	Not applicable	5	
	Ignored	88	
Margins (n = 24; 24%)	Positive	5	20.8%
	Negative	19	79.2%
	Not applicable	4	
	Ignored	72	
Surgical technique of mastectomy (n = 10, 10%)	Halsted	1	10%
	Pattey	1	10%
	Madden	2	20%
	Not applicable	6	60%
	Ignored	90	
FA surgical technique (n = 3; 3%)	Prudent	0	
	Other	3	100%
	Not applicable	4	
	Ignored	93	
Chest wall resection (n = 23; 23%)	Present	14	60.9%
	Absent	9	39.1%
	Not applicable	4	
	Ignored	73	
Closing technique (n = 25; 25%)	Primary	9	36%
	Myocutaneous flap	6	24%
	Extremity free flap	4	16%
	Fasciocutaneous flap	3	12%
	Skin-free graft	2	8%
	Free	1	4%
	osteomyocutaneous flap		
	Not applicable	4	
Myocutaneous flap (n = 18; 18%)	Ignored	72	
	Latissimus dorsi flap	2	11.1%
	Other	8	44.4%
	Absent	8	44.4%
	Not applicable	82	

FA: forequarter amputation

Table 3. Complications after forequarter amputation (FA) and its impacts on quality of life.

Category	Variable	N	Valid %
Complications (n = 40; 40%)	Yes	10	25%
	Missing	30	75%
	Not applicable	4	
	Ignored	56	
Pleural effusion (n = 29; 29%)	Yes	5	17.25%
	No	24	82.75%
	Not applicable	4	
	Ignored	67	
Infection (n = 24; 24%)	Yes	1	4.2%
	No	23	95.8%
	Not applicable	4	
	Ignored	67	
Dehiscence (n = 29; 29%)	Yes	3	10.4%
	No	26	89.6%
	Not applicable	4	
	Ignored	67	
Delayed healing (n = 27; 27%)	Yes	3	11.1%
	No	24	88.9%
	Not applicable	4	
	Ignored	69	
Necrosis (n = 31; 31%)	Yes	7	22.6%
	No	24	77.4%
	Not applicable	4	
	Ignored	65	
Other complications (n = 21; 21%)	Yes	3	14.3%
	No	18	85.7%
	Not applicable	4	
	Ignored	75	
Pain (n = 25; 25%)	Relief	13	52%
	Phantom pain	6	24%
	Absent	6	24%
	Not applicable	4	
	Ignored	71	
Gratitude (n = 11; 11%)	Yes	10	90.9%
	No	1	9.1%
	Not applicable	4	
	Ignored	85	
Physical, social, and/or emotional well-being (n = 14; 14%)	Yes	14	100%
	Not applicable	4	
	Ignored	78	
Quality of life assessment tool (n = 1; 1%)	Merimsky	1	100%
	Not applicable	4	
	Ignored	95	

FA: forequarter amputation.

Table 4. Actuarial survival as a function of the main situations related to the indication of forequarter amputation (FA)*

Variable	Category	n	12 months	24 months	36 months	60 months	p
Intention	Curative	39	71.6%	60.7%	60.7%	50.6%	< 0.001
	Palliative	32	52.6%	26.3%	17.5%	17.5%	
	Not realized	3	0	0	0	0	
Condition	RIS	13	67.6%	59.2%	49.4%	49.4%	0.048
	STS	39	61.9%	42.3%	30.2%	30.2%	
	Recurrence	23	73.9%	44.0%	44.0%	22.0%	
	LABC	4	60.0%	40.0%	40.0%	40.0%	
	Metastatic	6	16.7%	0	0	0	
Indication	Symptom	36	64.4%	44.0%	38.5%	38.5%	0.194
	STS	31	66.0%	47.1%	33.7%	33.7%	
	RIS	9	66.7%	55.6%	55.6%	55.6%	
	Axillary and unresectable rec.	12	50.0%	20.0%	20.0%	0	
Moment	Upfront	37	65.4%	51.1%	46.0%	46.0%	0.579
	After primary surgery	13	53.8%	53.8%	53.8%	0	
	After adjuvant	13	75.0%	30.0%	0	0	
Everyone	-	88	65.6%	42.8%	36.4%	32.4%	-

* Reported grouping of variables. RIS: radio-induced sarcoma; STS: Stewart & Treves Syndrome; Rec.: recurrence; LABC: locally advanced breast cancer.

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Clinical characteristics of published cases (n = 100)

Category	Variable	N	Valid %
Pre-treatment clinical stage (n = 17; 17%)	IIa	4	23.5%
	IIb	4	23.5%
	IIIa	1	5.9%
	IIIb	1	5.9%
	IIIc	6	35.3%
	IV	1	5.9%
	Ignored	83	
T (n = 13; 13%)	T1	1	7.7%
	T2	6	46.1%
	T4b	3	23.1%
	T4c	2	15.4%
	T4d	1	7.7%
	Ignored	87	
N (n = 23; 23%)	N0	5	21.7%
	N1	6	26.1%
	L2	3	13.1%
	N3	8	34.8%
	Nx	1	4.4%
	Ignored	77	
M (n = 22; 22%)	M0	20	90.9%
	M1	1	4.5%
	Mx	1	4.5%
	Ignored	78	
Histological type (n = 40; 40%)	Invasive breast carcinoma of no special type	30	75%
	Phyllodes tumor	1	2.5%
	Other	9	22.5%
	Ignored	60	
Histological type with no report of primary tumor (n = 3; 3%)	Angiosarcoma	2	66.7%
	Radio-induced sarcoma	1	33.3%
	Not applicable	97	
Estrogen receptor (n = 11; 11%)	Positive	3	27.3%
	Negative	6	54.5%
	Other histology	2	18.2%
	Ignored	89	
Progesterone receptor (n = 10; 10%)	Positive	4	40%
	Negative	4	40%
	Other histology	2	20%
	Ignored	90	
Her 2 (n = 11; 11%)	Positive	3	27.3%
	Negative	6	54.5%
	Other histology	2	18.2%
	Ignored	89	
Molecular subtype (n = 10; 10%)	Luminal B HER 2 negative	2	20%

	Luminal B HER 2 positive	2	20%
	Triple negative	4	40%
	Other histology	2	20%
	Ignored	90	
Nottingham histological grade (n = 10; 10%)	1	1	10%
	2	2	20%
	3	7	70%
	Ignored	90	

Supplementary Table 2. Characteristics of the primary treatment of invasive breast carcinoma

Category	Variable	N	Valid %
Initial surgical treatment of the breast (n = 93; 93%)	Mastectomy	78	83.9%
	Quadrantectomy / Sectorectomy	10	10.7%
	FA	5	5.4%
	Ignored	7	
Surgical treatment of the axilla (n = 74; 74%)	Axillary lymphadenectomy	67	90.5%
	Sentinel lymphnode biopsy	2	2.7%
	FA	5	6.7%
	Ignored	25	
Adjuvant chemotherapy (n = 39; 39%)	No	14	35.9%
	Yes	25	64.1%
	Ignored	61	
Adjuvant chemotherapy (n = 39; 39%)	No	14	35.9%
	Yes	25	64.1%
	Ignored	61	
Neoadjuvant chemotherapy (n = 38; 38%)	No	34	89.5%
	Yes	4	10.5%
	Ignored	62	
Chemotherapy prior to FA (n = 17; 17%)	No	9	52.9%
	Yes	8	47.1%
	Not applicable	1	
	Ignored	82	
Palliative chemotherapy (n = 18; 18%)	No	5	27.8%
	Yes	13	72.2%
	Not applicable	1	
	Ignored	81	
Palliative chemotherapy - when: (n = 13; 13%)	Before surgery	2	15.4%
	After surgery	9	69.2%
	Other	2	15.4%
	Not applicable	5	
	Ignored	82	
Adjuvant radiotherapy (n = 84; 84%)	No	6	7.2%
	Yes	78	92.8%
	Ignored	16	
Neoadjuvant radiotherapy (n = 48; 48%)	No	45	93.7%
	Yes	3	6.3%
	Not applicable	15	
	Ignored	37	
Radiotherapy prior to DIET (n = 26; 26%)	No	15	57.7%
	Yes	11	42.3%
	Not applicable	2	
	Ignored	72	
Palliative radiotherapy (n = 19; 19%)	No	7	36.8%
	Yes	12	63.2%
	Not applicable	2	
	Ignored	79	

Palliative radiotherapy - when: (n = 12; 12%)	Before surgery	2	16.7%
	After surgery	8	66.6%
	Other	2	16.7%
	Not applicable	87	
	Ignored	1	
Adjunctive hormone therapy (n = 12; 12%)	No	5	41.7%
	Yes	7	58.3%
	Not applicable	3	
	Ignored	85	
Neoadjuvant hormone therapy (n = 9; 9%)	No	8	88.9%
	Yes	1	11.1%
	Not applicable	3	
	Ignored	88	
Hormone therapy prior to DIET (n = 9; 9%)	No	8	88.9%
	Yes	1	11.1%
	Not applicable	3	
	Ignored	88	
Palliative hormone therapy (n = 10; 10%)	No	6	60%
	Yes	4	40%
	Not applicable	3	
	Ignored	87	
Palliative hormone therapy – when: (n = 4; 4%)	Before surgery	2	50%
	After surgery	2	50%
	Not applicable	95	
	Ignored	1	

FA: forequarter amputation;

Supplementary Table 3. Features related to Stewart & Treves Syndrome and radio-induced sarcoma

Category	Variable	N	Valid %
Stewart & Treves Syndrome	Yes	47	47%
	No	53	53%
Diagnosis	Clinical	0	100%
	Biopsy	47	
	Not applicable	53	
Time from primary treatment to lymphedema (n = 17; 17%)	Mean	4.0 ± 5.7 years	
Time from surgery to STS (n = 31, 31%)	Mean	15.8 ± 18.9 years	
Time from lymphedema to diagnosis of STS (n = 20, 20%)	Mean	13.7 ± 23.5 years	
Time from onset of symptoms to indication of FA (n = 13, 13%)	Mean	5.4 ± 5.4 months	
Radio-induced sarcoma	Yes	14	14%
	Absent	86	86%
Diagnosis	Clinical	0	100%
	Biopsy	14	
	Not applicable	86	
Histology	Fibrosarcoma	3	21.4%
	Malignant fibrous histiocytoma	2	14.4%
	Osteosarcoma	1	7.1%
	Other	1	7.1%
	Ignored	7	50%
	Not applicable	86	
Margins	Ignored	14	100%
	Not applicable	86	
Time from primary diagnosis to RIS (n = 6.6%)	Mean	9.0 ± 4.1 years	
Time from radiotherapy to RIS (n = 2.2%)	Mean	6.5 ± 6.4 years	
Time from symptom onset to FA (n = 2; 2%)	Mean	10.0 ± 4.2 months	

SST: Stewart & Treves Syndrome; RIS: radioinduced sarcoma; FA: forequarter amputation

Supplementary Table 4. Characteristics of the patients at the time of Forequarter amputation indication.

Category	Variable	N	Valid %
Local recurrence (n = 65, 65%)	Yes	31	47.7%
	No	34	52.3%
	Ignored	35	
Breast (n = 20, 20%)	Yes	6	30%
	No	14	70%
	Not applicable	35	
	Ignored	45	
Axilla (n = 28; 28%)	Yes	28	100%
	No	0	0%
	Not applicable	34	
	Ignored	38	
Breast and axilla (n = 12, 12%)	Yes	3	25%
	No	9	75%
	Not applicable	42	
	Ignored	46	
Others (n = 16; 16%)	Yes	2	12.5%
	No	14	87.5%
	Not applicable	36	
	Ignored	48	
Locoregional recurrence (n = 55; 55%)	Yes	17	30.9%
	No	38	69.1%
	Ignored	45	
Supraclavicular region (n = 10; 10%)	Yes	4	40%
	No	6	60%
	Not applicable	39	
	Ignored	51	
Infraclavicular region (n = 10; 10%)	Yes	5	50%
	No	5	50%
	Not applicable	39	
	Ignored	51	
Chest wall (n = 13; 13%)	Yes	12	92.3%
	No	1	7.7%
	Not applicable	39	
	Ignored	48	
Back (n = 6; 6%)	Yes	1	16.7%
	No	5	83.3%
	Not applicable	39	
	Ignored	55	
Contralateral breast (n = 7.7%)	Yes	1	14.3%
	No	6	85.7%
	Not applicable	39	
Contralateral axilla (n = 9.9%)	Yes	2	22.2%
	No	7	77.8%
	Not applicable	52	
Distant metastasis (n = 66; 66%)	Yes	16	24.3%
	No	50	75.7%
	Ignored	34	
Bone (n = 9; 9%)	Yes	2	22.2%
	No	7	77.8%
	Not applicable	50	
	Ignored	41	

Lung (n = 13; 13%)	Yes	5	38.5%
	No	8	61.5%
	Not applicable	50	
	Ignored	37	
Liver (n = 9; 9%)	Yes	0	
	No	9	100%
	Not applicable	50	
	Ignored	41	
Central nervous system (n = 10; 10%)	Yes	1	10%
	No	9	90%
	Not applicable	50	
	Ignored	40	
Other sites in the distance (n = 9; 9%)	Yes	6	66.7%
	No	3	33.3%
	Not applicable	50	
	Ignored	41	
Response to pretreatment (n = 93; 93%)	No prior treatment	4	4.3%
	Stable disease	4	4.3%
	Disease progression	24	25.8%
	Not applicable	1	1.0%
	2nd primary (STS or RIS)	60	64.5%
	Ignored	7	
Edema (n = 61; 61%)	Yes	54	88.5%
	No	7	11.5%
	Ignored	39	
Breast ulcer (n = 34; 34%)	Yes	7	20.6%
	No	27	79.4%
	Not applicable	3	
	Ignored	63	
Axillary ulcer (n = 40; 40%)	Yes	24	60%
	No	16	40%
	Ignored	60	
Fixed metastasis in axilla (n = 28; 28%)	Yes	13	46.4%
	No	15	53.6%
	Ignored	72	
Brachial plexopathy (n = 28; 28%)	Yes	18	64.3%
	No	10	35.7%
	Ignored	72	
Fixed shoulder joint (n = 20; 20%)	Yes	4	20%
	No	16	80%
	Ignored	80	
Dysfunctional upper limb (n = 40; 40%)	Yes	33	82.5%
	No	7	17.5%
	Ignored	60	
Pain (n = 46; 46%)	Yes	41	89.1%
	No	5	10.9%
	Ignored	54	
Infection (n = 19; 19%)	Yes	4	21.1%
	No	15	78.9%
	Ignored	81	
Axillary tumor mass (n = 34; 34%)	Yes	23	67.6%
	No	11	32.4%
	Ignored	66	
Wound dressings	Yes	11	45.8%

(n = 24; 24%)	No	13	54.2%
	Ignored	76	
Bleeding (n = 28; 28%)	Yes	15	53.6%
	No	13	46.4%
	Ignored	72	
Fungal infection (n = 19; 19%)	Yes	4	21.1%
	No	15	78.9%
	Ignored	81	
Necrosis (n = 18; 18%)	Yes	3	16.7%
	No	15	83.3%
	Ignored	82	
Blisters (n = 17, 17%)	Yes	1	5.9%
	No	16	94.1%
	Ignored	83	

FA: forequarter amputation; STS: Stewart & Treves Syndrome; RIS: radio-induced sarcoma.

Supplementary Table 5. Follow-up after forequarter amputation

Category	Variable	N	Valid %
Recurrence (n = 83; 83%)	Yes	52	62.6%
	No	31	37.4%
	Ignored	17	
Local recurrence (n = 66, 66%)	Yes	22	33.3%
	No	44	66.7%
	Ignored	34	
Axilla (n = 2; 2%)	Yes	2	100%
	Not applicable	44	
	Ignored	54	
Breast and axilla (n = 1; 1%)	Yes	1	100%
	Not applicable	44	
	Ignored	55	
Others (n = 3; 3%)	Yes	3	100%
	Not applicable	44	
	Ignored	53	
Locoregional recurrence (n = 62; 62%)	Yes	14	22.6%
	No	48	77.4%
	Ignored	38	
Supraclavicular region (n = 0)	Not applicable	48	
	Ignored	52	
Infraclavicular region (n = 1; 1%)	Yes	1	100%
	Not applicable	48	
	Ignored	51	
Chest wall (n = 12; 12%)	Yes	12	100%
	Not applicable	48	
	Ignored	40	
Back (n = 2; 2%)	Yes	2	100%
	Not applicable	48	
	Ignored	50	
Opposite breast (n = 1; 1%)	Yes	1	100%
	Not applicable	48	
	Ignored	51	
Opposite axilla (n = 1; 1%)	Yes	1	100%
	Not applicable	48	
	Ignored	51	
Distant metastasis (n = 74; 74%)	Yes	37	50%
	No	37	50%
	Ignored	26	
Bone (n = 1; 1%)	Yes	1	100%
	Not applicable	37	
	Ignored	62	
Lung (n = 13; 13%)	Yes	13	100%
	Not applicable	37	
	Ignored	50	
Liver (n = 0)	Not applicable	37	
	Ignored	63	
Central nervous system (n = 4; 4%)	Yes	4	100%
	Not applicable	37	
	Ignored	58	
Other sites of distant metastasis (n = 1; 1%)	Yes	1	100%
	Not applicable	37	

	Ignored	62	
Follow-up time since FA (n = 10; 10%)	Mean	35.0 ± 41.6 months	
Time from FA to local recurrence (n = 18; 18%)	Mean	9.1 ± 24.1 months	
Time from FA to locoregional recurrence (n = 12; 12%)	Mean	8.4 ± 10.7 months	
Time from FA to distant recurrence (n = 19; 19%)	Mean	9.1 ± 8.2 months	
Time from FA to death or loss to follow-up (n = 85; 85%)	Mean	24.6 ± 31.1 months	
Time from diagnosis to death or loss to follow-up (n = 54; 54%)	Mean	128.7 ± 82.0 months	
Patient's condition in the last report (n = 95; 95%)	Death from neoplasia	43	45.3%
	Alive without disease	33	34.7%
	Death from associated disease	4	4.2%
	Unspecified death	4	4.2%
	Alive with recurrence	3	3.1%
	Loss to follow-up	3	3.1%
	Other	5	5.3%
	Ignored	5	

FA: forequarter amputation.

Supplementary Table 6. Follow-up times (continuous variables).

Category	Variable	N	Total	N	Healing intention	N	Palliative intention
Follow-up time since FA - curative intention	Mean	10	37.3 ± 43.1 months	10	37.3 ± 43.1 months		
Time from FA to local recurrence	Mean	18	9.1 ± 24.1 months	6	19.7 ± 41.7 months	7	4.8 ± 3.7 months
Time from FA to locoregional recurrence	Mean	12	8.4 ± 10.7 months	7	6.5 ± 8.0 months	4	12.2 ± 16.3 months
Time from FA to distant recurrence	Mean	19	9.1 ± 8.2 months	5	22.0 ± 7.6 months	7	8.5 ± 6.6 months
Time from FA to death or loss to follow-up	Mean	85	23.9 ± 30.8 months	38	29.6 ± 36.6 months	32	18.5 ± 27.5 months
Time from diagnosis to death or loss to follow-up	Mean	54	128.7 ± 82.0 months	25	149.8 ± 92.7 months	23	99.3 ± 66.3 months

FA: forequarter amputation.

Supplementary Table 7. Points to be addressed in future studies.

Points to be addressed in future studies

Standardization of data included in reports and case series

Highlight the treatment performed by each patient in the case series

To assess the quality of life of patients undergoing forequarter amputation
through validated quality of life questionnaires

Standardize the reports of time from diagnosis and intervention to outcome

Grouping of data collected from reports and case series

Preparation of a protocol for systematic review of case reports and case
series

Supplementary Table 8. Data to be included in systematic reviews with reports or case series.

Data from reports or case series to be included in systematic reviews

Patient identification: gender, age, comorbidities

Symptoms and clinical information

Diagnosis and staging, if applicable

Main diagnostic methods performed and their results

Interventions or therapies performed and their types

Outcomes of therapies

Complications and/or difficulties of interventions

Prognosis

Impact of the intervention on quality of life

Patient's status at the last report

Follow-up time from main intervention to outcomes

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CONCLUSÃO

No câncer de mama, as pacientes submetidas a DIET geralmente constituem pacientes com Síndrome de Stewart-Treves, recorrência da neoplasia mamária e sarcoma radioinduzido. A maioria das cirurgias foi com intenção curativa. Esta cirurgia encontra-se associada a baixa complicação pós-operatória. Melhores resultados de sobrevida são observados em pacientes submetidos a cirurgia curativa, ou tendo a indicação associada ao SRI. Assim, a DIET, mesmo se tratando de uma amputação e, por consequência, uma cirurgia desfigurante, é plenamente justificada para controle local da doença e manejo de sintomas, fato que influencia positivamente na qualidade de vida.

ANEXOS

Anexo 1: Registo no PROSPERO - International Prospective Register of Systematic Reviews

Forequarter amputation for breast cancer. Systematic review and survival analysis.

Flavia Cardoso Franca, Rene Aloisio da Costa Vieira, Idam de Oliveira-Junior

Citation

Flavia Cardoso Franca, Rene Aloisio da Costa Vieira, Idam de Oliveira-Junior.
Forequarter amputation for breast cancer. Systematic review and survival analysis. .
PROSPERO 2025 CRD420251118259. Available from
<https://www.crd.york.ac.uk/PROSPERO/view/CRD420251118259>.

REVIEW TITLE AND BASIC DETAILS

Review title

Forequarter amputation for breast cancer. Systematic review and survival analysis.

Condition or domain being studied

Breast neoplasm; Forequarter Amputation; Curative care; Salvage surgery; Palliative surgery; Survival ; Recurrence free survival; Progression-Free Survival; Postoperative Complication

Rationale for the review

Owing to its morbidity and case selection criteria, forequarter amputation is not frequently indicated. In breast cancer, due to the multiple associated conditions, the use of forequarter amputation is usually described in the form of case reports or case series. However, no studies have evaluated the indications, surgical results, complications, recurrence and overall survival associated with the use of this procedure. Thus, to better understand the multiple factors associated with forequarter amputation in the context of breast cancer, a systematic review of the literature is necessary to understand the benefits of this procedure.

Review objectives

What is the impact of forequarter amputation on the treatment of breast cancer and/or tumors resulting from the treatment of breast cancer with indication or undergoing this surgery?

