UNIVERSITÉ DU QUÉBEC À TROIS-RIVIÈRES

LES APPROCHES CONSERVATRICES UTILISÉES DANS LA RÉADAPTATION PHYSIQUE DES PATIENTES ATTEINTES D'UN CANCER DU SEIN DEVANT SUBIR OU AYANT SUBI UNE MASTECTOMIE : UNE REVUE INTÉGRATIVE DE LA LITTÉRATURE

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RÉSUMÉ

Introduction : La mastectomie est l'approche thérapeutique utilisée en première instance pour plus de 90 % des patientes atteintes d'un cancer du sein. Les répercussions physiques associées à cette procédure chirurgicale sont nombreuses, affectant négativement la qualité de vie de ces femmes. Malgré de récentes études soutenant l'efficacité des interventions de réadaptation pour réduire les déficits fonctionnels de l'épaule causés par la mastectomie, les établissements affiliés au Centre intégré universitaire de santé et de services sociaux de la Mauricie-et-du-Centre-du-Québec (CIUSSS-MCQ) offrent des ressources limitées en matière de réadaptation périchirurgicale pour cette population. Afin de favoriser le développement d'interventions dont les modalités répondront aux besoins de ces patientes et refléteront les particularités du continuum de soins spécifique au cancer du sein, il est nécessaire d'établir un portrait global des stratégies de réadaptation et des mesures de résultats cliniques ayant déjà été utilisées pour cette population.

Objectif : (1) Identifier et décrire les interventions conservatrices et les mesures de résultats cliniques utilisées pour la réadaptation physique des femmes atteintes d'un cancer du sein devant subir ou ayant subi une mastectomie. (2) Rendre compte des barrières et des facteurs ayant facilité l'engagement à ces programmes de réadaptation.

Méthodologie : Une revue intégrative de la littérature a été réalisée, comprenant une recherche systématique dans les bases de données pertinentes, de leur création jusqu'à janvier 2021. Nous avons inclus les études publiées en anglais et en français, dans des journaux révisés par les pairs, correspondant à des devis quantitatifs, et décrivant des interventions conservatrices et des mesures de résultats cliniques utilisées pour la

réadaptation physique des femmes atteintes d'un cancer du sein de bas grade (0-III), ayant subi ou devant subir une mastectomie. Deux évaluateurs ont indépendamment passé en revue tous les articles en utilisant un processus de sélection en deux étapes. Les données extraites des études éligibles ont fait l'objet d'une analyse descriptive.

Résultats : Cette stratégie de recherche a permis d'identifier 5605 articles et 12 articles ont été trouvés de sources supplémentaires. Des 46 études éligibles, 60.9% des interventions identifiées étaient multimodales et comprenaient toutes des exercices, combinées à l'éducation aux patientes (45.7%), à la thérapie manuelle (23.9%) ou au drainage lymphatique (17.4%). La majorité des interventions ont été initiées après la chirurgie (84.8%) et d'abord réalisées sous supervision en milieu hospitalier (