Keywords

Breast Neoplasms; forequarter amputation; disarticulation; interscapulothoracic disarticulation; stewart treves syndrome; Radiation-induced sarcoma

Country

Brazil

ELIGIBILITY CRITERIA

Population

Included

patients with primary or recurrent invasive breast carcinoma, lymphangiosarcoma or radiation-induced sarcoma following primary treatment for breast cancer with indications for or undergoing forequarter amputation

Intervention(s) or exposure(s)

Included

Forequarter Amputation; Disarticulation

Comparator(s) or control(s)

This review does not have any comparators

Study design

Both randomized and nonrandomized study types will be included.

Included

case studies, case series or reports of patients

Context

The selection criteria were publications including case studies, case series or reports of patients with primary or recurrent invasive breast carcinoma, lymphangiosarcoma or radiation-induced sarcoma following primary treatment for breast cancer with indications for or undergoing forequarter amputation, with no restrictions on the period or type of treatment and written in English, Portuguese, Spanish, French or German. The exclusion criteria were as follows: a) older articles lacking abstracts, abstracts only, or articles published in journals unavailable on the internet or that cannot be retrieved

TIMELINE OF THE REVIEW

Date of first submission to PROSPERO

02 August 2025

Review timeline

Start date: 2 August 2021. End date: 31 August 2025.

Date of registration in PROSPERO

02 August 2025

AVAILABILITY OF FULL PROTOCOL

Availability of full protocol

A full protocol has been written and uploaded to PROSPERO. The protocol may be accessed through this link

<https://www.crd.york.ac.uk/PROSPEROFILES/96ad0900c4a368de52091f4b9b5ecab3.pdf>.

SEARCHING AND SCREENING

Search for unpublished studies

Both published and unpublished studies will be sought.

Main bibliographic databases that will be searched

The main databases to be searched are *CINAHL - Cumulative Index to Nursing and Allied Health Literature*, *CLIB - The Cochrane Library*, *Embase - Embase via Ovid*, *Embase.com*, *LILACS - Latin American and Caribbean Health Sciences Literature*, *MEDLINE*, *PubMed* and *Scopus*.

Other important or specialist databases that will be searched

Cochrane, CINAHL Complete, Embase, Lilacs, PubMed, Scielo, Scopus and Web of Science

Search language restrictions

There are no language restrictions.

Search date restrictions

There are no search date restrictions.

Other methods of identifying studies

Other studies will be identified by: *looking through all the articles that cite the papers included in the review ("snowballing")*, *reference list checking* and *searching trial or study registers*.

Link to search strategy

A full search strategy has been uploaded to PROSPERO. The PDF may be accessed through this link

<https://www.crd.york.ac.uk/PROSPEROFILES/2f5fe14d56c3038ab30e607cbe2ac8e7.pdf>.

Selection process

Studies will be screened independently by at least two people (or person/machine combination) with a process to resolve differences.

Other relevant information about searching and screening

None

DATA COLLECTION PROCESS

Data extraction from published articles and reports

Data will be extracted by one person (or a machine) and checked by at least one other person (or machine).

Authors will not be contacted for further information.

Study risk of bias or quality assessment

Risk of bias/study quality will not be assessed.

Reporting bias assessment

Risk of bias due to missing results will be assessed

Certainty assessment

These data were then tabulated and analyzed with the IBM SPSS software□ for Mac□. Descriptive statistics are presented, and the Kaplan–Meier method was used to assess survival, with differences between survival curves assessed with the log-rank method. Univariate and multivariate analysis (conditional forward) was performed.

OUTCOMES TO BE ANALYSED

Main outcomes

Patient data, including age; characteristics of the neoplasm at the time of diagnosis and its primary treatment; characteristics of the tumor at the time of indication for forequarter amputation, such as local, locoregional and systemic recurrence, and clinical presentation of the disease; forequarter amputation indications; nature of surgery and its characteristics; specific information related to Stewart-Treves Syndrome and radiation-induced surgery; complications; quality of life; recurrence; and survival were collected in a standardized form from the articles. The intention of the surgery was recorded as that reported by the author; if it was not defined, this information was considered ignored data. These data were then tabulated and analyzed with the IBM SPSS software□ for Mac□. Descriptive statistics are presented, and the Kaplan–Meier method was used to assess survival, with differences between survival curves assessed with the log-rank method. Univariate and multivariate analysis (conditional forward) was performed.

Additional outcomes

There are no additional outcomes.

PLANNED DATA SYNTHESIS

Strategy for data synthesis

Patient data, including age; characteristics of the neoplasm at the time of diagnosis and its primary treatment; characteristics of the tumor at the time of indication for forequarter amputation, such as local, locoregional and systemic recurrence, and clinical presentation of the disease; forequarter amputation indications; nature of surgery and its characteristics; specific information related to Stewart-Treves Syndrome and Radiation-induced sarcoma; complications; quality of life; recurrence; and survival were collected in a standardized form from the articles. The intention of the surgery was recorded as that reported by the author; if it was not defined, this information was considered ignored data. These data were then tabulated and analyzed with the IBM SPSS software□ for Mac□. Descriptive statistics are presented, and the Kaplan–Meier method was used to assess survival, with differences between survival curves assessed with the log-rank method. Univariate and multivariate analysis (conditional forward) was performed.

CURRENT REVIEW STAGE

Stage of the review at this submission

Review stage	Started	Completed
Pilot work	✓	

Review stage	Started	Completed
Formal searching/study identification	✓	
Screening search results against inclusion criteria	✓	
Data extraction or receipt of IPD		
Risk of bias/quality assessment		
Data synthesis		

Review status

The review is currently planned or ongoing.

Publication of review results

Results of the review will be published in English.

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members

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No conflict of interest declared.

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No conflict of interest declared.

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No conflict of interest declared.

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Review affiliation

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Funding source

Review has no funding and no agreed support from an academic institution and is done in authors' own time.

Peer review

This systematic review will be presented to a panel of four professors to obtain a doctorate degree in Postgraduate Program in Tocogynecology - Botucatu School of Medicine (Botucatu - SP), São Paulo State University (UNESP).

ADDITIONAL INFORMATION

Review conflict of interest

Declared individual interests are recorded under team member details.. No additional interests are recorded for this review.

Medical Subject Headings

Breast Neoplasms; Survival Analysis; Surgical Oncology; Amputation

SIMILAR REVIEWS

Check for similar records already in PROSPERO

PROSPERO identified a number of existing PROSPERO records that were similar to this one (last check made on 2 August 2025). These are shown below along with the reasons given by that the review team for the reviews being different and/or proceeding.

- Quality of life of male patients after treatment for breast cancer: a systematic review [published 16 February 2024] [CRD42024510200]. The review was judged **not to be similar**
- Impact of cancer treatment on cardiovascular and cognitive outcomes of breast cancer patients: A systematic review and meta-analysis. [published 13 November 2024] [CRD42024608835]. The review was judged **not to be similar**
- Impact of postoperative complications on the initiation of adjuvant treatment and satisfaction levels after breast oncoplastic surgery in women with breast cancer: a systematic review. [published 14 October 2024] [CRD42024589617]. The review was judged **not to be similar**

PROSPERO version history

- [Version 1.0, published 02 Aug 2025](#)

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Any enquiries about the record should be referred to the named review contact

Anexo 2: Dispensa do Comitê de Ética em Pesquisa



UNIVERSIDADE ESTADUAL PAULISTA
"JULIO DE MESQUITA FILHO"
Câmpus de Botucatu



Deliberação nº: 351/2020

Data da Congregação: 24/07/2020

Assunto: Proposta para que subprojetos desenvolvidos no âmbito da Pós-Graduação, pertencentes a projetos "guarda-chuvas" que não apresentem modificações da proposta inicial, não sejam submetidos novamente à apreciação ética.

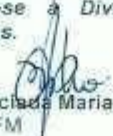
A CONGREGAÇÃO DA FACULDADE DE MEDICINA - UNESP, em reunião ordinária realizada no dia 24 de julho de 2020, após ampla discussão sobre as deliberações da Congregação 650/2001 e 489/2002 deliberou o que segue:

1) Todos os projetos de pesquisa da Unidade envolvendo seres humanos e/ou animais de experimentação deverão ser encaminhados para análise do Comitê de Ética em Pesquisa - CEP e/ou Comissão de Experimentação no Uso de Animais - CEUA, excetuando-se as pesquisas citadas no Parágrafo Único do Artigo 1º da Resolução nº 510/2016 - do Conselho Nacional de Saúde que estabelece: "Não serão registradas nem avaliadas pelo sistema CEP/CONEP: I - pesquisa de opinião pública com participantes não identificados; II - pesquisa que utilize informações de acesso público, nos termos da Lei nº 12.527, de 18 de novembro de 2011; III - pesquisa que utilize informações de domínio público; IV - pesquisa censitária; V - pesquisa com bancos de dados, cujas informações são agregadas, sem possibilidade de identificação individual; e VI - pesquisa realizada exclusivamente com textos científicos para revisão da literatura científica; VII - pesquisa que objetiva o aprofundamento teórico de situações que emergem espontaneamente e contingencialmente na prática profissional, desde que não revelem dados que possam identificar o sujeito; e VIII - atividade realizada com o intuito exclusivamente de educação, ensino ou treinamento sem finalidade de pesquisa científica, de alunos de graduação, de curso técnico, ou de profissionais em especialização."

2) Subprojetos desenvolvidos a partir de um projeto maior (genericamente conhecidos como guarda-chuva), que mudem seu título sem alterar procedimentos operacionais ou metodológicos aprovados pelo CEP ou CEUA não precisam ser ressubmetidos. Caberá ao pesquisador responsável que esteja identificado no parecer consubstanciado, manifestar-se em documento oficial indicando a situação acima mencionada bem como citar que o aluno que desenvolveu o subprojeto faz parte da equipe.

Essa deliberação revoga as deliberações 650 de 03 de agosto de 2001 e 489 de 08 de maio de 2002.

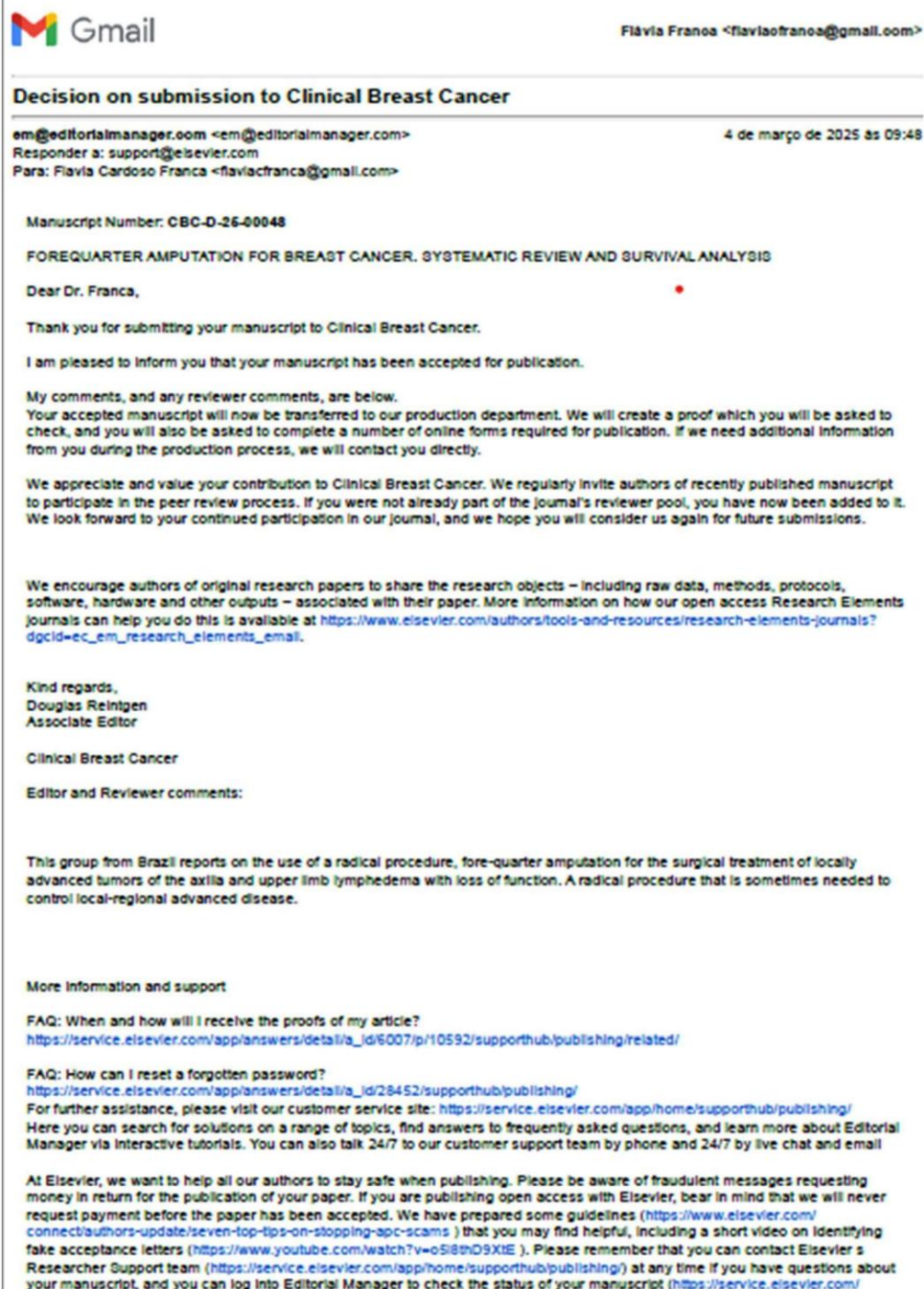
Encaminhe-se à Divisão Técnica Acadêmica (DTA), para as demais providências.


Profa. Associada Maria Cristina P. Lima
Diretora da FM

Faculdade de Medicina de Botucatu - Seção Técnica Acadêmica
Av. Prof. Manoel Rubens Guimarães Montenegro, s/n - CEP 13618-887 - Botucatu/SP
e-mail: sts@fmb.unesp.br

Anexo 3: Documentos de submissão de trabalho derivado de tese de doutorado para publicação:

Anexo 3.1: carta de aceite de trabalho na *Clinical Breast Cancer*:



Anexo 3.2: submissão de trabalho na European Journal of Surgical Oncology e no Journal of Surgical Oncology

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My Submissions René Aloisio da Costa

Start a new submission for *Journal of Surgical Oncology*

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My Submissions	Journal	Submission Status	Author Role
	All Journals	All Submission Statuses	Submitting Author Only
	Journal of Surgical Oncology		
	Review Article		

FOREQUARTER AMPUTATION FOR BREAST CANCER.
SYSTEMATIC REVIEW AND SURVIVAL ANALYSIS

Submission Status Rejected

Learn about what to do if your manuscript was rejected.

Manuscript ID	JSO-2024-2184
Rejected On	4 January 2025 by Editorial Office
Submitted On	28 December 2024 by René Aloisio da Costa Vieira

Submission overview →

Decision letter (Initial Submission)
JSO-2024-2184- Manuscript Decision

×

From: jso@wiley.com
To: reneacv@gmail.com

04-Jan-2025

Dear Dr. Vieira:

Your manuscript entitled, "FOREQUARTER AMPUTATION FOR BREAST CANCER. SYSTEMATIC REVIEW

AND

SURVIVAL ANALYSIS," (JSO-2024-2184) was reviewed by the Editorial Committee of Journal of Surgical Oncology. After careful consideration, the manuscript was not recommended for publication in the Journal. This decision reflects the priority that the manuscript was assigned in relation to competing submissions.

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Submissions are increasing each year and the JSO can publish less than 15% of them, so acceptance is chosen on priority. I am sorry that the answer on this occasion must be negative and hope that it will not dissuade you from submitting other manuscripts to the Journal in the future.

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Reviewer Comments to the Author:

Thank you for your interest in Journal of Surgical Oncology and for giving us the opportunity to review your manuscript.

Sincerely yours,

Dr. David Bentrem
Editor-in-Chief
Journal of Surgical Oncology

Fwd: Decision on submission to European Journal of Surgical Oncology

Flávia Franca <flaviacfranca@gmail.com>

Caixa de entrada

ter., 14 de jan., 20:25

para mim ▾

 Traduza para o português

×

----- Mensagem encaminhada -----

From: <em@editorialmanager.com>

Data: ter., 14 de jan. de 2025 às 20:18

Assunto: Decision on submission to European Journal of Surgical Oncology

Para: Flavia Cardoso Franca <flaviacfranca@gmail.com>

Manuscript Number: EJSO-D-25-00113

FOREQUARTER AMPUTATION FOR BREAST CANCER. SYSTEMATIC REVIEW AND SURVIVAL ANALYSIS

Dear Ms Franca,

Thank you for your submission to European Journal of Surgical Oncology.

After careful evaluation, I have determined there are other journals that may better suit your work.

The alternative journals I recommend are listed here:

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These journals all participate in Elsevier's Article Transfer Service, which means you do not have to resubmit or reformat your manuscript, saving you valuable time and effort during the submission process. While this does not constitute a guarantee that your paper will be published in one of the suggested journals, we hope this arrangement will help expedite the process for promising papers.

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We appreciate you submitting your manuscript to European Journal of Surgical Oncology and thank you for giving us the opportunity to consider your work.

Kind regards,

Riccardo A. Audisio, MD, PhD(Hon), FRCS, FEBS

Editor in Chief

European Journal of

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comments (if applicable):

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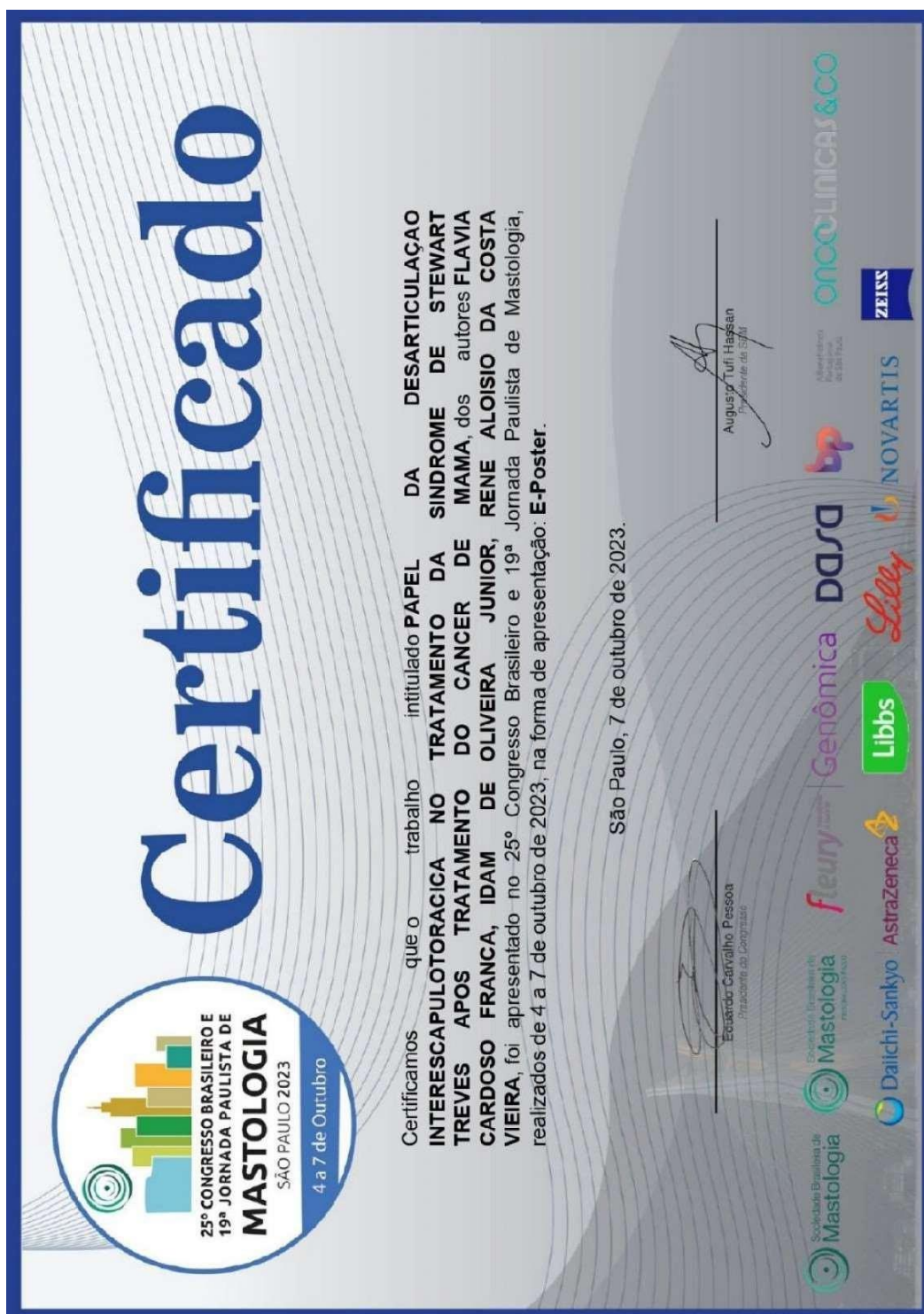
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Anexo 4: apresentação de trabalhos em congressos, jornadas e simpósios.

Anexo 4.1: 19ª Jornada Paulista de Mastologia e 25º Congresso Brasileiro de Mastologia.



Anexo 4.2: XVI Congresso Brasileiro de Cirurgia Oncológica



XVI CONGRESSO
BRASILEIRO DE
CIRURGIA
ONCOLÓGICA

15 A 18 DE NOVEMBRO DE 2023
RIO DE JANEIRO

Certificamos que o trabalho

**DESARTICULAÇÃO INTERESCAPULOTORÁRICA EM PACIENTES COM CÂNCER DE MAMA:
UMA REVISÃO SISTEMÁTICA.**

dos autores: FLÁVIA CARDOSO FRANCA; FLÁVIA CARDOSO FRANCA; IDAM DE OLIVEIRA-JUNIOR; ANTÔNIO BAILÃO JUNIOR; RODRIGO CASTANHO DE CAMPOS LEITE; RENÉ ALOISIO DA COSTA VIEIRA, foi apresentado na modalidade Pôster Eletrônico - XVI Congresso Brasileiro de Cirurgia Oncológica, no evento XVI Congresso Brasileiro de Cirurgia Oncológica ocorrido de 15 a 18 de novembro de 2023, no Windsor Barra Hotel em Rio de Janeiro/RJ.

18 de novembro de 2023

Para validar, acesse <http://www.cbcocongressos.com.br/validacao/?cod=60661097>



Dr. Héber Salvador de Castro Ribeiro
Presidente da SBCO 2021-2023



Dr. Reitan Ribeiro
Presidente da Comissão Organizadora
do XVI Congresso Brasileiro de Cirurgia Oncológica

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CERTIFICADO

BBCS

BRAZILIAN
BREAST CANCER
SYMPOSIUM 2024

May 16 - 18, 2024

C E R T I F I C A T E

We hereby certify that **FOREQUARTER AMPUTATION IN PATIENTS WITH BREAST CANCER: A SYSTEMATIC LITERATURE REVIEW** was presented in the Brazilian Breast Cancer Symposium under the category **commented poster presentation** by the following authors: **Flávia Cardoso Franca; René Aloisio da Costa Vieira; Idam de Oliveira-Junior.**

Brasília, May 18th, 2024.


Dr. Ruffo de Freitas Junior
General Coordinator - BBCS 2024


Dra. Rosemar Macedo Sousa Rahal
Commissions Coordinator and Logistics
Coordinator - BBCS 2024


Dra. Ana Carolina Salles de M. Ferreira
Scientific Committee - BBCS 2024


Dr. Leonardo Ribeiro Soares
Award and Abstracts Coordinator - BBCS 2024

<https://doi.org/10.29289/259453942024V34S1020>

Forequarter amputation in patients with breast cancer: a systematic literature review

Flávia Cardoso Franca¹, René Aloisio da Costa Vieira^{1,2,3}, Idam de Oliveira-Junior²

¹Botucatu Faculty of Medicine.

²Barretos Cancer Hospital.

³Muriae Cancer Hospital.

Objective: The objective of this study was to carry out a systematic review of the literature, evaluating the impact of forequarter amputation in locoregional control and survival of patients with breast cancer. **Methodology:** Based on resolution 466/12, the Research Ethics Committee evaluation was not necessary. Systematic literature review using eight databases. The PICOS and PRISMA methodologies were used. Two evaluators selected the articles, and the data were summarized in a standardized form. **Results:** Of 1326 articles initially selected on December 31, 2022, 55 articles served as the basis for the review, and 104 cases were observed. The indication 78 (75.0%) were primary tumors and 7 (6.7%) were local recurrences. The main histological type of the primary tumor was invasive ductal carcinoma. The main indication was due to Stewart-Treves syndrome (43.3%), followed by local recurrence of breast cancer (23.1%), radio-induced tumor (14.4%), and locally advanced primary (5.8%). Surgery was considered potentially curative in 50.0%, palliative in 31.7%, and not performed in 2.9%. In patients where the complication rate was reported, it was around 27.3%, the main ones being necrosis, pleural effusion, dehiscence, and infection, with no mortality observed. When evaluating well-being (n=22), all reported improvement in this aspect. In 71 patients, local recurrence was evaluated, being in the order of 32.4%. In 89 patients, it was possible to assess survival. The overall actuarial survival at 24, 36, and 60 months was 37.1%, 31.6%, and 28.0%, respectively. The type of surgery had an impact on survival (p=0.002), 47.2% of patients undergoing curative surgery were alive at 60 months, and 15.3% of patients undergoing palliative surgery were alive at 24 months. **Conclusion:** In breast cancer, forequarter amputation is associated with high morbidity and absence of mortality, allowing a high rate of local control and pain control. When performed on a curative basis, it allows a high survival rate.

Keywords: breast neoplasms, disarticulation, stewart treves syndrome, surgical amputation, forequarter amputation.

APÊNDICES

Apêndice 1: estratégia de busca nos bancos de dados

Estratégia de busca 1

- **MESH:**
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((Amputation OR Amputations) OR (Disarticulation OR Disarticulations) OR (Forequarter) OR (Periscapular) OR (Interscapulothoracic)))

- **DECS:** (Neoplasias da Mama OR Breast Neoplasms OR Neoplasias de la Mama OR Carcinoma Mamário Humano OR Carcinoma de Mama OR Carcinomas Mamários Humanos OR Carcinomas da Mama OR Câncer Mamário OR Câncer da Mama OR Câncer de Mama OR Câncer de Seio OR Câncer do Seio OR Cânceres de Mama OR Neoplasia Maligna da Mama OR Neoplasia Maligna de Mama OR Neoplasia Mamária OR Neoplasia Mamária Humana OR Neoplasia da Mama OR Neoplasias Malignas de Mama OR Neoplasias Mamárias OR Neoplasias Mamárias Humanas OR Neoplasias de Mama OR Tumor Maligno da Mama OR Tumor da Mama OR Tumor de Mama OR Tumor de Seio OR Tumores Malignos da Mama OR Tumores Mamários OR Tumores da Mama OR Tumores de Mama OR Tumores de Seio) AND ((Amputação OR Amputation OR Amputación) OR (Desarticulação OR Disarticulation OR Desarticulación) OR (Forequarter) OR (Quarto Dianteiro) OR (Periscapular) OR (Periescapular) OR (Interscapulothoracic) OR (Interescapulotorácica))
- Scielo: (Neoplasias da Mama OR Carcinoma Mamário Humano OR Carcinoma de Mama OR Carcinomas Mamários Humanos OR Carcinomas da Mama OR Câncer Mamário OR Câncer da Mama OR Câncer de Mama OR Câncer de Seio OR Câncer do Seio OR Cânceres de Mama OR Neoplasia Maligna da Mama OR Neoplasia Maligna de Mama OR Neoplasia Mamária OR Neoplasia Mamária Humana OR Neoplasia da Mama OR Neoplasias Malignas de Mama OR Neoplasias Mamárias OR Neoplasias Mamárias Humanas OR Neoplasias de Mama OR Tumor Maligno da Mama OR Tumor da Mama OR Tumor de Mama OR Tumor de Seio OR Tumores Malignos da Mama OR Tumores Mamários OR Tumores da Mama OR Tumores de Mama OR Tumores de Seio) AND ((Amputação) OR (Desarticulação) OR (Quarto Dianteiro) OR (Periescapular) OR (Interescapulotorácica))
- Lilacs: (Neoplasias da Mama OR Carcinoma Mamário Humano OR Carcinoma de Mama OR Carcinomas Mamários Humanos OR Carcinomas da Mama OR Câncer Mamário OR Câncer da Mama OR Câncer de Mama OR Câncer de Seio OR Câncer do Seio OR Cânceres de Mama OR Neoplasia Maligna da Mama OR Neoplasia Maligna de Mama OR Neoplasia Mamária OR Neoplasia Mamária Humana OR Neoplasia da Mama OR Neoplasias Malignas de Mama OR Neoplasias Mamárias OR Neoplasias Mamárias Humanas OR Neoplasias de Mama OR Tumor Maligno da Mama OR Tumor da Mama OR Tumor de Mama OR Tumor de Seio OR Tumores Malignos da Mama OR Tumores Mamários OR Tumores da Mama OR Tumores de Mama OR Tumores de Seio) AND ((Amputação) OR (Desarticulação) OR (Quarto Dianteiro) OR (Periescapular) OR (Interescapulotorácica))
- **EMTREE:** (Breast tumor OR breast gland tumor OR breast gland tumour OR breast mass OR breast neoplasms OR breast neoplasms, male OR breast tumour OR female breast neoplasm OR female breast tumor OR female breast tumour OR male breast neoplasms OR mamma tumor OR mamma tumour OR mammary gland tumor OR mammary gland tumour OR mammary neoplasms OR mammary tumor OR mammary tumor cell OR mammary tumour OR mammary tumour cell OR unilateral breast neoplasms) AND

(Amputation OR physiologic amputation OR post amputation syndrome OR reamputation OR Disarticulation OR exarticulatio OR exarticulation OR Forequarter OR Periscapular OR Interscapulothoracic)

- Embase: ('breast tumor'/exp OR 'breast gland tumor' OR 'breast gland tumour' OR 'breast mass' OR 'breast neoplasms' OR 'breast neoplasms, male' OR 'breast tumor' OR 'breast tumour' OR 'female breast neoplasm' OR 'female breast tumor' OR 'female breast tumour' OR 'male breast neoplasms' OR 'mamma tumor' OR 'mamma tumour' OR 'mammary gland tumor' OR 'mammary gland tumour' OR 'mammary neoplasms' OR 'mammary tumor' OR 'mammary tumor cell' OR 'mammary tumour' OR 'mammary tumour cell' OR 'unilateral breast neoplasms') AND ('amputation'/exp OR 'amputation' OR 'physiologic amputation' OR 'post amputation syndrome' OR 'reamputation' OR 'disarticulation'/exp OR 'disarticulation' OR 'exarticulatio' OR 'exarticulation' OR 'forequarter amputation'/exp OR 'interscapulothoracic amputation'/exp OR 'periscapular')

Estratégia de busca 2: SARCOMA E STEWART TREVES

- **MESH**

((Breast Neoplasms OR Breast Neoplasm OR Neoplasm, Breast OR Breast Tumors OR Breast Tumor OR Tumor, Breast OR Tumors, Breast OR Neoplasms, Breast OR Breast Cancer OR Cancer, Breast OR Mammary Cancer OR Cancer, Mammary OR Cancers, Mammary OR Mammary Cancers OR Malignant Neoplasm of Breast OR Breast Malignant Neoplasm OR Breast Malignant Neoplasms OR Malignant Tumor of Breast OR Breast Malignant Tumor OR Breast Malignant Tumors OR Cancer of Breast OR Cancer of the Breast OR Mammary Carcinoma, Human OR Carcinoma, Human Mammary OR Carcinomas, Human Mammary OR Human Mammary Carcinomas OR Mammary Carcinomas, Human OR Human Mammary Carcinoma OR Mammary Neoplasms, Human OR Human Mammary Neoplasm OR Human Mammary Neoplasms OR Neoplasm, Human Mammary OR Neoplasms, Human Mammary OR Mammary Neoplasm, Human OR Breast Carcinoma OR Breast Carcinomas OR Carcinoma, Breast OR Carcinomas, Breast) AND ((Amputation OR Amputations) OR (Disarticulation OR Disarticulations) OR (Forequarter) OR (Periscapular) OR (Interscapulothoracic)) AND ((**Sarcoma OR Sarcomas OR Sarcoma, Soft Tissue OR Sarcomas, Soft Tissue OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Sarcoma, Epithelioid OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcomas, Epithelioid OR Sarcoma, Spindle Cell OR Sarcomas, Spindle Cell OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas**) **OR** (Lymphangiosarcoma OR Lymphangiosarcomas OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas))

- PUBMED: ((Breast Neoplasms OR Breast Neoplasm OR Neoplasm, Breast OR Breast Tumors OR Breast Tumor OR Tumor, Breast OR Tumors, Breast OR Neoplasms, Breast OR Breast Cancer OR Cancer, Breast OR Mammary Cancer OR Cancer, Mammary OR Cancers, Mammary OR Mammary Cancers OR Malignant Neoplasm of Breast OR Breast Malignant Neoplasm OR Breast Malignant Neoplasms OR Malignant Tumor of Breast OR Breast Malignant Tumor OR Breast Malignant Tumors OR Cancer of Breast OR Cancer of the Breast OR Mammary Carcinoma, Human OR Carcinoma, Human Mammary OR Carcinomas, Human Mammary OR Human Mammary Carcinomas OR Mammary Carcinomas, Human OR Human Mammary Carcinoma OR

Mammary Neoplasms, Human OR Human Mammary Neoplasm OR Human Mammary

Neoplasms OR Neoplasm, Human Mammary OR Neoplasms, Human Mammary OR Mammary Neoplasm, Human OR Breast Carcinoma OR Breast Carcinomas OR Carcinoma, Breast OR Carcinomas, Breast) AND ((Amputation OR Amputations) OR (Disarticulation OR Disarticulations) OR (Forequarter) OR (Periscapular) OR (Interscapulothoracic)) AND ((Sarcoma OR Sarcomas OR Sarcoma, Soft Tissue OR Sarcomas, Soft Tissue OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Sarcoma, Epithelioid OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcomas, Epithelioid OR Sarcoma, Spindle Cell OR Sarcomas, Spindle Cell OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Lymphangiosarcomas OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas)))

- Scopus: ((breast AND neoplasms OR breast AND neoplasm OR neoplasm, AND breast OR breast AND tumors OR breast AND tumor OR tumor, AND breast OR tumors, AND breast OR neoplasms, AND breast OR breast AND cancer OR cancer, AND breast OR mammary AND cancer OR cancer, AND mammary OR cancers, AND mammary OR mammary AND cancers OR malignant AND neoplasm AND of AND breast OR breast AND malignant AND neoplasm OR breast AND malignant AND neoplasms OR malignant AND tumor AND of AND breast OR breast AND malignant AND tumor OR breast AND malignant AND tumors OR cancer AND of AND breast OR cancer AND of AND the AND breast OR mammary AND carcinoma, AND human OR carcinoma, AND human AND mammary OR carcinomas, AND human AND mammary OR human AND mammary AND carcinomas OR mammary AND carcinomas, AND human OR human AND mammary AND carcinoma OR mammary AND neoplasms, AND human OR human AND mammary AND neoplasm OR human AND mammary AND neoplasms OR neoplasm, AND human AND mammary OR neoplasms, AND human AND mammary OR mammary AND neoplasm, AND human OR breast AND carcinoma OR breast AND carcinomas OR carcinoma, AND breast OR carcinomas, AND breast) AND ((amputation OR amputations) OR (disarticulation OR disarticulations) OR (forequarter) OR (periscapular) OR (interscapulothoracic)) AND ((sarcoma OR sarcomas OR sarcoma, AND soft AND tissue OR sarcomas, AND soft AND tissue OR soft AND tissue AND sarcoma OR soft AND tissue AND sarcomas OR sarcoma, AND epithelioid OR epithelioid AND sarcoma OR epithelioid AND sarcomas OR sarcomas, AND epithelioid OR sarcoma, AND spindle AND cell OR sarcomas, AND spindle AND cell OR spindle AND cell AND sarcoma OR spindle AND cell AND sarcomas) OR (lymphangiosarcoma OR lymphangiosarcomas OR lymphangioendothelioma, AND malignant OR lymphangioendotheliomas, AND malignant OR malignant AND lymphangioendothelioma OR malignant AND lymphangioendotheliomas)))
- Web of Science: ((Breast Neoplasms OR Breast Neoplasm OR Neoplasm, Breast OR Breast Tumors OR Breast Tumor OR Tumor, Breast OR Tumors, Breast OR Neoplasms, Breast OR Breast Cancer OR Cancer, Breast OR Mammary Cancer OR Cancer, Mammary OR Cancers, Mammary OR Mammary Cancers OR Malignant Neoplasm of Breast OR Breast Malignant Neoplasm OR Breast Malignant Neoplasms OR Malignant Tumor of Breast OR Breast Malignant Tumor OR Breast Malignant Tumors OR Cancer of Breast OR Cancer of the Breast OR Mammary Carcinoma, Human OR Carcinoma, Human Mammary OR Carcinomas, Human Mammary OR Human Mammary Carcinomas OR Mammary Carcinomas, Human OR Human Mammary Carcinoma OR Mammary Neoplasms, Human OR Human Mammary Neoplasm OR Human Mammary Neoplasms OR Neoplasm, Human Mammary OR

Neoplasms, Human Mammary OR Mammary Neoplasm, Human OR Breast Carcinoma OR Breast Carcinomas OR Carcinoma, Breast OR Carcinomas, Breast) AND ((Amputation OR Amputations) OR (Disarticulation OR Disarticulations) OR (Forequarter) OR (Periscapular) OR (Interscapulothoracic)) AND ((Sarcoma OR Sarcomas OR Sarcoma, Soft Tissue OR Sarcomas, Soft Tissue OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Sarcoma, Epithelioid OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcomas, Epithelioid OR Sarcoma, Spindle Cell OR Sarcomas, Spindle Cell OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Lymphangiosarcomas OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas)))

<https://www.webofscience.com/wos/woscc/summary/bb193bd1-0315-45d1-ab18-74d059f953ce-7cca760a/relevance/1>

- CINAHL complete: ((Breast Neoplasms OR Breast Neoplasm OR Neoplasm, Breast OR Breast Tumors OR Breast Tumor OR Tumor, Breast OR Tumors, Breast OR Neoplasms, Breast OR Breast Cancer OR Cancer, Breast OR Mammary Cancer OR Cancer, Mammary OR Cancers, Mammary OR Mammary Cancers OR Malignant Neoplasm of Breast OR Breast Malignant Neoplasm OR Breast Malignant Neoplasms OR Malignant Tumor of Breast OR Breast Malignant Tumor OR Breast Malignant Tumors OR Cancer of Breast OR Cancer of the Breast OR Mammary Carcinoma, Human OR Carcinoma, Human Mammary OR Carcinomas, Human Mammary OR Human Mammary Carcinomas OR Mammary Carcinomas, Human OR Human Mammary Carcinoma OR Mammary Neoplasms, Human OR Human Mammary Neoplasm OR Human Mammary Neoplasms OR Neoplasm, Human Mammary OR Neoplasms, Human Mammary OR Mammary Neoplasm, Human OR Breast Carcinoma OR Breast Carcinomas OR Carcinoma, Breast OR Carcinomas, Breast) AND ((Amputation OR Amputations) OR (Disarticulation OR Disarticulations) OR (Forequarter) OR (Periscapular) OR (Interscapulothoracic)) AND ((Sarcoma OR Sarcomas OR Sarcoma, Soft Tissue OR Sarcomas, Soft Tissue OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Sarcoma, Epithelioid OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcomas, Epithelioid OR Sarcoma, Spindle Cell OR Sarcomas, Spindle Cell OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Lymphangiosarcomas OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas)))
- Cochrane: ((Breast Neoplasms OR Breast Neoplasm OR Neoplasm, Breast OR Breast Tumors OR Breast Tumor OR Tumor, Breast OR Tumors, Breast OR Neoplasms, Breast OR Breast Cancer OR Cancer, Breast OR Mammary Cancer OR Cancer, Mammary OR Cancers, Mammary OR Mammary Cancers OR Malignant Neoplasm of Breast OR Breast Malignant Neoplasm OR Breast Malignant Neoplasms OR Malignant Tumor of Breast OR Breast Malignant Tumor OR Breast Malignant Tumors OR Cancer of Breast OR Cancer of the Breast OR Mammary Carcinoma, Human OR Carcinoma, Human Mammary OR Carcinomas, Human Mammary OR Human Mammary Carcinomas OR Mammary Carcinomas, Human OR Human Mammary Carcinoma OR Mammary Neoplasms, Human OR Human Mammary Neoplasm OR Human Mammary Neoplasms OR Neoplasm, Human Mammary OR Neoplasms, Human Mammary OR Mammary Neoplasm, Human OR Breast Carcinoma OR Breast Carcinomas OR Carcinoma, Breast OR Carcinomas, Breast) AND ((Amputation OR Amputations) OR (Disarticulation OR Disarticulations) OR (Forequarter) OR (Periscapular) OR

((Interscapulothoracic)) AND ((Sarcoma OR Sarcomas OR Sarcoma, Soft Tissue OR Sarcomas, Soft Tissue OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Sarcoma, Epithelioid OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcomas, Epithelioid OR Sarcoma, Spindle Cell OR Sarcomas, Spindle Cell OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Lymphangiosarcomas OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas)))

- **DECS:** (Neoplasias da Mama OR Breast Neoplasms OR Neoplasias de la Mama OR Carcinoma Mamário Humano OR Carcinoma de Mama OR Carcinomas Mamários Humanos OR Carcinomas da Mama OR Câncer Mamário OR Câncer da Mama OR Câncer de Mama OR Câncer de Seio OR Câncer do Seio OR Cânceres de Mama OR Neoplasia Maligna da Mama OR Neoplasia Maligna de Mama OR Neoplasia Mamária OR Neoplasia Mamária Humana OR Neoplasia da Mama OR Neoplasias Malignas de Mama OR Neoplasias Mamárias OR Neoplasias Mamárias Humanas OR Neoplasias de Mama OR Tumor Maligno da Mama OR Tumor da Mama OR Tumor de Mama OR Tumor de Seio OR Tumores Malignos da Mama OR Tumores Mamários OR Tumores da Mama OR Tumores de Mama OR Tumores de Seio) AND ((Amputação OR Amputation OR Amputación) OR (Desarticulação OR Disarticulation OR Desarticulación) OR (Forequarter) OR (Quarto Dianteiro) OR (Periscapular) OR (Periescapular) OR (Interscapulothoracic) OR (Interescapulotorácica)) AND ((Sarcoma OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcoma, Epithelioid OR Sarcoma, Soft Tissue OR Sarcoma, Spindle Cell OR Sarcomas OR Sarcomas, Epithelioid OR Sarcomas, Soft Tissue OR Sarcomas, Spindle Cell OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Linfangiosarcoma OR Linfangiossarcoma OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Lymphangiosarcomas OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas)))
- Scielo: (ab:((Neoplasias da Mama OR Breast Neoplasms OR Neoplasias de la Mama OR Carcinoma Mamário Humano OR Carcinoma de Mama OR Carcinomas Mamários Humanos OR Carcinomas da Mama OR Câncer Mamário OR Câncer da Mama OR Câncer de Mama OR Câncer de Seio OR Câncer do Seio OR Cânceres de Mama OR Neoplasia Maligna da Mama OR Neoplasia Maligna de Mama OR Neoplasia Mamária OR Neoplasia Mamária Humana OR Neoplasia da Mama OR Neoplasias Malignas de Mama OR Neoplasias Mamárias OR Neoplasias Mamárias Humanas OR Neoplasias de Mama OR Tumor Maligno da Mama OR Tumor da Mama OR Tumor de Mama OR Tumor de Seio OR Tumores Malignos da Mama OR Tumores Mamários OR Tumores da Mama OR Tumores de Mama OR Tumores de Seio) AND ((Amputação OR Amputation OR Amputación) OR (Desarticulação OR Disarticulation OR Desarticulación) OR (Forequarter) OR (Quarto Dianteiro) OR (Periscapular) OR (Periescapular) OR (Interscapulothoracic) OR (Interescapulotorácica)) AND ((Sarcoma OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcoma, Epithelioid OR Sarcoma, Soft Tissue OR Sarcoma, Spindle Cell OR Sarcomas OR Sarcomas, Epithelioid OR Sarcomas, Soft Tissue OR Sarcomas, Spindle Cell OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Linfangiosarcoma OR Linfangiossarcoma OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant

OR Lymphangiosarcomas OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas))))

- Lilacs: (Neoplasias da Mama OR Breast Neoplasms OR Neoplasias de la Mama OR Carcinoma Mamário Humano OR Carcinoma de Mama OR Carcinomas Mamários Humanos OR Carcinomas da Mama OR Câncer Mamário OR Câncer da Mama OR Câncer de Mama OR Câncer de Seio OR Câncer do Seio OR Cânceres de Mama OR Neoplasia Maligna da Mama OR Neoplasia Maligna de Mama OR Neoplasia Mamária OR Neoplasia Mamária Humana OR Neoplasia da Mama OR Neoplasias Malignas de Mama OR Neoplasias Mamárias OR Neoplasias Mamárias Humanas OR Neoplasias de Mama OR Tumor Maligno da Mama OR Tumor da Mama OR Tumor de Mama OR Tumor de Seio OR Tumores Malignos da Mama OR Tumores Mamários OR Tumores da Mama OR Tumores de Mama OR Tumores de Seio) AND ((Amputação OR Amputation OR Amputación) OR (Desarticulação OR Disarticulation OR Desarticulación) OR (Forequarter) OR (Quarto Dianteiro) OR (Periscapular) OR (Periescapular) OR (Interscapulothoracic) OR (Interescapulotorácica)) AND ((Sarcoma OR Epithelioid Sarcoma OR Epithelioid Sarcomas OR Sarcoma, Epithelioid OR Sarcoma, Soft Tissue OR Sarcoma, Spindle Cell OR Sarcomas OR Sarcomas, Epithelioid OR Sarcomas, Soft Tissue OR Sarcomas, Spindle Cell OR Soft Tissue Sarcoma OR Soft Tissue Sarcomas OR Spindle Cell Sarcoma OR Spindle Cell Sarcomas) OR (Lymphangiosarcoma OR Linfangiosarcoma OR Linfangiossarcoma OR Lymphangioendothelioma, Malignant OR Lymphangioendotheliomas, Malignant OR Lymphangiosarcomas OR Malignant Lymphangioendothelioma OR Malignant Lymphangioendotheliomas))
- **EMTREE:** ((Breast tumor) OR (breast gland tumor) OR (breast gland tumour) OR (breast mass) OR (breast neoplasms) OR (breast neoplasms, male) OR (breast tumour) OR (female breast neoplasm) OR (female breast tumor) OR (female breast tumour) OR (male breast neoplasms) OR (mamma tumor) OR (mamma tumour) OR (mammary gland tumor) OR (mammary gland tumour) OR (mammary neoplasms) OR (mammary tumor) OR (mammary tumor cell) OR (mammary tumour) OR (mammary tumour cell) OR (unilateral breast neoplasms)) AND (Amputation OR (physiologic amputation) OR (post amputation syndrome) OR reamputation OR Disarticulation OR exarticulatio OR exarticulation OR Forequarter OR Periscapular OR Interscapulothoracic) AND (Sarcoma OR lymphangiosarcoma)
- - Embase: ('breast tumor'/exp OR 'breast tumor' OR (('breast'/exp OR breast) AND ('tumor'/exp OR tumor)) OR 'breast gland tumor'/exp OR 'breast gland tumor' OR (('breast'/exp OR breast) AND ('gland'/exp OR gland) AND ('tumor'/exp OR tumor)) OR 'breast gland tumour'/exp OR 'breast gland tumour' OR (('breast'/exp OR breast) AND ('gland'/exp OR gland) AND ('tumour'/exp OR tumour)) OR 'breast mass'/exp OR 'breast mass' OR (('breast'/exp OR breast) AND ('mass'/exp OR mass)) OR 'breast neoplasms'/exp OR 'breast neoplasms' OR (('breast'/exp OR breast) AND ('neoplasms'/exp OR neoplasms)) OR 'breast neoplasms, male'/exp OR 'breast neoplasms, male' OR (('breast'/exp OR breast) AND ('neoplasms,'/exp OR neoplasms,) AND ('male'/exp OR male)) OR 'breast tumour'/exp OR 'breast tumour' OR (('breast'/exp OR breast) AND ('tumour'/exp OR tumour)) OR 'female breast neoplasm'/exp OR 'female breast neoplasm' OR (('female'/exp OR female) AND ('breast'/exp OR breast) AND ('neoplasm'/exp OR neoplasm)) OR 'female breast

tumor'/exp OR 'female breast tumor' OR (('female'/exp OR female) AND ('breast'/exp OR breast) AND ('tumor'/exp OR tumor)) OR 'female breast tumour'/exp OR 'female breast tumour' OR (('female'/exp OR female) AND ('breast'/exp OR breast) AND ('tumour'/exp OR tumour)) OR 'male breast neoplasms'/exp OR 'male breast neoplasms' OR (('male'/exp OR male) AND ('breast'/exp OR breast) AND ('neoplasms'/exp OR neoplasms)) OR 'mamma tumor'/exp OR 'mamma tumor' OR (('mamma'/exp OR mamma) AND ('tumor'/exp OR tumor)) OR 'mamma tumour'/exp OR 'mamma tumour' OR (('mamma'/exp OR mamma) AND ('tumour'/exp OR tumour)) OR 'mammary gland tumor'/exp OR 'mammary gland tumor' OR (mammary AND ('gland'/exp OR gland) AND ('tumor'/exp OR tumor)) OR 'mammary gland tumour'/exp OR 'mammary gland tumour' OR (mammary AND ('gland'/exp OR gland) AND ('tumour'/exp OR tumour)) OR 'mammary neoplasms'/exp OR 'mammary neoplasms' OR (mammary AND ('neoplasms'/exp OR neoplasms)) OR 'mammary tumor'/exp OR 'mammary tumor' OR (mammary AND ('tumor'/exp OR tumor)) OR 'mammary tumor cell'/exp OR 'mammary tumor cell' OR (mammary AND ('tumor'/exp OR tumor) AND ('cell'/exp OR cell)) OR 'mammary tumour'/exp OR 'mammary tumour' OR (mammary AND ('tumour'/exp OR tumour)) OR 'mammary tumour cell'/exp OR 'mammary tumour cell' OR (mammary AND ('tumour'/exp OR tumour) AND ('cell'/exp OR cell)) OR 'unilateral breast neoplasms'/exp OR 'unilateral breast neoplasms' OR (unilateral AND ('breast'/exp OR breast) AND ('neoplasms'/exp OR neoplasms))) AND ('amputation'/exp OR amputation OR 'physiologic amputation'/exp OR 'physiologic amputation' OR (physiologic AND ('amputation'/exp OR amputation)) OR 'post amputation syndrome'/exp OR 'post amputation syndrome' OR (post AND ('amputation'/exp OR amputation) AND ('syndrome'/exp OR syndrome)) OR 'reamputation'/exp OR reamputation OR 'disarticulation'/exp OR disarticulation OR 'exarticulatio'/exp OR exarticulatio OR 'exarticulation'/exp OR exarticulation OR forequarter OR periscapular OR interscapulothoracic) AND ('sarcoma'/exp OR sarcoma OR 'lymphangiosarcoma'/exp OR lymphangiosarcoma)

Apêndice 2: Ficha padronizada de coleta de dados

HISTÓRICO E ESTADIAMENTO			
1	Número do caso	1	
2	Autor	2	
3	Tipo de publicação (1) Relato de casos (2) série de casos (3) revisão não sistemática (4) outro _____	3	
4	Ano da publicação aaaa	4	
5	Identificação da paciente no artigo	5	
6	Gênero (1) Feminino (2) Masculino	6	
7	Idade ao diagnóstico da neoplasia primária Anos	7	
8	Idade à indicação de DIET Anos	8	
9	Lado da lesão (1) Direito; (2) Esquerdo; (3) Bilateral; (99) Ignorado	9	
10	Status ao diagnóstico da neoplasia mamária (1) primário; (2) metastático sem tratamento prévio; (3) recorrência local sem metástase à distância; (4) recorrência local com metástase à distância; (5) recorrência local sem informação sobre metástase à distância (6) outros _____ (99) Ignorado	10	
11	Tempo de sintomas ao diagnóstico meses	11	
12	Tempo do tratamento (cirurgia primária) até a recorrência que levou a DIET meses	12	
13	Tempo do tratamento (cirurgia primária) até a DIET meses	13	
14	Comorbidades (1) Diabetes Melitus; (2) obesidade; (3) HAS; (4) tabagismo; (5) outros (99) ignorado	14	
15	Estádio clínico pré tratamento (0) 0; (1) I; (2) II A; (3) IIB; (4) IIIA; (5) IIIB; (6) IIIC; (7) IV; (8) X; (99) ignorado	15	
16	Maior tamanho clínico total do tumor Cm	16	
17	Estádio clínico - T: pré tratamento (0) Tis; (1) T1; (2) T2; (3) T3; (4) T4a; (5) T4b; (6) T4c; (7) T4d; (99) Ignorado	17	
18	Estádio clínico - N: pré tratamento (0) N0; (1) N1; (2) N2; (3) N3; (4) Nx; (99) ignorado	18	
19	Estádio clínico - M: pré tratamento (0) M0; (1) M1; (2) Mx; (99) ignorado	19	
PATOLOGIA BIOPSIA			
20	Tipo histológico mama (1) CDI; (2) CDis; (3) CLI; (4) tumor filóides; (5) combinação: _____; (7) Outro: _____; (99) Ignorado	20	
21	Tipo histológico (quando não há relato de tumor primário) (1) Angiossarcoma (2) sarcoma radioinduzido (88) não se aplica	21	

22	RE (0) negativo; (1) positivo; (2) outra histologia; (99) Ignorado	22	
23	RP (0) negativo; (1) positivo; (2) outra histologia; (99) Ignorado	23	
24	HER2 (0) negativo; (1) positivo; (2) outra histologia; (99) Ignorado	24	
25	Subtipo Molecular (1) Luminal A; (2) Luminal B HER 2 negative ; (3) Luminal B HER 2 positive ; (4) Her2; (5) Triplo negativo; (6) outra histologia; (99) Ignorado	25	
26	Grau nuclear (1) G I; (2) G II; (3) G III; (99) Ignorado	26	
27	Grau Nottingham (1) G 1; (2) G 2; (3) G 3; (99) Ignorado	27	
TRATAMENTO CIRÚRGICO DO CÂNCER DE MAMA			
28	Tratamento cirúrgico inicial - MAMA (1) mastectomia; (2) quadrantectomia / setorectomia / lumpectomia; (3) outro (4) nenhum (5) DIET upfront (99) Ignorado	28	
29	Tratamento cirúrgico inicial - AXILA (1) BLS; (2) linfadenectomia axilar; (3) outro; (4) nenhum (5) DIET upfront (99) Ignorado	29	
QUIMIOTERAPIA			
30	Adjuvante: (0) não; (1) sim; (2) não se aplica; (99) ignorado	30	
31	Neoadjuvante: (0) não; (1) sim; (2) não se aplica; (99) ignorado	31	
32	Resgate (Salvage – adjuvant treatment given prior to referral for DIET): (0) não; (1) sim; (2) não se aplica; (99) ignorado	32	
33	Paliativa: (0) não; (1) sim; (2) não se aplica; (99) ignorado	33	
34	Paliativa - quando: (0) antes da cirurgia; (1) após a cirurgia; (2) outro; (3) não se aplica; (99) ignorado	34	
RADIOTERAPIA			
35	Adjuvante: (0) não; (1) sim; (2) não se aplica; (99) ignorado	35	
36	Neoadjuvante: (0) não; (1) sim; (2) não se aplica; (99) ignorado	36	
37	Resgate (Salvage – adjuvant treatment given prior to referral for DIET): (0) não; (1) sim; (2) não se aplica; (99) ignorado	37	
38	Paliativa: 1. (0) não; (1) sim; (2) não se aplica; (99) ignorado	38	
39	Paliativa - quando: (0) antes da cirurgia; (1) após a cirurgia; (2) outro; (3) não se aplica; (99) ignorado	39	
HORMONIOTERAPIA			
40	Adjuvante: (0) não; (1) sim; (2) não se aplica; (99) ignorado	40	
41	Neoadjuvante: (0) não; (1) sim; (2) não se aplica; (99) ignorado	41	

42	Resgate (Salvage – adjuvant treatment given prior to referral for DIET): (0) não; (1) sim; (2) não se aplica; (99) ignorado	42	
43	Paliativa: (0) não; (1) sim; (2) não se aplica; (99) ignorado	43	
44	Paliativa - quando: (0) antes da cirurgia; (1) após a cirurgia; (2) outro; (3) não se aplica; (99) ignorado	44	
TUMOR NA DIET			
45	Condição (1) Primário localmente avançado; (2) recorrência do câncer de mama; (3) metastático; (4) radio induzido; (5) Síndrome de Stewart Treves; (6) metástase óssea na articulação do ombro; (7) outros _____; (8) ignorado; (99) NA	45	
46	Recorrência local (0) não; (1) sim; (99) Ignorado	46	
47	Recorrência local mama (0) não; (1) sim; (2) não se aplica; (99) ignorado	47	
48	Recorrência local axila (0) não; (1) sim; (2) não se aplica; (99) ignorado	48	
49	Recorrência local mama + axila (0) não; (1) sim; (2) não se aplica; (99) ignorado	49	
50	Recorrência local outros _____ (0) não; (1) sim; (2) não se aplica; (99) ignorado	50	
51	Sítio de recorrência locorregional (0) não; (1) sim; (99) Ignorado	51	
52	Recorrência locorregional fossa supraclavicular (FSC) (0) não; (1) sim; (2) não se aplica; (99) ignorado	52	
53	Recorrência locorregional fossa infraclavicular (FIC) (0) não; (1) sim; (2) não se aplica; (99) ignorado	53	
54	Recorrência locorregional parede torácica (0) não; (1) sim; (2) não se aplica; (99) ignorado	54	
55	Recorrência locorregional dorso (0) não; (1) sim; (2) não se aplica; (99) ignorado	55	
56	Recorrência locorregional mama oposta (0) não; (1) sim; (2) não se aplica; (99) ignorado	56	
57	Recorrência locorregional axila oposta (0) não; (1) sim; (2) não se aplica; (99) ignorado	57	
58	Metástase à distância: (0) não; (1) sim; (99) ignorado	58	
59	Metástase óssea (0) não; (1) sim; (2) não se aplica; (99) ignorado	59	
60	Metástase pulmão (0) não; (1) sim; (2) não se aplica; (99) ignorado	60	
61	Metástase fígado (0) não; (1) sim; (2) não se aplica; (99) ignorado	61	
62	Metástase SNC (0) não; (1) sim; (2) não se aplica; (99) ignorado	62	
63	Metástase à distância – outros _____ (0) não; (1) sim; (2) não se aplica; (99) ignorado	63	

64	Resposta ao tratamento prévio: (0) sem tratamento prévio; (1) doença estável; (2) progressão de doença; (3) não se aplica; (4) 2º primário (STS ou RIS); (99) ignorado	64	
65	Tamanho clínico do tumor no momento da DIET cm	65	
66	Edema/linfedema: (0) não; (1) sim; (2) não se aplica; (99) ignorado	66	
67	Úlcera mamária: (0) não; (1) sim; (2) não se aplica; (99) ignorado	67	
68	Úlcera axilar: (0) não; (1) sim; (2) não se aplica; (99) ignorado	68	
69	Metástase fixa em axila: (0) não; (1) sim; (2) não se aplica; (99) ignorado	69	
70	Plexopatia braquial / invasão do plexo braquial (0) não; (1) sim; (2) não se aplica; (99) ignorado	70	
71	Articulação do ombro fixa (0) não; (1) sim; (2) não se aplica; (99) ignorado	71	
72	Membro superior disfuncional (0) não; (1) sim; (2) não se aplica; (99) ignorado	72	
73	Dor (0) não; (1) sim; (2) não se aplica; (99) ignorado	73	
74	Infecção (0) não; (1) sim; (2) não se aplica; (99) ignorado	74	
75	Massa tumoral axilar (0) não; (1) sim; (2) não se aplica; (99) ignorado	75	
76	Curativo de feridas (0) não; (1) sim; (2) não se aplica; (99) ignorado	76	
77	Hemorragia (0) não; (1) sim; (2) não se aplica; (99) ignorado	77	
78	Infecção fúngica (0) não; (1) sim; (2) não se aplica; (99) ignorado	78	
79	Necrose (0) não; (1) sim; (2) não se aplica; (99) ignorado	79	
80	Bolhas (0) não; (1) sim; (2) não se aplica; (99) ignorado	80	
DIET - cirurgia			
81	Intenção (1) curativa; (2) paliativa; (3) não cirurgia/indicado, porém não operou (99) Ignorado	81	
82	DIET não indicada – motivos: (1) Comorbidade (2) recusa (3) metástase à distância (4) metástase locorreional (5) metástase locorreional (6) outros _____ (88) NA	82	
83	Status da paciente quando não indicada DIET: (0) Vivo sem doença; (1) Vivo com recorrência; (2) Óbito pela neoplasia; (3) Óbito por doença associada; (4) Óbito sem especificação; (5) Perda de seguimento; (5) Outro: _____ (88) NA	83	
84	Tempo da indicação da DIET (T0) até desfecho (morte, recidiva ou perda de seguimento) – PACIENTE SUBMETIDA A DIET _____ (meses)	84	

85	Tempo da indicação da DIET (T0) até desfecho (morte ou recidiva) – PACIENTE QUE NÃO REALIZOU CIRURGIA (meses)	85	
86	DIET Cirurgia realizada (0) não: _____; (1) sim; (99) ignorado	86	
87	Indicação principal (0) Ausente; (1) linfedema; (2) disfunção de membro superior; (3) dor; (4) infecção; (5) infecção fúngica; (6) curativo de ferida; (7) tumor axilar recorrente e irresssecável (extensão para tórax e/ou feixe neurovascular); (8) radionecrose; (9) ulceração; (10) hemorragia; (11) paralisia; (12) SST; (13) RIS; (14) tumor localmente avançado; (15) outro: _____; (88) não se aplica (99) Ignorado	87	
88	Tamanho da peça ressecada Cm	88	
89	Tamanho patológico do tumor Cm	89	
90	Tipo de ressecção (0) R0; (1) R1; (2) R2 (88) não aplica (99) Ignorado	90	
91	Margens (0) Negativas; (1) positivas; (88) não se aplica (99) ignoradas	91	
92	Momento da cirurgia (1) Up front; (2) após tratamento adjuvante; (3) após cirurgia de ressecção tumoral/ preservação do membro superior; (4) após tratamento de resgate/adjuvante preservadora do membro; (88) não se aplica (99) ignorado	92	
93	Técnica cirúrgica da mastectomia (0) Ausente; (1) halsted; (2) Madden; (3) Pattey; (4) outra; (88) não se aplica (99) Ignorado	93	
94	Técnica da DIET (1) Prudente; (2) outra; (88) não se aplica; (99) ignorado	94	
95	Ressecção de parede torácica (0) Ausente; (1) presente; (3) pneumonectomia; (88) não se aplica; (99) ignorado	95	
96	Fechamento (1) primário; (2) retalho fasciocutâneo; (3) retalho miocutâneo; (4) enxerto livre de pele; (5) omentoplastia pediculada; (6) free filet extremity flap; (7) retalho osteomiocutâneo livre; (88) não se aplica; (99) Ignorado	96	
97	Retalho miocutâneo (0) ausente; (1) toracoabdominal; (2) oblíquo; (3) grande dorsal (4) outro: _____; (88) não se aplica (99) Ignorado	97	
SÍNDROME DE STEWART TREVES (SST)			
98	Síndrome de Stewart Treves (0) Ausente (1) presente (88) não se aplica	98	
99	Diagnóstico (1) Clínico (2) biópsia (3) imagem (4) outro (88) não se aplica	99	
100	Tempo de tratamento primário (cirurgia) até linfedema: anos (88) não se aplica	100	
101	Tempo de linfedema até SST anos (88) não se aplica	101	
102	Tempo da cirurgia até SST Anos (88) não se aplica	102	
103	Tempo de início dos sintomas à DIET meses (88) não se aplica	103	

SARCOMA RADIOINDUZIDO (SRI)			
104	Sarcoma radioinduzido (SRI) (0) Ausente (1) presente (88) não se aplica	104	
105	Diagnóstico (1) Clínico (2) biópsia (3) imagem (4) outro (88) não se aplica	105	
106	Tempo de diagnóstico primário até SRI _____anos (88) não se aplica	106	
107	Tempo de radioterapia até SRI _____anos (88) não se aplica	107	
108	Tempo de início dos sintomas à DIET _____Meses (88) não se aplica	108	
109	Histologia (1) Malignant fibrous histiocytoomas, (2) neurofibrosarcoma, (3) leiomyosarcoma, (4) osteosarcoma, (5) fibrosarcoma, (6) angiosarcoma, (7) spindle cell sarcoma; (8) outro (88) não se aplica (99) Ignorado	109	
110	Margens (MSTS) (1) intralesional (margin was through the tumor tissue), (2) marginal (margin was through the reactive zone around the tumor—this zone contains edema, inflammatory cells, fibrous tissue, and satellites of tumor cells), (3) wide (margin is through normal tissue outside the reactive zone), (4) radical (the entire compartment containing the tumor was removed). (88) não se aplica (99) ignorado	110	
COMPLICAÇÕES			
112	Complicações (0) Ausente; (1) Presente; (99) Ignorado	112	
112	Efusão pleural (0) Ausente; (1) Presente; (99) Ignorado	112	
113	Infecção (0) Ausente; (1) Presente; (99) Ignorado	113	
114	Deiscência (0) Ausente; (1) Presente; (99) Ignorado	114	
115	Cicatrização demorada (0) Ausente; (1) Presente; (99) Ignorado	115	
116	Necrose (0) Ausente; (1) Presente; (99) Ignorado	116	
117	Outras complicações (99) ignorado	117	
QUALIDADE DE VIDA			
118	Dor (0) ausência (1) alívio (2) presente controlada com medicamentos (3) presente sem controle com medicamentos (4) dor fantasma (99) ignorado	118	
119	Gratidão (0) ausente (1) presente (88) não se aplica (99) ignorado	119	
120	Bem-estar físico, social e/ou emocional (0) ausente (1) presente (88) não se aplica (99) ignorado	120	
121	Ferramenta de avaliação de qualidade de vida (99) ignorado	121	
SEGUIMENTO			

122	Recorrência (0) ausente (1) presente (88) não se aplica (99) ignorado	122	
123	Recorrência local (0) não; (1) sim; (99) Ignorado	123	
124	Recorrência local mama (0) não; (1) sim; (2) não se aplica; (99) ignorado	124	
125	Recorrência local axila (0) não; (1) sim; (2) não se aplica; (99) ignorado	125	
126	Recorrência local mama + axila (0) não; (1) sim; (2) não se aplica; (99) ignorado	126	
127	Recorrência local outros _____ (0) não; (1) sim; (2) não se aplica; (99) ignorado	127	
128	Sítio de recorrência locorregional (0) não; (1) sim; (99) Ignorado	128	
129	Recorrência locorregional fossa supraclavicular (FSC) (0) não; (1) sim; (2) não se aplica; (99) ignorado	129	
130	Recorrência locorregional fossa infraclavicular (FIC) (0) não; (1) sim; (2) não se aplica; (99) ignorado	130	
131	Recorrência locorregional parede torácica (0) não; (1) sim; (2) não se aplica; (99) ignorado	131	
132	Recorrência locorregional dorso (0) não; (1) sim; (2) não se aplica; (99) ignorado	132	
133	Recorrência locorregional mama oposta (0) não; (1) sim; (2) não se aplica; (99) ignorado	133	
134	Recorrência locorregional axila oposta (0) não; (1) sim; (2) não se aplica; (99) ignorado	134	
135	Metástase à distância: (0) não; (1) sim; (99) ignorado	135	
136	Metástase óssea (0) não; (1) sim; (2) não se aplica; (99) ignorado	136	
137	Metástase pulmão (0) não; (1) sim; (2) não se aplica; (99) ignorado	137	
138	Metástase fígado (0) não; (1) sim; (2) não se aplica; (99) ignorado	138	
139	Metástase SNC (0) não; (1) sim; (2) não se aplica; (99) ignorado	139	
140	Metástase à distância – outros _____ (0) não; (1) sim; (2) não se aplica; (99) ignorado	140	
141	Intenção curativa - Tempo de seguimento desde a DIET (sobrevida livre de doença) Meses	141	
SEGUIMENTO – PALIATIVO			
142	Tempo da DIET até a recorrência local Meses	142	
143	Tratamento de resgate após recorrência local (0) ausente (1) quimioterapia (2) radioterapia (3) hormonioterapia (4) cirurgia (88) não se aplica (99) ignorado	143	

144	Tempo da DIET até a recorrência locorregional Meses	144	
145	Tempo da DIET até a recorrência à distância Meses	145	
146	Tempo da DIET até a morte ou perda de seguimento (?) (sobrevida livre de recorrência) Meses	146	
147	<i>Tempo do diagnóstico até a morte ou perda de seguimento (sobrevida global)*****</i> Meses	147	
CONDIÇÃO FINAL			
148	Estado do paciente no último relato (1) Vivo sem doença; (2) Vivo com recorrência; (3) Óbito pela neoplasia; (4) Óbito por doença associada; (5) Óbito sem especificação; (6) Perda de seguimento; (7) Outro: _____ (8) vivo com metástase sistêmica (99) ignorado	148	
149	OBS	149	

Apêndice 3. Tabela sumária com os artigos e os casos incluídos nas análises

Caso	Referência	Autor	Ano da Publicação	Tratamento cirúrgico inicial da Mama	Tratamento cirúrgico inicial da Axila	Condição do tumor à indicação da DIET	Intenção cirúrgica da DIET	Indicação principal da DIET	Síndrome de Stewart-Treves	Sarcoma Radioinduzido	Tempo da DIET até óbito ou perda de seguimento	Tempo do diagnóstico até óbito ou perda de seguimento	Estado do paciente ao último relato
1	(31)	Adam	1977	Mastectomia	Linfadenectomia axilar	Sarcoma radioinduzido	Paliativa	Paralisia		Sim	26,0	39,0	Óbito pela neoplasia
2	(38)	Alan	2016	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim		-----	-----	Ignorado
3	(4)	Ariel	1987	Mastectomia	Ignorado	Recorrência do câncer de mama	Paliativa	Ulceração			9,0	-----	Óbito pela neoplasia
4	(4)	Ariel	1987	Ignorado	Ignorado	Carcinoma mamário invasivo metastático	Paliativa	Dor			12,0	-----	Óbito pela neoplasia
5	(4)	Ariel	1987	DIET	DIET	CMLA	Curativa	Dor			60,0	-----	Perda de seguimento
6	(4)	Ariel	1987	DIET	DIET	CMLA	Curativa	Dor			72,0	-----	Perda de seguimento
7	(39)	Aygit	1999	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Paliativa	Síndrome de Stewart-Treves	Sim		7,0	127,0	Óbito pela neoplasia
8	(8)	Ayvaz	2011	DIET	DIET	Metástase óssea do carcinoma mamário invasivo em ombro	Paliativa	Dor			11,0	-----	Óbito pela neoplasia
9	(40)	Barnett	1969	Cirurgia conservadora	Ignorado	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim		-----	160,0	Viva sem doença
10	(40)	Barnett	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	DIET indicada, porém não realizou procedimento	Linfedema	Sim		-----	96,0	Óbito pela neoplasia

11	(40)	Barnett	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Paliativa	Disfunção de membro superior	Sim		16,0	180,0	Viva com metástase óssea
12	(12)	Behnke	2013	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			13,0	36,0	Óbito pela neoplasia
13	(12)	Behnke	2013	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			24,0	257,0	Viva com recorrência
14	(12)	Behnke	2013	Cirurgia conservadora	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			17,0	66,0	Viva com recorrência
15	(12)	Behnke	2013	Cirurgia conservadora	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			22,0	108,0	Viva com recorrência
16	(41)	Bhargavan	2018	Mastectomia	Linfadenectomia axilar	Linfedema	Curativa	Disfunção de membro superior			-----	-----	Viva sem doença
17	(42)	Bilski	2007	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim		6,0	162,0	Óbito pela neoplasia
18	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	10,0	-----	Óbito pela neoplasia
19	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	6,0	-----	Óbito pela neoplasia
20	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	17,0	-----	Óbito pela neoplasia
21	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	30,0	-----	Viva sem doença
22	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	48,0	-----	Viva sem doença

23	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	48,0	-----	Viva sem doença
24	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	18,0	-----	Viva sem doença
25	(29)	Bobin	1994	Mastectomia	Ignorado	Sarcoma radioinduzido	Curativa	Sarcoma radioinduzido		Sim	60,0	-----	Viva sem doença
26	(43)	Borman	2021	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim		20,0	128,0	Óbito por doença associada
27	(15)	Borman H	1998	Cirurgia conservadora	Linfadenectomia axilar	Sarcoma radioinduzido	Curativa	Disfunção de membro superior		Sim	-----	-----	Ignorado
28	(44)	Adolfsson	1973	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim		4,0	276,0	Óbito pela neoplasia
29	(45)	Caldarola	1975	Mastectomia	Nenhum	Recorrência do câncer de mama	Paliativa	Carcinoma mamário invasivo recorrente na axila			9,0	216,0	Óbito sem especificação
30	(46)	Coster	1988	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	DIET indicada, porém não realizou procedimento	Síndrome de Stewart-Treves	Sim		-----	84,0	Óbito por doença associada
31	(47)	Da Silva	1958	DIET	DIET	CMLA	Curativa	CMLA			-----	-----	Ignorado
32	(48)	DeJong	2012	Ignorado	Ignorado	Sarcoma radioinduzido	Curativa	Isquemia após radioterapia de membro superior ipsilateral ao carcinoma mamário invasivo		Sim	-----	-----	Viva sem especificações

33	(49)	Dragu	2011	Cirurgia conservadora	Linfadenectomia axilar	Sarcoma radioinduzido	Paliativa	Carcinoma mamário invasivo recorrente na axila		Sim	1,5	85,5	Óbito pela neoplasia
34	(50)	Fanous	1976	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			2,0	-----	Óbito pela neoplasia
35	(50)	Fanous	1976	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			22,0	-----	Óbito pela neoplasia
36	(35)	Felmerer	2016	Ignorado	Ignorado	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		36,0	-----	Óbito sem especificação
37	(9)	Goodman	2005	Cirurgia conservadora	Linfadenectomia axilar	Recorrência do câncer de mama	Curativa	Disfunção de membro superior			35,0	60,0	Perda de seguimento
38	(51)	Guleç	2014	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Paliativa	Dor	Sim		25,0	-----	Viva sem doença
39	(3)	Holleb	1959	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			60,0	132,0	Óbito por outras causas
40	(3)	Holleb	1959	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Ulceração			13,0	23,0	Óbito pela neoplasia
41	(3)	Holleb	1959	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			17,0	38,0	Óbito pela neoplasia
42	(3)	Holleb	1959	Mastectomia	Linfadenectomia axilar	Radionecrose	Curativa	Hemorragia			59,0	224,0	Viva sem doença
43	(3)	Holleb	1959	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior			18,0	114,0	Viva sem doença
44	(3)	Holleb	1959	Mastectomia	Linfadenectomia axilar	Sarcoma radioinduzido	Curativa	Dor			7,0	150,0	Viva sem doença

45	(52)	Manju	2018	Mastectomia	Linfadenectomia axilar	Linfedema	Curativa	Linfedema		1,0	178,0	Viva sem doença
46	(53)	Martin	1984	Cirurgia conservadora	Biópsia de linfonodo sentinela	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	24,0	366,0	Viva sem doença
47	(54)	Martini	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim	4,0	304,0	Viva sem doença
48	(5)	Mussey	1956	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Disfunção de membro superior		22,0	47,0	Óbito pela neoplasia
49	(5)	Mussey	1956	Mastectomia	Ignorado	Recorrência do câncer de mama	Paliativa	Carcinoma mamário invasivo recorrente na axila		4,0	14,0	Óbito pela neoplasia
50	(55)	Nemoto	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Paliativa	Linfedema	Sim	7,0	101,0	Óbito pela neoplasia
51	(55)	Nemoto	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim	----	201,0	Viva sem doença
52	(55)	Nemoto	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	CMLA	Sim	1,0	112,0	Óbito pela neoplasia
53	(55)	Nemoto	1969	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	18,0	123,0	Viva sem doença
54	(34)	Mesli	2017	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Linfedema	Sim	8,0	248,0	Óbito pela neoplasia
55	(19)	Osanai	2004	Cirurgia conservadora	Ignorado	Recorrência do câncer de mama	Paliativa	Carcinoma mamário invasivo recorrente na axila		10,0	70,0	Viva sem doença

56	(56)	Piza-Katze	2005	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Carcinoma mamário invasivo recorrente na axila		9,0	69,0	Óbito por doença associada
57	(57)	Pressman	1974	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Curativa	Disfunção de membro superior		48,0	72,0	Viva sem doença
58	(57)	Pressman	1974	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Curativa	Disfunção de membro superior		24,0	72,0	Viva sem doença
59	(58)	Echenique	2004	Mastectomia	Ignorado	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim	46,0	-----	Viva sem doença
60	(58)	Echenique	2004	Mastectomia	Ignorado	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim	12,0	-----	Óbito sem especificação
61	(59)	Lu	2022	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim	13,0	169,0	Viva sem doença
62	(24)	Lindford	2012	Cirurgia conservadora	Ignorado	Carcinoma mamário invasivo metastático	Paliativa	Carcinoma mamário invasivo recorrente na axila		17,0	125,0	Óbito pela neoplasia
63	(10)	Pundi	2015	Mastectomia	Biópsia de linfonodo sentinela	Recorrência do câncer de mama	Curativa	Carcinoma mamário invasivo recorrente na axila		60,0	34,0	Óbito pela neoplasia
64	(60)	Ramsey	1968	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	2,0	110,0	Viva sem doença
65	(13)	Roy	2004	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	3,0	-----	Viva sem doença
66	(13)	Roy	2004	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	16,0	-----	Viva sem doença

67	(13)	Roy	2004	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim		135,0	----	Viva sem doença
68	(13)	Roy	2004	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim		23,0	----	Viva sem doença
69	(13)	Roy	2004	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	DIET indicada, porém não realizou procedimento	Síndrome de Stewart-Treves	Sim		----	216,0	Óbito por neoplasia de esôfago
70	(61)	Sakamura	2001	Mastectomia	Ignorado	CMLA	Curativa	CMLA			22,0	22,0	Óbito pela neoplasia
71	(62)	Schmied	2014	Mastectomia	Linfadenectomia axilar	Recorrência do câncer de mama	Paliativa	Carcinoma mamário invasivo recorrente na axila			2,0	17,0	Óbito pela neoplasia
72	(20)	Schwarz	2002	Mastectomia	Linfadenectomia axilar	Sarcoma radioinduzido	Curativa	Ulceração		Sim	180,0	288,0	Viva sem doença
73	(20)	Schwarz	2002	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim		----	----	Viva sem doença
74	(63)	Shaw	1968	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim		11,0	120,0	Viva sem doença
75	(63)	Shaw	1968	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Paliativa	Síndrome de Stewart-Treves	Sim		2,0	72,0	Óbito pela neoplasia
76	(64)	Silverberg	1970	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim		----	----	Ignorado
77	(64)	Silverberg	1970	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		----	----	Ignorado

78	(30)	Souba	1986	Mastectomia	Ignorado	Sarcoma radioinduzido	Paliativa	Sarcoma radioinduzido		Sim	12,0	180,0	Óbito pela neoplasia
79	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		6,0	-----	Óbito pela neoplasia
80	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		2,0	-----	Óbito pela neoplasia
81	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		27,0	-----	Óbito pela neoplasia
82	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		24,0	-----	Óbito pela neoplasia
83	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		8,0	-----	Óbito pela neoplasia
84	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		17,0	-----	Óbito pela neoplasia
85	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		4,0	-----	Óbito pela neoplasia
86	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		72,0	-----	Viva sem doença
87	(27)	Stewart	1995	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		15,0	-----	Óbito pela neoplasia
88	(65)	Tomita	1988	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sixm		18,0	-----	Óbito pela neoplasia
89	(65)	Tomita	1988	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Ignorado	Síndrome de Stewart-Treves	Sim		48,0	228,0	Viva sem doença

90	(11)	Tsai	2014	Cirurgia conservadora	Ignorado	Recorrência do câncer de mama	Curativa	Carcinoma mamário invasivo recorrente na axila		36,0	144,0	Viva sem doença
91	(23)	Wittig	2001	Ignorado	Ignorado	Carcinoma mamário invasivo metastático	Paliativa	Dor		4,0	-----	Óbito pela neoplasia
92	(23)	Wittig	2001	Ignorado	Ignorado	Carcinoma mamário invasivo metastático	Paliativa	Dor		4,0	-----	Óbito pela neoplasia
93	(23)	Wittig	2001	Ignorado	Ignorado	Carcinoma mamário invasivo metastático	Curativa	Dor		5,0	-----	Óbito pela neoplasia
94	(18)	Vieira	2020	Mastectomia	Linfadenectomia axilar	CMLA	Curativa	Disfunção de membro superior		7,0	9,0	Óbito pela neoplasia
95	(66)	Merimsky	2001	Ignorado	Ignorado	Recorrência do câncer de mama	Paliativa	Carcinoma mamário invasivo recorrente na axila		18,0	-----	Óbito pela neoplasia
96	(36)	Puhaindran	2012	DIET	DIET	CMLA	Curativa	Disfunção de membro superior		-----	-----	Óbito sem especificação
97	(59)	Lu	2022	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Paliativa	Síndrome de Stewart-Treves	Sim	156,0	168,0	Viva sem doença
98	(67)	Silva	2003	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	18,0	78,0	Viva sem doença
99	(68)	Vojtsek	2020	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	Curativa	Síndrome de Stewart-Treves	Sim	4,0	105,0	Óbito pela neoplasia
100	(69)	Maldonado	2002	Mastectomia	Linfadenectomia axilar	Síndrome de Stewart-Treves	DIET indicada, porém não realizou procedimento	Síndrome de Stewart-Treves	Sim	-----	127,0	Óbito por doença associada

DIET: desarticulação interescapulotorácica; CMLA: câncer de mama localmente avançado.

Apêndice 4. Material submetido e aprovado para publicação no Clinical Breast Cancer



Forequarter Amputation for Breast Cancer. Systematic Review and Survival Analysis

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René Aloisio da Costa Vieira^{1,2,4,5}

Abstract

Introduction: Forequarter amputation (FA) or Interscapulothoracic disarticulation is indicated in patients with invasive breast carcinoma (BC) in selected cases: primary resection of a locally advanced or recurrent tumor, Stewart & Treves syndrome (STS), or sarcoma secondary to radiation due to breast cancer (radiation-induced sarcoma, RIS). However, no studies have robustly evaluated the indications, results, complications, recurrence and overall survival in the context of FA in patients with BC. **Material and Methods:** We performed a systematic review of 8 databases according to the PICOS and PRISMA methodology through December 31, 2022. Descriptive statistics are presented, and Kaplan–Meier survival curves were generated and compared with the log-rank method. **Results:** We identified 54 articles and collected data from 100 patients. The intention of FA was curative for 48 patients (57.1%) and palliative in 32 (38.1%). The procedure was performed due to STS (35%), upper limb dysfunction (18%), lymphedema (10%), recurrent axillary tumors (10%) and RIS (9%). Complications were low. The survival rates at 12, 24, 36, and 60 months were 65.6%, 42.8%, 36.4%, and 32.4%, respectively. The main factors associated with survival were tumor's condition ($P = .05$) and surgical intent ($P < .001$; multivariate analysis). **Conclusion:** FA has few complications and attenuates symptoms in patients treated with both curative and palliative intent. Surgery is justified in select cases, such as locally advanced tumors, infiltration of axillary structures, upper limb lymphedema with loss of function, and STS and RIS, and often represents the best chance for local disease control and improvement in quality of life.

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Keywords: Breast neoplasms, Disarticulation, Interscapulothoracic disarticulation, Locally advanced breast cancer, Stewart Treves syndrome, Radiation-induced neoplasms

Introduction

The first publication in the English literature on forequarter amputation (FA) or interscapulothoracic disarticulation (ISTD) in breast cancer patients dates back to 1956, describing the case of 2 patients with recurrent neoplasia following primary treatment presenting with edema, pain, axillary tumors and loss of functionality of the upper limb ipsilateral to the site of surgery.¹ However, over time, the use of this procedure in the context of locally advanced tumor resection² (curative or palliative),^{3,4} recurrent disease,^{5–9} brachial plexopathy,⁸ Stewart & Treves syndrome

(STS),^{10–12} sarcoma secondary to radiation due to breast cancer (radiation-induced sarcoma, RIS)^{13,14} and metastatic bone disease¹⁵ has been reported. Histological types associated with the use of FA include carcinoma^{8,9} malignant phyllodes tumors,¹⁶ and RISs such as angiosarcoma,¹⁰ fibrosarcoma and chondrosarcoma.¹⁴

Owing to its morbidity and case selection criteria, this surgery is not frequently indicated. In breast cancer, due to the multiple associated conditions, the use of FA is usually described in the form of case reports or case series.^{4,8,17–21} However, no studies have evaluated the indications, surgical results, complications, recurrence, and overall survival associated with the use of this procedure. Thus, to better understand the multiple factors associated with FA in the context of breast cancer, a systematic review of the literature is necessary to understand the benefits of this procedure.

Materials and Methods

This was a systematic review of the literature conducted in 8 databases (Cochrane, CINAHL Complete, Embase, Lilacs, PubMed, Scielo, Scopus, and Web of Science) through December 31, 2022, according to the PRISMA methodology²² (Figure 1). Two searches were conducted with the PICOS methodology, the

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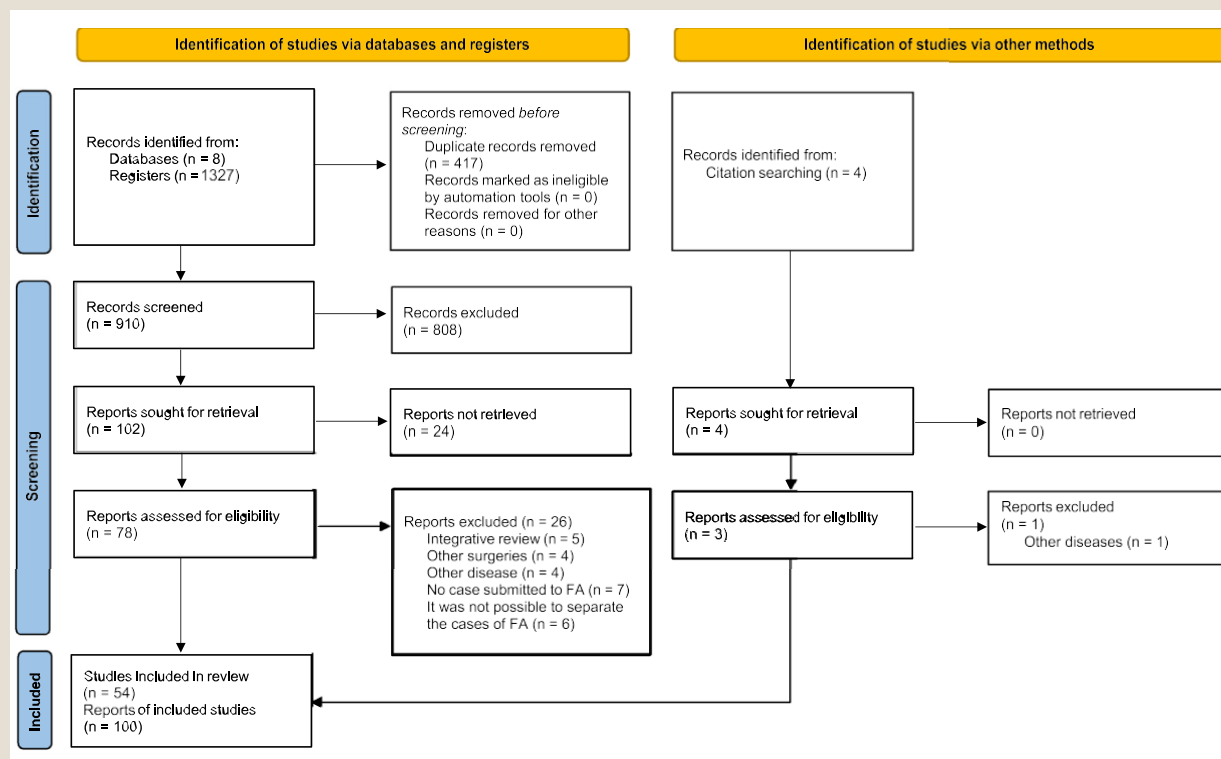
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Figure 1 Prisma Flowchart. FA: forequarter amputation.
 From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi:10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>.



first including the keywords (“Breast neoplasm”) AND ((amputation) OR amputations) OR (disarticulation OR disarticulations) OR (forequarter) OR (periscapular) OR (interscapulothoracic)). The second search included (“Breast Neoplasm”) AND ((amputation) OR amputations) OR (disarticulation OR disarticulations) OR (forequarter) OR (periscapular) OR (interscapulothoracic)) AND ((Sarcoma) OR (Lymphangiosarcoma)). Other equivalent controlled terms were employed depending on the database. In addition to those studies retrieved from the database search, 4 studies were identified from a search of the citations of the retrieved studies.

The literature review was performed by 2 independent reviewers who, after excluding duplicates, selected articles on the basis of the title and abstract. The reviewers’ databases were pooled and compared, and in cases of disagreement, the full texts of the articles were evaluated. The selection criteria were publications including case studies, case series, or reports of patients with primary or recurrent invasive breast carcinoma, lymphangiosarcoma, or RIS following primary treatment for breast cancer with indications for or undergoing FA, with no restrictions on the period or type of treatment and written in English, Portuguese, Spanish, French or German. The exclusion criteria were as follows: (1) older articles lacking abstracts, abstracts only, or articles published in journals unavailable on the internet or that cannot be retrieved from the

Regional Library of Medicine (BIREME/Brazil); (2) patients who underwent FA for other causes, such as other neoplasms, or who underwent other surgeries; and c) publications that did not allow the individualization of patients treated with FA. The full texts of the articles that met these criteria were subsequently evaluated.

Patient data, including age; characteristics of the neoplasm at the time of diagnosis and its primary treatment; characteristics of the tumor at the time of indication for FA, such as local, locoregional, and systemic recurrence, and clinical presentation of the disease; FA indications; nature of surgery and its characteristics; specific information related to STS and RIS; complications; quality of life; recurrence; and survival were collected in a standardized form from the articles. The intention of the surgery was recorded as that reported by the author; if it was not defined, this information was considered ignored data. These data were then tabulated and analyzed with the IBM SPSS software for Mac OS. Descriptive statistics are presented, and the Kaplan–Meier method was used to assess survival, with differences between survival curves assessed with the log-rank method. Univariate and multivariate analysis (conditional forward) was performed.

As this is a review of the literature, the present study fits Resolution 510/2016 of the National Health Council, which waives the need for registration and evaluation through the Research Ethics Committee (Comitê de Ética em Pesquisa, CEP)/National Research

Ethics Commission (Comissão Nacional de Ética em Pesquisa, CONEP) system. This systematic review was not registered.

Results

A total of 1327 articles were identified, among which 417 duplicates were excluded, resulting in 910 articles whose titles and abstracts were evaluated by 2 independent reviewers. Of these, 106 articles were selected for a full text reading. After applying the inclusion and exclusion criteria, 54 articles encompassing 100 patients with indications or who underwent FA due to BC (primary or recurrent), lymphangiosarcoma (STS) or RIS after primary treatment for BC (Figure 1) were selected for data collection. These data came from single-case reports,^{2,5-7,9,13,16,23-50} 2-case reports,^{1,42,51-55} and case series^{8,10,17-21,56,57} whose median and mean number of cases per article were 1 and 1.8 (range 1 to 9 cases), respectively.

The articles were published from 1955 to 2022 and consisted of 69% of case reports and 29% of case series; 62% of cases reported in the literature of patients indicated for or undergoing FA were published from the 1990s onwards. Table 1 shows the main clinical characteristics of the published cases. The mean age at diagnosis of the primary neoplasm was 52.95 ± 9.56 years; 96% of the patients were female, and 78% were diagnosed with primary BC.

Information on the pretreatment clinical stage, histological type and histological grade, and immunohistochemical classification was not provided in most case reports (Supplemental Tables 1 and 2). Mastectomy (78%) and axillary lymphadenectomy (67%) were the most commonly performed surgeries for the treatment of primary breast cancer, and FA was performed as the first surgical treatment in 5% of cases. Among studies that reported adjuvant treatment, adjuvant radiotherapy was the most commonly described and performed (92.8%).

Regarding the tumor conditions at the time of FA indication, 47% of the cases had STS, 23% had recurrent BC, and 15% had RIS (Table 1 and Supplemental Table 3). The most commonly reported symptoms were edema (88.5%), pain (89.1%), and upper limb dysfunction (82.5%). In terms of recurrence, 31% reported local recurrence, and 16% described distant metastases, with the most common site being the lung (Supplemental Table 4).

In the 100 patients evaluated, FA was indicated with curative intent in 48 patients (57.1%) and palliative intent in 32 patients (38.1%); It was not possible to judge the intention of surgery for the remaining 20 patients. Four patients did not undergo FA despite presenting with indications for the procedure due to refusal, comorbidities or presence of distant metastases. Among the 96 patients who underwent the surgery, the main indications were STS (35%), upper limb dysfunction (18%), lymphedema (10%), recurrent and uncontrollable axillary tumors (10%) and RIS (9%). A total of 44 patients (60.3%) underwent surgery as the first treatment for the condition that indicated the need for FA, 14 (19.2%) underwent the procedure after adjuvant treatment, and 13 (17.8%) were treated after tumor resection surgery.

The chest wall was partial resected at the time of FA in 14 cases (60.9%), among whom primary closure was possible in 9 cases, and 16 cases required some type of flap or graft, such as myocutaneous flaps (2 requiring latissimus dorsi myocutaneous flaps) or extremity free flaps (Table 2). Complications after FA were

reported in 10 cases, the most common of which were skin necrosis (22.6%), pleural effusion (17.25%) and delayed healing (11.1%). Thirteen reports described pain alleviation after surgery, 6 each described complete pain relief and phantom pain, and 10 (90.9%) and 14 (100%) reports described a sense of gratitude and physical/emotional well-being, respectively (Table 3).

After surgery, recurrence was present in 62.6% of cases, with distant recurrence being the most common (50%), followed by local recurrence (33.3%) (Supplemental Tables 5 and 6). Local recurrence was reported in 22/66 patients, occurring mainly when FA was used for STS (13/30), symptom control (10/30), and recurrent disease (7/15), irrespective of treatment intention [curative (7/35) or palliative (8/20)], tumor status or time of surgery.

The overall mean time from primary diagnosis to death or loss to follow-up was 128.7 ± 82.0 months; for patients treated with curative intent, the mean time was 149.8 ± 92.7 months, and for those treated with palliative intent, the mean time was 99.3 ± 66.3 months. At the time of the last follow-up, 45.3% of the patients had died due to cancer, and 34.7% were alive without disease. The overall follow-up time after FA was 23.9 ± 30.8 months; 29.6 ± 36.6 months for curative intention; 18.5 ± 27.4 months for palliative intention and 3.3 ± 3.0 months for patients not submitted to FA.

The survival rates at 12, 24, 36, and 60 months were 65.6%, 42.8%, 36.4%, and 32.4%, respectively. Evaluating factors associated to survival (Table 4, Figure 2), main indication ($P = .194$), moment of surgery ($P = .579$), surgical condition ($P = .048$), and factors intention of surgery ($P < .001$), 2 factors were observed. Multivariate analysis showed that treatment intention was the main factor associated to survival, since the inclusion ($P = .003$) or not-inclusion ($P = .001$) of missing data, and patients who underwent curative surgery had better survival.

Discussion

In a series of patients who underwent FA, the indication for the procedure in approximately 12.5% of the patients was breast cancer.⁵⁸ This procedure is usually performed for patients with metastatic disease²⁰ and recurrent disease^{5-7,20} and with palliative intent^{6,8}. In this review, the main indication for the procedure was STS,^{12,59} followed by breast cancer recurrence,^{5,6,8} RIS,^{13,14} and metastatic disease.¹⁵

In terms of metastasis, one patient with breast cancer who progressed to bone metastasis required FA to treat or prevent pathological fracture, and one patient with locally advanced breast cancer experienced recurrence in the ipsilateral axillary cavity.^{9,15} Other descriptions related to breast cancer involved the evaluation of chest wall reconstruction.^{16,24} In patients with STS and RIS, surgery is usually intended to be curative (21/25 patients); in the presence of recurrent/unresectable axillary disease or to control symptoms, it tends to be palliative (28/54 patients). In this sample, potential bias should be considered in the selection of cases, as patients with better performance are usually selected for surgery. Among the 4 patients who did not undergo surgery, the mean survival time was 4.1 ± 3.2 months, indicating that even in unfavorable and palliative scenarios, surgery helps control symptoms, potentially improving quality of life.

Forequarter Amputation for Breast Cancer

Table 1 Clinical Characteristics of Published Cases (n = 100)

Category	Variables	N	Valid %
Gender (n = 98; 98%)	Feminine	96	97.9%
	Masculine	2	2.1%
	Ignored	2	
Age at diagnosis of primary neoplasia (n = 56; 56%)	Mean	52.95 ± 9.56 y	
Side of the neoplasia (n = 57; 57%)	Right	27	47.4%
	Left	30	52.6%
	Ignored	43	
Status at diagnosis of primary Neoplasm (n = 86; 86%)	Primary	78	90.7%
	Local recurrence with distant metastasis	5	5.8%
	Local recurrence without information on distant metastasis	2	2.3%
	Locally advanced primary neoplasm	1	1.2%
Tumor conditions at the time of FA indication (n = 100; 100%)	Ignored	14	
	STS	47	47%
	Breast cancer recurrence	23	23%
	RIS	15	15%
	Locally advanced primary neoplasm	6	6%
	Metastatic	5	5%
	Other	3	3%
	Bone metastasis in the shoulder joint	1	1%
Age at FA indication (n = 66; 66%)	Mean	60.8 ± 11.6 y	
Time from symptom onset to diagnosis (n = 11; 11%)	Mean	46.0 ± 64.3 mo	
Larger clinical tumor size (n = 5; 5%)	Mean	10.4 ± 5.7 cm	
Time from treatment (primary surgery) to recurrence leading to FA (n = 49; 49%)	Mean	74.5 ± 49.4 mo	
Time from treatment (primary surgery) to FA (n = 48; 48%)	Average	95.7 ± 79.9 mo	
FA intent (n = 84; 84%)	Curative	48	57.1%
	Palliative	3)	38.1%
	Surgery indicated but not performed	4	4.8%
	Ignored	16	
FA performed (n = 100; 100%)	Yes	96	96%
	No	4	4%
Reasons for FA not indicated (n = 4)	Comorbidities	1	25%
	Refusal	2	50%
	Distant metastasis	1	25%
	Not applicable	96	
Patient status when FA not indicated (n = 4; 4%)	Death from neoplasia	1	25%
	Death from associated disease	2	50%
	Follow-up loss	1	25%
	Ignored	96	
Time from FA indication to outcome in a patient who did not undergo surgery (n = 3; 3%)	Mean	4.1 ± 3.2 mo	
Main indication of FA (n = 100; 100%)	STS	35	35%
	Upper limb dysfunction	18	18%
	Lymphedema	10	10%
	Recurrent, unresectable axillary tumor	10	10%
	Pain	9	9%
	RIS	9	9%
	Ulceration	3	3%

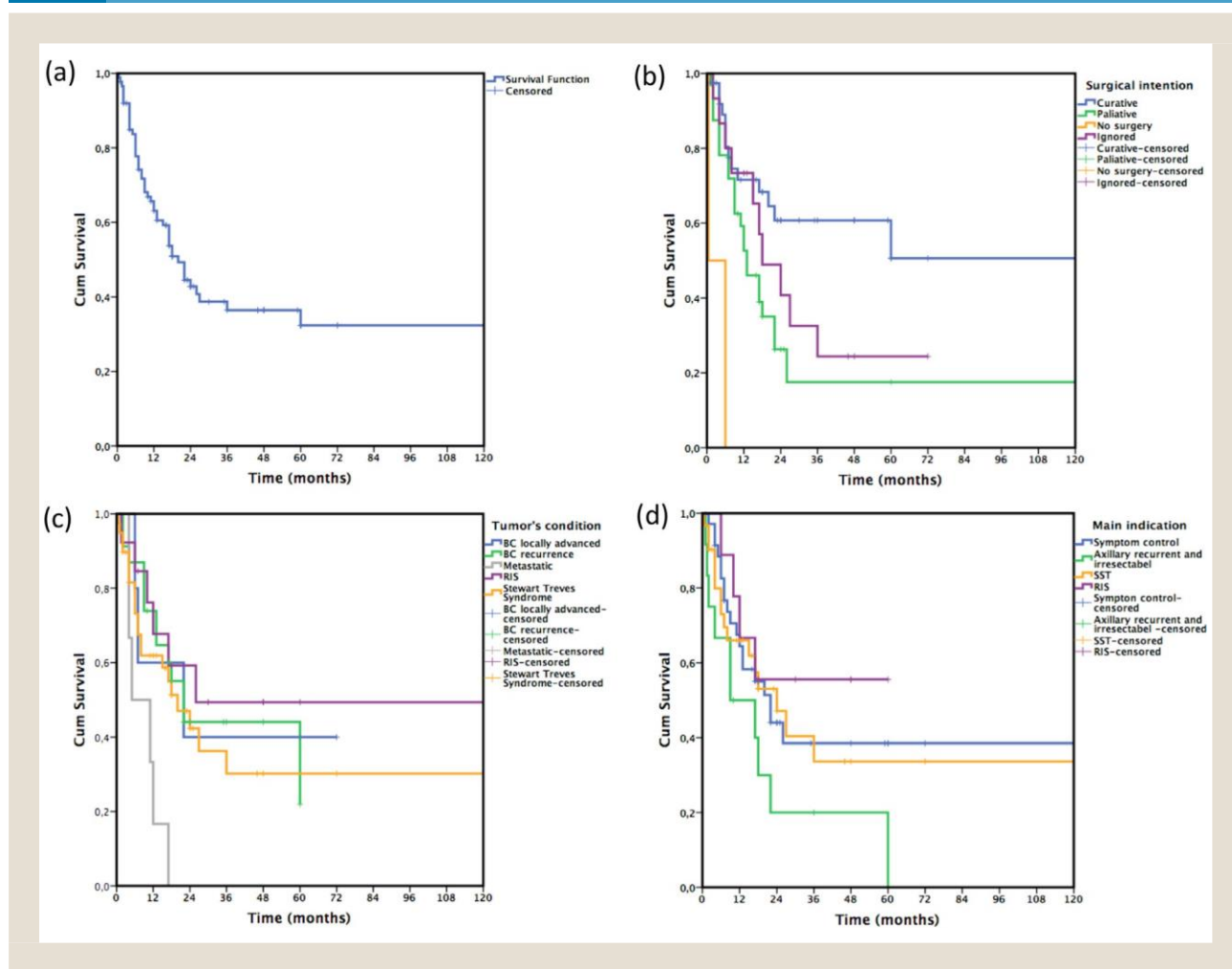
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Table 1 (continued)

Category	Variables	N	Valid %
Timing of surgery (n = 73; 73%)	Locally advanced breast cancer	3	3%
	Bleeding	1	1%
	Paralysis	1	1%
	Other	1	1%
	First surgical treatment for the reason for indication of FA	44	60.3%
	After adjuvant treatment	14	19.2%
	After tumor resection surgery	13	17.8%
Time from indication of FA to outcome in a patient undergoing surgery (n = 76; 76%)	After limb-preserving adjuvant salvage treatment	2	2.7%
	Not applicable	4	
	Ignored	23	
	Mean	24.1 ± 29.5 mo	

STS, Stewart & Treves Syndrome; FA, forequarter amputation; RIS, radio-induced sarcoma.

Figure 2 Actuarial survival according to conditions related to clinical indication. Cum. Survival: cumulative survival. BC: breast cancer. RIS: radio-induced sarcoma



Forequarter Amputation for Breast Cancer

Table 2 Aspects Related to Forequarter Amputation (FA)

Category	Variable	N	Valid %
Size of the excised piece (n = 4; 4%)	Mean	32.7 ± 28.5 cm	
Pathological tumor size (n = 2; 2%)	Mean	12.5 ± 1.0 cm	
Type of resection (n = 7; 7%)	R0	5	71.4%
	R1	0	0
	R2	2	28.6%
	Not applicable	5	
	Ignored	88	
Margins (n = 24; 24%)	Positive	5	20.8%
	Negative	19	79.2%
	Not applicable	4	
	Ignored	72	
Surgical technique of mastectomy (n = 10; 10%)	Halsted	1	10%
	Pattey	1	10%
	Madden	2	20%
	Not applicable	6	60%
	Ignored	90	
FA surgical technique (n = 3; 3%)	Prudent	0	
	Other	3	100%
	Not applicable	4	
	Ignored	93	
Chest wall resection (n = 23; 23%)	Present	14	60.9%
	Absent	9	39.1%
	Not applicable	4	
	Ignored	73	
Closing technique (n = 25; 25%)	Primary	9	36%
	Myocutaneous flap	6	24%
	Extremity free flap	4	16%
	Fasciocutaneous flap	3	12%
	Skin-free graft	2	8%
	Free osteomyocutaneous flap	1	4%
	Not applicable	4	
	Ignored	72	
Myocutaneous flap (n = 18; 18%)	Latissimus dorsi flap	2	11.1%
	Other	8	44.4%
	Absent	8	44.4%
	Not applicable	82	

FA, forequarter amputation.

The results of this review indicated that the interval between the initial treatment and the development of RIS and STS was 9.0 ± 4.1 years and 15.8 ± 18.9 years, respectively (Supplemental Table 3). Factors such as the type of radiotherapy may have affected these values, since STS has become less prevalent with new forms of energy associated to radiotherapy.

One of the main points to consider in FA is the closure of the resected area, which can be performed using part of the skin of the affected limb, skin grafts, and myocutaneous flaps.^{2,5,6,8} Few articles have reported surgical results, such as margins (free in 19/24

patients), chest wall resection (present in 14/23 patients), and the need for flaps to close the defect (9/25), usually with a primary or free graft (2/25).

In classical FA, the complication rate is relatively low and usually related to skin necrosis, local dehiscence, and pleural effusion.⁵⁻⁸ These complications can be considered limited and do not negatively impact the postoperative outcome⁶. Among the complications reported are necrosis of the flap or its edge and delayed healing. In this sample (Table 3), the complication rate was approximately 25% (10/40); the primary complications included

Table 3 Complications After Forequarter Amputation (FA) and Its Impacts on Quality of Life

Category	Variable	N	Valid %
Complications (n = 40; 40%)	Yes	10	25%
	Missing	30	75%
	Not applicable	4	
	Ignored	56	
Pleural effusion (n = 29; 29%)	Yes	5	17.25%
	No	24	82.75%
	Not applicable	4	
	Ignored	67	
Infection (n = 24; 24%)	Yes	1	4.2%
	No	23	95.8%
	Not applicable	4	
	Ignored	67	
Dehiscence (n = 29; 29%)	Yes	3	10.4%
	No	26	89.6%
	Not applicable	4	
	Ignored	67	
Delayed healing (n = 27; 27%)	Yes	3	11.1%
	No	24	88.9%
	Not applicable	4	
	Ignored	69	
Necrosis (n = 31; 31%)	Yes	7	22.6%
	No	24	77.4%
	Not applicable	4	
	Ignored	65	
Other complications (n = 21; 21%)	Yes	3	14.3%
	No	18	85.7%
	Not applicable	4	
	Ignored	75	
Pain (n = 25; 25%)	Relief	13	52%
	Phantom pain	6	24%
	Absent	6	24%
	Not applicable	4	
Gratitude (n = 11; 11%)	Ignored	71	
	Yes	10	90.9%
	No	1	9.1%
	Not applicable	4	
Physical, social, and/or emotional well-being (n = 14; 14%)	Ignored	85	
	Yes	14	100%
	Not applicable	4	
	Ignored	78	
Quality of life assessment tool (n = 1; 1%)	Merimsky	1	100%
	Not applicable	4	
	Ignored	95	

FA, forequarter amputation.

necrosis (7/31 = 22.6%), pleural effusion (5/29 = 17.3%), dehiscence (3/29=10.4%), delayed healing (3/27=11.1%) and infection (1/24=4.2%), fully justifying the surgery.

The lack of standardization among the reports, as well as the wide range of indications and follow-up times, limits the evaluation of the immediate results of the procedures, especially when used for symptom control. According to this review, pain relief (13/25)

or control (6/25), phantom pain (6/25), and senses of gratitude (10/11), and physical, social and/or emotional well-being (14/14) have been reported following FA.

A review of the literature on patients undergoing FA for recurrent disease (n = 28) revealed better survival with a curative intent, with a mean of 23 months, whereas palliative intent was associated with a mean survival of 13 months when used both for symptom control

Table 4 Actuarial Survival as a Function of the Main Situations Related to the Indication of Forequarter Amputation (FA)*

Variable	Category	n	12 mo	24 mo	36 mo	60 mo	P
Intention	Curative	39	71.6%	60.7%	60.7%	50.6%	<.001
	Palliative	32	52.6%	26.3%	17.5%	17.5%	
	Not realized	3	0	0	0	0	
Condition	RIS	13	67.6%	59.2%	49.4%	49.4%	.048
	STS	39	61.9%	42.3%	30.2%	30.2%	
	Recurrence	23	73.9%	44.0%	44.0%	22.0%	
	LABC	4	60.0%	40.0%	40.0%	40.0%	
Indication	Metastatic	6	16.7%	0	0	0	.194
	Symptom	36	64.4%	44.0%	38.5%	38.5%	
	STS	31	66.0%	47.1%	33.7%	33.7%	
	RIS	9	66.7%	55.6%	55.6%	55.6%	
	Axillary and unresectable rec.	12	50.0%	20.0%	20.0%	0	
Moment	Upfront	37	65.4%	51.1%	46.0%	46.0%	.579
	After primary surgery	13	53.8%	53.8%	53.8%	0	
	After adjuvant	13	75.0%	30.0%	0	0	
Everyone	-	88	65.6%	42.8%	36.4%	32.4%	-

*Reported grouping of variables. RIS: radio-induced sarcoma; STS: Stewart & Treves Syndrome; Rec.: recurrence; LABC: locally advanced breast cancer.

and for patients with systemic disease.⁶ In this review (n = 100), we included patients in different situations who underwent FA, with mean survival times of 29.6 ± 36.6 months and 18.5 ± 27.5 months following treatment with curative and palliative intent, respectively. Given its systematic nature, this review includes the largest number of patients to date, which allows us to compare groups using survival estimation. The results indicated that patients undergoing curative surgery had significantly greater survival (*P* < .001); nevertheless, of the patients who underwent palliative surgery, half were alive at 12 months, and a quarter were alive at 24 months, so it is important to evaluate indicators of quality of life in future studies.

Another factor associated with survival was the condition that led to surgical treatment. Survival was significantly associated with the surgical condition (*P* = .048); specifically, patients with RIS and those with metastatic disease had longer and shorter survival times, respectively. In RIS, surgery allows the degree of discomfort associated with local invasion, usually located in the shoulder, supraclavicular and infraclavicular regions, and scapula, to be reduced.²¹ The overall survival of patients who developed RIS after treatment for breast cancer following FA was 12 to 24 months; in this group, death was mainly due to lung metastases.^{23,25} In a series of 7 patients with RIS after radiotherapy for breast cancer treated with FA, all of which were resected with macroscopically free margins, 5 patients survived with survival of 18 to 60 months after the second primary diagnosis, and 2 died due to metastases at 6 and 17 months after the diagnosis. No patient who survived experienced local recurrence, but one patient developed lung metastases.²¹ FA was chosen as an option for alleviating symptoms and curing patients with RIS.²⁵ This series included 13 patients, with a mean follow-up of 35.6 ± 47.1 months and RIS is associated with the best prognosis.

FA for the treatment of STSs has been described in the literature since 1948, in a 6-case series published by Stewart and Treves, who

gave the syndrome its name.¹² In a series of 8 patients with STS who underwent FA, local progression-free survival ranged from 1 to 27 months, with one patient surviving without evidence of disease for 6 years.¹⁹ Four patients with STS treated with FA survived without evidence of disease for a mean time of 44.2 months.⁴ STS patients have the highest local recurrence rate (10/23). In this study, in a group of 39 patients, the mean follow-up was 22.2 ± 32.7 months, and the 24-month survival rate was 42.3%.

In the treatment of BC, FA is primarily indicated for local and/or locoregional recurrence, especially axillary recurrence.^{5,6,8} In a case series from the literature, Pundi et al.⁶ reported a mean survival of 23.4 ± 14.6 months in patients with recurrent breast cancer who underwent FA with curative intent, while Goodman presented a survival of 22 to 48 months in a separate case report.⁵ Patients with axillary breast cancer recurrence who progressed to brachial plexopathy due to local extension of the disease without evidence of distant disease demonstrated an overall survival of 13 to 22 months and progression-free survival of 2 to 9 months.⁸ Patients with locally advanced primary, recurrent and metastatic disease presented with follow-up times of 33.4 ± 30.7 months, 21.5 ± 15.5 months and 8.8 ± 5.3 months, respectively.

Palliative surgery is indicated for the partial or complete relief of local symptoms such as uncontrolled pain, ulceration, foul odors, recurrent infections, ulceration requiring dressing changes, bleeding, upper limb edema, and paralysis and/or loss of functionality of the ipsilateral upper limb,²⁴ with the goal of local control and disease-free survival.⁶ In the palliative setting, survival ranged from 4 to 22 months in patients with recurrent disease and from 4 to 60 months in patients with metastatic disease,⁵ while a median survival of approximately 13 months has been reported.⁶ Progression-free survival of 6 weeks and overall survival of 4, 5, 6, or 17 months have been reported in patients with disease progression.^{6,20,24} In this series, patients with recurrent disease had a better prognosis than

did patients with metastatic disease, among whom only 16.7% were alive at 12 months.

In this review, we sought to evaluate the main data associated with FA exclusively in the context of breast cancer through a rigorous analysis of the literature, extracting key conclusions that allowed us to evaluate the main groups treated with this procedure as well as their survival. Despite these strengths, a number of limitations should be noted, including the retrospective nature of the study, in which we observed a large variation in the quantity and quality of the information present in the studies, possibly due to the characteristics of the publications, which were typically case reports and small case series. Nevertheless, to the best of our knowledge, this is the first study to estimate the survival rates of these patients. Another major limitation was the lack of adequate evaluation of outcomes associated with improvements in symptoms and quality of life, which is necessary to better understand the benefits of this surgery in palliative contexts and especially metastatic patients. To address this issue, we present the main points to be addressed in future studies (Supplemental Table 7).

We suggest conducting systematic reviews of case reports or series. The standardization of data to be used to conduct case reports, CARE⁶⁰ (CASEREporting), dates from 2013, but it is still not used frequently. We performed a systematic review according to the PRISMA methodology²² with the goal of identifying relevant articles and extracting key data. We are aware of the need to standardize data to be used in future studies, so we suggest that review articles⁶¹ or systematic reviews, including case reports, consider the information in Supplemental Table 8.

Despite the extensiveness of the surgery and wide range of disease-free and overall survival, FA is associated with few complications and high success in relieving symptoms, both in curative and palliative contexts,^{5,8,20} leading to improvements in quality of life.⁹ Surgery is fully justified in carefully selected cases, such as locally advanced tumors, infiltration of axillary structures, significant upper limb lymphedema with loss of function, and both STS and RIS, and often represents the best chance for local disease control, improvement in patient survival,⁶² possibly contributing positively to quality of life.

Conclusions

Despite its nature as an amputative and, consequently, disfiguring surgery, FA has value as part of the surgical arsenal for managing patients with breast cancer. Better results are observed when employed in a curative context and for patients with RIS. It results in few complications, and those that occur are not very morbid and has little impact on the subsequent management of the primary tumor.⁵ When used in palliative contexts, the goal is mainly to control symptoms. It allows the relief of pain and discomfort caused by swelling of the upper limbs and infiltration of axillary tumors into neurovascular bundles and/or ulcers, increasing patient quality of life.⁹

Disclosure

The authors have stated that they have no conflicts of interest.

CRedit authorship contribution statement

Flávia Cardoso Franca: Conceptualization, Data curation, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Idam de Oliveira-Junior:** Data curation, Investigation, Visualization, Writing – original draft, Writing – review & editing. **René Aloisio da Costa Vieira:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Supplementary material

Supplemental Table 1 Clinical Characteristics of Published Cases (n = 100)

Category	Variable	N	Valid %
Pretreatment clinical stage (n = 17; 17%)	Ila	4	23.5%
	IIb	4	23.5%
	IIIa	1	5.9%
	IIIb	1	5.9%
	IIIc	6	35.3%
	IV	1	5.9%
	Ignored	83	
T (n = 13; 13%)	T1	1	7.7%
	T2	6	46.1%
	T4b	3	23.1%
	T4c	2	15.4%
	T4d	1	7.7%
	Ignored	87	
N (n = 23; 23%)	N0	5	21.7%
	N1	6	26.1%
	L2	3	13.1%
	N3	8	34.8%
	Nx	1	4.4%
	Ignored	77	
M (n = 22; 22%)	M0	20	90.9%
	M1	1	4.5%
	Mx	1	4.5%
	Ignored	78	
Histological type (n = 40; 40%)	Invasive breast carcinoma of no special type	30	75%
	Phyllodes tumor	1	2.5%
	Other	9	22.5%
	Ignored	60	
Histological type with no report of primary tumor (n = 3; 3%)	Angiosarcoma	2	66.7%
	Radio-induced sarcoma	1	33.3%
	Not applicable	97	
Estrogen receptor (n = 11; 11%)	Positive	3	27.3%
	Negative	6	54.5%
	Other histology	2	18.2%
	Ignored	89	
Progesterone receptor (n = 10; 10%)	Positive	4	40%
	Negative	4	40%
	Other histology	2	20%
	Ignored	90	
Her 2 (n = 11; 11%)	Positive	3	27.3%
	Negative	6	54.5%
	Other histology	2	18.2%
	Ignored	89	
Molecular subtype (n = 10; 10%)	Luminal B HER 2 negative	2	20%
	Luminal B HER 2 positive	2	20%
	Triple negative	4	40%
	Other histology	2	20%
	Ignored	90	
Nottingham histological grade (n = 10; 10%)	1	1	10%
	2	2	20%
	3	7	70%
	Ignored	90	

Forequarter Amputation for Breast Cancer

Supplemental Table 2 Characteristics of the Primary Treatment of Invasive Breast Carcinoma

Category	Variable	N	Valid %
Initial surgical treatment of the breast (n = 93; 93%)	Mastectomy	78	83.9%
	Quadrantectomy / Sectorectomy	10	10.7%
	FA	5	5.4%
Surgical treatment of the axilla (n = 74%)	Ignored	7	
	Axillary lymphadenectomy	67	90.5%
	Sentinel lymphnode biopsy	2	2.7%
	FA	5	6.7%
	Ignored	25	
Adjuvant chemotherapy (n = 39; 39%)	None	1	
	No	14	35.9%
	Yes	25	64.1%
Adjuvant chemotherapy (n = 39; 39%)	Ignored	61	
	No	14	35.9%
	Yes	25	64.1%
Neoadjuvant chemotherapy (n = 38; 38%)	Ignored	61	
	No	34	89.5%
	Yes	4	10.5%
Chemotherapy prior to FA (n = 17; 17%)	Ignored	62	
	No	9	52.9%
	Yes	8	47.1%
	Not applicable	1	
Palliative chemotherapy (n = 18; 18%)	Ignored	82	
	No	5	27.8%
	Yes	13	72.2%
	Not applicable	1	
Palliative chemotherapy – when: (n = 13; 13%)	Ignored	81	
	Before surgery	2	15.4%
	After surgery	9	69.2%
	Other	2	15.4%
	Not applicable	5	
Adjuvant radiotherapy (n = 84; 84%)	Ignored	82	
	No	6	7.2%
	Yes	78	92.8%
Neoadjuvant radiotherapy (n = 48; 48%)	Ignored	16	
	No	45	93.7%
	Yes	3	6.3%
Radiotherapy prior to DIET (n = 26; 26%)	Not applicable	15	
	Ignored	37	
	No	15	57.7%
	Yes	11	42.3%
Palliative radiotherapy (n = 19; 19%)	Not applicable	2	
	Ignored	72	
	No	7	36.8%
Palliative radiotherapy – when: (n = 12; 12%)	Yes	12	63.2%
	Not applicable	2	
	Ignored	79	
	Before surgery	2	16.7%
	After surgery	8	66.6%
	Other	2	16.7%
	Not applicable	87	
	Ignored	1	

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Supplemental Table 2 (continued)

Category	Variable	N	Valid %
Adjunctive hormone therapy (n = 12; 12%)	No	5	41.7%
	Yes	7	58.3%
	Not applicable	3	
Neoadjuvant hormone therapy (n = 9; 9%)	Ignored	85	
	No	8	88.9%
	Yes	1	11.1%
	Not applicable	3	
Hormone therapy prior to FA (n = 9; 9%)	Ignored	88	
	No	8	88.9%
	Yes	1	11.1%
	Not applicable	3	
Palliative hormone therapy (n = 10; 10%)	Ignored	88	
	No	6	60%
	Yes	4	40%
	Not applicable	3	
Palliative hormone therapy - when: (n = 4; 4%)	Ignored	87	
	Before surgery	2	50%
	After surgery	2	50%
	Not applicable	95	
	Ignored	1	

FA, forequarter amputation.

Supplemental Table 6 Follow-Up Times (Continuous Variables).

Category	Variable	N	Total	N	Healing Intention	N	Palliative Intention
Follow-up time since FA – curative intention	Mean	10	37.3 ± 43.1 mo	10	37.3 ± 43.1 mo		
Time from FA to local recurrence	Mean	18	9.1 ± 24.1 mo	6	19.7 ± 41.7 mo	7	4.8 ± 3.7 mo
Time from FA to locoregional recurrence	Mean	12	8.4 ± 10.7 mo	7	6.5 ± 8.0 mo	4	12.2 ± 16.3 mo
Time from FA to distant recurrence	Mean	19	9.1 ± 8.2 mo	5	22.0 ± 7.6 mo	7	8.5 ± 6.6 mo
Time from FA to death or loss to follow-up	Mean	85	23.9 ± 30.8 mo	38	29.6 ± 36.6 mo	32	18.5 ± 27.5 mo
Time from diagnosis to death or loss to follow-up	Mean	54	128.7 ± 82.0 mo	25	149.8 ± 92.7 mo	23	99.3 ± 66.3 mo

FA, forequarter amputation.

Supplemental Table 3 Features Related to Stewart & Treves Syndrome and Radio-Induced Sarcoma

Category	Variable	N	Valid %
Stewart & Treves syndrome	Yes	47	47%
	No	53	53%
Diagnosis	Clinical	0	
	Biopsy	47	100%
	Not applicable	53	
Time from primary treatment to lymphedema (n = 17; 17%)	Mean	4.0 ± 5.7 y	
Time from surgery to STS (n = 31, 31%)	Mean	15.8 ± 18.9 y	
Time from lymphedema to diagnosis of STS (n = 20, 20%)	Mean	13.7 ± 23.5 y	
Time from onset of symptoms to indication of FA (n = 13, 13%)	Mean	5.4 ± 5.4 mo	
Radio-induced sarcoma	Yes	14	14%
	Absent	86	86%
Diagnosis	Clinical	0	
	Biopsy	14	100%
	Not applicable	86	
Histology	Fibrosarcoma	3	21.4%
	Malignant fibrous histiocytoma	2	14.4%
	Osteosarcoma	1	7.1%
	Other	1	7.1%
	Ignored	7	50%
Margins	Not applicable	86	
	Ignored	14	100%
	Not applicable	86	
Time from primary diagnosis to RIS (n = 6.6%)	Mean	9.0 ± 4.1 y	
Time from radiotherapy to RIS (n = 2.2%)	Mean	6.5 ± 6.4 y	
Time from symptom onset to FA (n = 2; 2%)	Mean	10.0 ± 4.2 mo	

SST: Stewart & Treves Syndrome; RIS: radioinduced sarcoma; FA: forequarter amputation

Supplementary Table 4 Characteristics of the Patients at the Time of Forequarter Amputation Indication

Category	Variable	N	Valid %
Local recurrence (n = 65; 65%)	Yes	31	47.7%
	No	34	52.3%
	Ignored	35	
Breast (n = 20; 20%)	Yes	6	30%
	No	14	70%
	Not applicable	35	
Axilla (n = 28; 28%)	Yes	28	100%
	No	0	0%
	Not applicable	34	
Breast and axilla (n = 12; 12%)	Yes	3	25%
	No	9	75%
	Not applicable	42	
Others (n = 16; 16%)	Yes	2	12.5%
	No	14	87.5%
	Not applicable	36	
Locoregional recurrence (n = 55; 55%)	Yes	17	30.9%
	No	38	69.1%
	Ignored	45	
Supraclavicular region (n = 10; 10%)	Yes	4	40%
	No	6	60%
	Not applicable	39	
Infraclavicular region (n = 10; 10%)	Yes	5	50%
	No	5	50%
	Not applicable	39	
Chest wall (n = 13; 13%)	Yes	12	92.3%
	No	1	7.7%
	Not applicable	39	
Back (n = 6; 6%)	Yes	1	16.7%
	No	5	83.3%
	Not applicable	39	
Contralateral breast (n = 7.7%)	Yes	1	14.3%
	No	6	85.7%
	Not applicable	39	
Contralateral axilla (n = 9.9%)	Yes	2	22.2%
	No	7	77.8%
	Not applicable	52	
Distant metastasis (n = 66; 66%)	Yes	16	24.3%
	No	50	75.7%
	Ignored	34	

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Forequarter Amputation for Breast Cancer

Supplementary Table 4 (continued)

Category	Variable	N	Valid %
Bone (n = 9; 9%)	Yes	2	22.2%
	No	7	77.8%
	Not applicable	50	
	Ignored	41	
Lung (n = 13; 13%)	Yes	5	38.5%
	No	8	61.5%
	Not applicable	50	
	Ignored	37	
Liver (n = 9; 9%)	Yes	0	
	No	9	100%
	Not applicable	50	
	Ignored	41	
Central nervous system (n = 10; 10%)	Yes	1	10%
	No	9	90%
	Not applicable	50	
	Ignored	40	
Other sites in the distance (n = 9; 9%)	Yes	6	66.7%
	No	3	33.3%
	Not applicable	50	
	Ignored	41	
Response to pretreatment (n = 93; 93%)	No prior treatment	4	4.3%
	Stable disease	4	4.3%
	Disease progression	24	25.8%
	Not applicable	1	1.0%
	2nd primary (STS or RIS)	60	64.5%
	Ignored	7	
Edema (n = 61; 61%)	Yes	54	88.5%
	No	7	11.5%
	Ignored	39	
Breast ulcer (n = 34; 34%)	Yes	7	20.6%
	No	27	79.4%
	Not applicable	3	
Axillary ulcer (n = 40; 40%)	Yes	24	60%
	No	16	40%
	Ignored	60	
Fixed metastasis in axilla (n = 28; 28%)	Yes	13	46.4%
	No	15	53.6%
	Ignored	72	
Brachial plexopathy (n = 28; 28%)	Yes	18	64.3%
	No	10	35.7%
	Ignored	72	
Fixed shoulder joint (n = 20; 20%)	Yes	4	20%
	No	16	80%
	Ignored	80	
Dysfunctional upper limb (n = 40; 40%)	Yes	33	82.5%
	No	7	17.5%
	Ignored	60	
Pain (n = 46; 46%)	Yes	41	89.1%
	No	5	10.9%
	Ignored	54	

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Supplementary Table 4 (continued)

Category	Variable	N	Valid %
Infection (n = 19; 19%)	Yes	4	21.1%
	No	15	78.9%
	Ignored	81	
Axillary tumor mass (n = 34; 34%)	Yes	23	67.6%
	No	11	32.4%
	Ignored	66	
Wound dressings (n = 24; 24%)	Yes	11	45.8%
	No	13	54.2%
	Ignored	76	
Bleeding (n = 28; 28%)	Yes	15	53.6%
	No	13	46.4%
	Ignored	72	
Fungal infection (n = 19; 19%)	Yes	4	21.1%
	No	15	78.9%
	Ignored	81	
Necrosis (n = 18; 18%)	Yes	3	16.7%
	No	15	83.3%
	Ignored	82	
Blisters (n = 17; 17%)	Yes	1	5.9%
	No	16	94.1%
	Ignored	83	

FA, forequarter amputation; STS, Stewart & Treves Syndrome; RIS, radio-induced sarcoma.

Supplemental Table 5 Follow-Up After Forequarter Amputation

Category	Variable	N	Valid %
Recurrence (n = 83; 83%)	Yes	52	62.6%
	No	31	37.4%
	Ignored	17	
Local recurrence (n = 66; 66%)	Yes	22	33.3%
	No	44	66.7%
	Ignored	34	
Axilla (n = 2; 2%)	Yes	2	100%
	Not applicable	44	
	Ignored	54	
Breast and axilla (n = 1; 1%)	Yes	1	100%
	Not applicable	44	
	Ignored	55	
Others (n = 3; 3%)	Yes	3	100%
	Not applicable	44	
	Ignored	53	
Locoregional recurrence (n = 62; 62%)	Yes	14	22.6%
	No	48	77.4%
	Ignored	38	
Supraclavicular region (n = 0)	Not applicable	48	
	Ignored	52	

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Forequarter Amputation for Breast Cancer

Supplemental Table 5 (continued)

Infraclavicular region (n = 1; 1%)	Yes	1	100%
	Not applicable	48	
	Ignored	51	
Chest wall (n = 12; 12%)	Yes	12	100%
	Not applicable	48	
	Ignored	40	
Back (n = 2; 2%)	Yes	2	100%
	Not applicable	48	
	Ignored	50	
Opposite breast (n = 1; 1%)	Yes	1	100%
	Not applicable	48	
	Ignored	51	
Opposite axilla (n = 1; 1%)	Yes	1	100%
	Not applicable	48	
	Ignored	51	
Distant metastasis (n = 74; 74%)	Yes	37	50%
	No	37	50%
	Ignored	26	
Bone (n = 1; 1%)	Yes	1	100%
	Not applicable	37	
	Ignored	62	
Lung (n = 13; 13%)	Yes	13	100%
	Not applicable	37	
	Ignored	50	
Liver (n = 0)	Not applicable	37	
	Ignored	63	
Central nervous system (n = 4; 4%)	Yes	4	100%
	Not applicable	37	
	Ignored	58	
Other sites of distant metastasis (n = 1; 1%)	Yes	1	100%
	Not applicable	37	
	Ignored	62	
Follow-up time since FA (n = 10; 10%)	Mean	35.0 ± 41.6 months	
Time from FA to local recurrence (n = 18; 18%)	Mean	9.1 ± 24.1 months	
Time from FA to locoregional recurrence (n = 12; 12%)	Mean	8.4 ± 10.7 months	
Time from FA to distant recurrence (n = 19; 19%)	Mean	9.1 ± 8.2 months	
Time from FA to death or loss to follow-up (n = 85; 85%)	Mean	24.6 ± 31.1 months	
Time from diagnosis to death or loss to follow-up (n = 54; 54%)	Mean	128.7 ± 82.0 months	
Patient's condition in the last report (n = 95; 95%)	Death from neoplasia	43	45.3%
	Alive without disease	33	34.7%
	Death from associated disease	4	4.2%
	Unspecified death	4	4.2%
	Alive with recurrence	3	3.1%
	Loss to follow-up	3	3.1%
	Other	5	5.3%
	Ignored	5	

FA, forequarter amputation.

Supplemental Table 7 Points to Be Addressed in Future Studies**Points to Be Addressed in Future Studies**

Standardization of data included in reports and case series
Highlight the treatment performed by each patient in the case series
To assess the quality of life of patients undergoing forequarter amputation through validated quality of life questionnaires
Standardize the reports of time from diagnosis and intervention to outcome
Grouping of data collected from reports and case series
Preparation of a protocol for systematic review of case reports and case series

Supplemental Table 8 Data to Be Included in Systematic Reviews With Reports or Case Series.**Data From Reports or Case Series to be Included in Systematic Reviews**

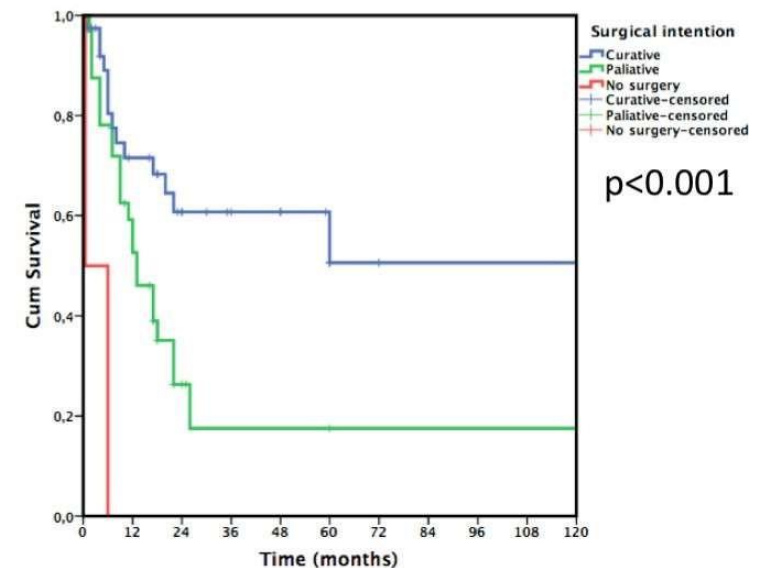
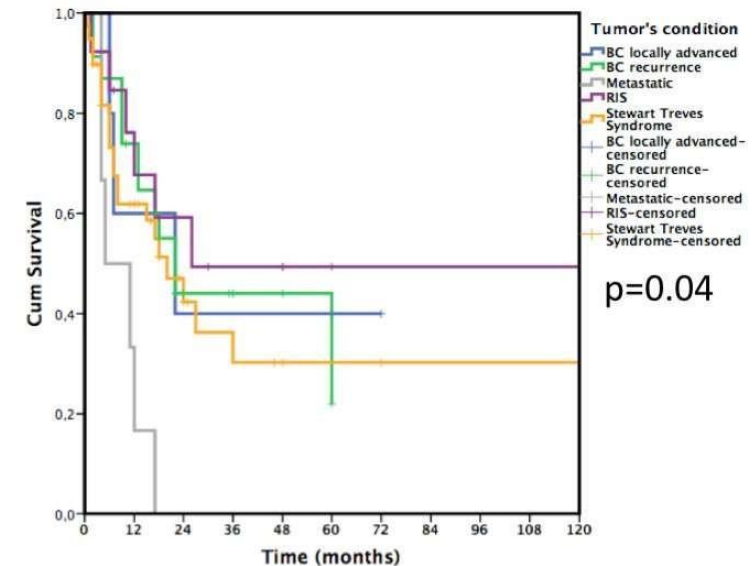
Patient identification: gender, age, comorbidities
Symptoms and clinical information
Diagnosis and staging, if applicable
Main diagnostic methods performed and their results
Interventions or therapies performed and their types
Outcomes of therapies
Complications and/or difficulties of interventions
Prognosis
Impact of the intervention on quality of life
Total follow-up time
Follow-up time from main intervention to outcomes
Patient's status at the last report

Apêndice 5. Graphical Abstract

Forequarter amputation for breast cancer

Present: Case reports and case series
Median 1.8 cases per study
Unknown prognostic factors

Current Study: Systematic review; 9 databases
PRISMA statement
54 articles; 100 cases



Main surgical indications:

Radio-induced Sarcoma, Stewart Treves Syndrome,
Recurrent disease, locally advanced breast cancer,
metastatic disease

Follow up after FA

- Overall: 23.9 ± 30.8 months;
- Curative intention: 29.6 ± 36.6 months
- Palliative intention: 18.5 ± 27.5 months
- No surgery: 3.3 ± 3.0 months

Prognostic factors: surgical indication;
surgical intention (main)

Apêndice 6. Publicação de Capítulo de Livro

ONCOPLASTIA E RECONSTRUÇÃO MAMÁRIA

2ª edição

Clécio Ênio Murta de Lucena
Régis Resende Paulinelli
José Luiz Pedrini
Cícero de Andrade Urban
Maurício de Aquino Resende



Sociedade Brasileira de
Mastologia

 **Medbook**



Desarticulação Interescapulotorácica

Flávia Cardoso Franca

Idam de Oliveira-Júnior

René Aloísio da Costa Vieira

INTRODUÇÃO

As cirurgias para ressecção de tumores localmente avançados com margens adequadas podem implicar extensas ressecções de pele e de músculos da parede torácica, entre outras estruturas, originando grandes defeitos e a necessidade de estratégias para fechamento^{1,2}. As principais são as rotações de retalhos locais dermogordurosos, fasciocutâneos ou retalhos miocutâneos, a depender do tamanho do defeito e da experiência e preferência da equipe cirúrgica^{1,2}. Uma das cirurgias realizadas em tumores avançados é a desarticulação interescapulotorácica (DIET), que consiste na ressecção do membro superior, clavícula e escápula e está indicada para ressecção de tumores primários ou metastáticos das cinturas escapulares que invadem o feixe neurovascular axilar.

A DIET é uma amputação descrita para tratamento, paliativo ou curativo, de tumores ósseos, sarcomas de partes moles e melanoma, bem como em situações benignas, como osteomielites e grandes ferimentos. A primeira publicação encontrada na literatura inglesa sobre a DIET em pacientes com câncer de mama data de 1956, apresentando duas pacientes portadoras de neoplasia recorrente após tratamento primário, com edema, dor, tumoração axilar e perda de funcionalidade do membro superior ipsilateral à cirurgia³. No entanto, é possível encontrar relatos na literatura de que o primeiro autor a conceber a DIET para tratamento de alguns casos avançados de câncer de mama foi um brasileiro, Antonio Prudente, de São Paulo, que realizou a primeira cirurgia em 1933⁴.

Prudente defendeu a DIET associada à mastectomia radical para tratamento de casos selecionados, como metástases fixas de linfonodos axilares, grande linfedema do membro superior ipsilateral ao câncer, membro superior disfuncional secundário a comprometimento local pelo câncer e de paciente com bom *status* nutricional e risco cirúrgico adequado³. Segundo Prudente, as contraindicações à DIET incluíam as pacientes com câncer de mama localmente avançado e metástases à distância disseminadas, com envolvimento profundo de estruturas torácicas, como arcos costais, que impossibilitassem a ressecção tumoral completa e adequada, e metástases fixas em linfonodos supraclaviculares com invasão do feixe neurovascular na base do pescoço⁴. Outras indicações estariam associadas a tumores primários localmente avançados ou recorrentes com invasão do plexo braquial, cavo axilar ou braço, síndrome de Stewart-Treves (SST) e sarcoma radioinduzido (SRI)⁵. Com a implementação das estratégias de rastreamento mamográfico, implicando diagnósticos mais precoces, e as mudanças na radioterapia, além de novos tratamentos sistêmicos, possibilitando melhor controle local da doença, tem sido observada a redução dos casos com indicação para DIET⁵.

SELEÇÃO DAS PACIENTES

A cirurgia é indicada em casos de tumores que evoluem com ulceração, radionecrose, tumoração fixa em axila, com extensão para vasos sanguíneos e/ou plexo braquial, dor intratável ou membro superior ipsilateral com linfedema e/ou sem função, geralmente aplicada a pacientes com *status* nutricional de razoável a bom e

como último recurso após tratamento padrão com cirurgia local, tratamento sistêmico e radioterapia^{6,7}. Além disso, é indicada para tratamento de sarcomas primários, na SST, em sarcomas pós-mastectomia e linfedema.

Quanto ao câncer de mama, observam-se descrições associadas à ressecção primária em tumor localmente avançado⁸, ressecção de doença recorrente⁹⁻¹², associada à plexopatia braquial¹², SST^{13,14} ou sarcoma secundário à radiação pelo câncer de mama^{15,16} e doença metastática óssea¹⁷. Na histologia após ressecção tumoral pela DIET, observa-se a presença de carcinomas^{12,18} e tumor *phylloides* maligno¹⁹, além de SRI como o angiossarcoma¹³, o fibrossarcoma e o condrossarcoma¹⁶. Para os casos de câncer de mama localmente avançados, a cirurgia pode ser curativa, porém na maioria das vezes é realizada com objetivo paliativo⁴.

Em 1948, Stewart e Treves publicaram seis casos de linfangiossarcoma em pacientes que evoluíram com linfedema de membro superior ipsilateral para mastectomia radical modificada secundária a câncer de mama e dois foram submetidos à DIET²⁰. Posteriormente, em 1952, a doença foi denominada síndrome de Stewart-Treves e foi sugerido que a amputação radical precoce (p. ex., a DIET) fosse indicada assim que estabelecido o diagnóstico²¹. Desde então, são encontradas várias descrições de casos de SST submetidos à DIET, tanto no contexto paliativo como curativo, com sobrevida global e sobrevida livre de doença variáveis¹³.

Em pacientes com câncer de mama, a radioterapia está associada a aumento do risco de desenvolvimento de uma segunda neoplasia não mamária, como o SRI²² ou sarcoma ósseo. Apesar da histologia agressiva, a DIET torna possível o controle locorregional, sendo descrito o caso de uma paciente com sobrevida de 4 anos, evidenciando que essa cirurgia pode ser útil no contexto das neoplasias radioinduzidas após tratamento do câncer de mama^{15,16}, apesar de ser um evento raro.

Em séries de pacientes submetidas à DIET, a associação ao câncer de mama representa cerca de 12,5% das causas²³, com maior representação (37,5%) quando se considera a DIET em pacientes com doença metastática²⁴, sendo a doença recorrente sua principal indicação^{9-11,24}, e em caráter paliativo^{10,12}. A literatura sobre o tema é limitada, observando-se apenas dois casos descritos na literatura latino-americana: uma paciente com câncer de mama que evoluiu com metástase óssea e necessidade de DIET para tratamento de fratura patológica ou para preveni-la²⁵ e uma paciente com câncer de mama localmente avançado com recorrência no cavo axilar ipsilateral (Figuras 59.1 e 59.2)¹⁸. Outras descri-

ções relacionadas com o câncer de mama são observadas quando se avaliam os casos de reconstrução da parede torácica^{19,26}.

Apesar de seu aspecto radical, a cirurgia promove controle locorregional, melhora dos sintomas, aumento do intervalo livre de doença e melhora da qualidade de vida, o que justifica sua realização em casos selecionados, tanto com intenção curativa como paliativa^{9,10,12}. Da mesma maneira, em pacientes com plexopatia braquial, envolvimento neurovascular da axila e disfunção do membro superior, é um procedimento a ser considerado¹².

▮ TÉCNICA

Como sucintamente apresentado nas Figuras 59.1 e 59.2, para realização da DIET é feita uma incisão na inserção do músculo esternocleidomastóideo na clavícula, estendida lateralmente ao longo de sua superfície anterior, dividida em Y na altura do acrômio. A incisão continua anteriormente no sulco deltopeitoral, sobre o músculo peitoral até a axila, e posteriormente ao longo da porção medial da escápula, até se juntar à incisão anterior no ângulo escapular. A clavícula é totalmente exposta para possibilitar a visualização do eixo neurovascular, sendo dividida lateralmente à inserção do músculo esternocleidomastóideo e então desarticulada do acrômio e do esterno.

O músculo peitoral maior é dividido no nível do peitoral menor. Os músculos peitoral menor, coracobraquial e bíceps são liberados de suas inserções para completar a exposição do eixo neurovascular. A veia e artéria subclávias e o plexo braquial são isolados e ligados. Os músculos romboides maior e menor são divididos de suas inserções escapulares, permitindo a elevação da escápula para dividir os músculos trapézio, elevador da escápula e latíssimo do dorso. O músculo serrátil anterior é liberado de sua inserção escapular. O membro superior é então removido em bloco. Quando há suspeita de acometimento tumoral de arcos costais, é possível removê-los em bloco com a peça cirúrgica mediante secção dos arcos costais acometidos. Drenos são posicionados, e um retalho miocutâneo vascularizado é usado para fechamento⁹.

Em pacientes portadoras do câncer de mama, Prudente descreveu a técnica para remoção do membro superior em bloco com a mama. A incisão começa na borda interna do músculo deltoide, passa pelo sulco deltopeitoral e se estende pela clavícula até sua articulação com o esterno. A partir desse ponto, a incisão circunda a mama, descendo a partir de sua borda medial, passando

pela inferior e ascendendo pela margem lateral da mama, cruzando a parede lateral torácica em direção à borda medial do músculo grande dorsal. A incisão continua superior e diagonalmente em direção à borda posterior do músculo deltoide, circundando-o até seu início.

A desarticulação da clavícula é realizada no esterno e na escápula. O músculo subclávio é seccionado e há a exposição do plexo braquial e da artéria e veia subclávias, que são ligados e seccionados. A mama é excisada em bloco, em conjunto com os músculos peitoral maior e menor. Linfadenectomia dos níveis I, II e III é realizada, bem como a ressecção dos nervos torácico longo e subescapular. O membro superior é rotacionado anteriormente, os músculos posteriores do úmero e da escápula são seccionados da parede torácica, e um retalho cutâneo a partir da região deltoide é confeccionado para ser utilizado como fechamento. Após essas etapas, é realizada a DIET em continuidade com a dissecação da fossa supraclavicular⁴.

Exibimos um caso de DIET previamente publicado pelos autores¹⁸ em paciente portadora de neoplasia mamária com comorbidades, que apresentou recorrência

do tumor mamário no cavo axilar (Figura 59.1A e B), tornando necessária a DIET para promover controle locorregional. Exemplificamos partes da cirurgia, como a desinserção da escápula (Figura 59.1C), o descolamento da clavícula (Figura 59.1D), a ressecção da peça (Figura 59.2A), o fechamento primário (Figura 59.2B) e o resultado final (Figura 59.2C).

COMPLICAÇÕES

Na DIET clássica, a taxa de complicação é relativamente baixa e geralmente associada a necrose de pele, deiscência local e derrame pleural⁹⁻¹². Essas complicações são limitadas e não impactam negativamente o resultado pós-operatório¹⁰. No entanto, por se tratar de cirurgia de grande porte, a possibilidade de importante perda sanguínea, complicações locais, como infecções, e tromboembolismo pulmonar deve ser considerada e incluída na comunicação com a paciente e no manejo perioperatório¹².

Um dos principais pontos a considerar diz respeito ao fechamento da área ressecada, o qual pode ser realizado por meio de enxertos cutâneos, aproveitamento de parte

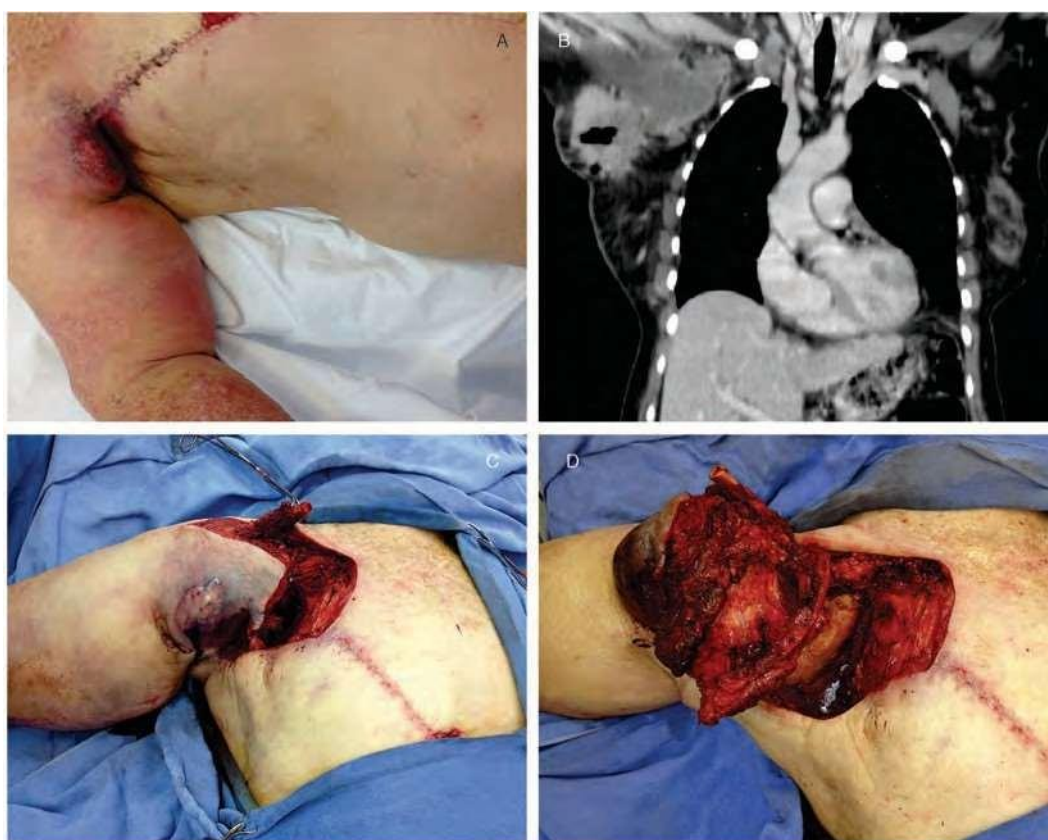


Figura 59.1 Paciente submetida a desarticulação interescapulotorácica por recorrência no cavo axilar. **A** Aspecto clínico. **B** Tomografia. **C** Desinserção da clavícula. **D** Descolamento da escápula.



Figura 59.2 Desarticação interescapulotorácica. Resultado após ressecção do membro. A e B Cirurgia. C Pós-operatório.

da pele do membro e rotação de retalhos miocutâneos^{8-10,12}. Entre as complicações relatadas estão necrose de retalho ou de sua borda e cicatrização demorada.

Algumas complicações tardias são inerentes às amputações e relatadas nas descrições de casos de pacientes com câncer de mama submetidas à DIET, como dor fantasma e necessidade de reabilitação das pacientes devido à ausência do membro. No entanto, com o auxílio de uma equipe multidisciplinar, elas podem ser manejadas adequadamente, de modo a contribuir para a melhora da qualidade de vida dessas pacientes¹².

► RECORRÊNCIA E SOBREVIDA

Uma série de casos mostrou que a sobrevida é maior quando a intenção da DIET é curativa – média de 23 meses –, diminuindo para 13 meses nos casos paliativos, tanto para controle de sintomas como para pacientes com doença sistêmica¹⁰.

A maioria das desarticulações interescapulotorácicas descritas para tratamento do câncer de mama é indicada para casos de recorrência local e/ou locorregional, principalmente axilar^{9,10,12}. No câncer de mama recorrente, a DIET pode ser curativa, na ausência de metástases à dis-

tância, ou paliativa e indicada para alívio dos sintomas locais, como dor não controlada, ulceração, odor fétido, infecções recorrentes, ulceração com necessidade de troca de curativos, sangramento, edema em membro superior, paralisia e/ou perda de funcionalidade do membro superior ipsilateral²⁶, ou para evitar esses desconfortos, visando ao controle local e à sobrevida livre de doença¹⁰.

Pundi e cols., em uma série de casos levantados na literatura, relatam sobrevida média de $23,4 \pm 14,6$ meses para as pacientes com câncer de mama recorrente que foram submetidas à DIET com intenção curativa¹⁰. Os casos levantados por Goodman apresentaram sobrevida de 22 a 48 meses⁹. As pacientes com recorrência axilar de câncer de mama que evoluíram com plexopatia braquial por extensão local da doença, sem evidência de doença à distância, apresentaram sobrevida global de 13 a 22 meses e sobrevida livre de progressão de 2 a 9 meses¹².

No contexto paliativo, a sobrevida varia de 4 a 22 meses nos casos de doença recorrente e de 4 a 60 meses nos de doença metastática⁹, e a sobrevida média é de aproximadamente 13 meses¹⁰. São encontradas sobrevida livre de progressão de 6 semanas e sobrevida global de 4 a 17 meses devido à evolução da doença^{10,24,26}.

Existe pequeno risco de SRI em pacientes com câncer de mama tratadas com radioterapia²⁷. A cirurgia é indicada de acordo com a extensão da doença e a possibilidade de ressecção completa, e a opção pela amputação pode promover a cura. A cirurgia também torna possível diminuir os desconfortos da invasão local do SRI, geralmente localizados no ombro, nas regiões supra e infraclaviculares e na escápula²⁸. A sobrevida global de pacientes com SRI após tratamento de câncer de mama submetidas à DIET é de 12 a 24 meses, com óbito em razão de metástases pulmonares^{29,30}. Em uma série de sete casos de SRI após radioterapia por câncer de mama tratados com DIET, todos ressecados com margens macroscopicamente livres, cinco pacientes estavam vivos, com sobrevida de 18 a 60 meses após o diagnóstico do segundo tumor primário, e duas evoluíram para óbito por metástases em 6 e 17 meses após o diagnóstico. Nenhuma paciente viva evoluiu com recorrência local, porém uma apresentou metástases pulmonares²⁸. Portanto, a DIET é uma opção para paliar sintomas e, em casos específicos, até mesmo curar pacientes selecionadas com SRI²⁹.

Para tratamento da SST, a DIET é descrita desde 1948, quando Stewart e Treves publicaram a série de seis casos que deu nome à síndrome²⁰. Em uma série de oito casos de pacientes com SST submetidas à DIET, a sobrevida livre de progressão local variou de 1 a 27 meses, e duas pacientes não apresentaram recorrência local. A sobrevida global variou de 2 a 72 meses, com relato de uma paciente viva sem evidência de doença por 6 anos³¹. Quatro casos de mulheres com SST tratadas com DIET, vivas e sem evidência de doença, sobreviveram por 3, 16, 23 e 135 meses, respectivamente³². Definir a extensão do linfangiossarcoma pode ser difícil, e a DIET pode ser uma opção para ressecção cirúrgica completa com margens negativas³¹.

Apesar da cirurgia extensa e das variáveis sobrevidas livre de doença e global, a DIET apresenta poucas complicações e elevado sucesso na atenuação dos sintomas, tanto nos casos com intenção curativa como paliativa^{9,12,24}, melhorando a qualidade de vida¹⁸. Logo, a cirurgia é plenamente justificada em casos selecionados, como tumores localmente avançados, infiltração de estruturas axilares, linfedema de membro superior importante com perda de função, SST e SRI, muitas vezes representando a principal possibilidade de controle local da doença e melhora da sobrevida dessas pacientes³³.

CONSIDERAÇÕES FINAIS

A DIET, mesmo se tratando de uma amputação e consequentemente de uma cirurgia desfigurante, tem valor no arsenal cirúrgico para manejo da paciente com

câncer de mama, apresentando poucas complicações, as quais, quando presentes, são pouco mórbidas e têm pequeno impacto na condução subsequente da neoplasia⁹. Além disso, o procedimento possibilita alívio da dor e do desconforto causados pelo membro superior edemaciado e tumorações axilares infiltrando o feixe neurovascular e/ou ulceradas, melhorando a qualidade de vida¹⁸.

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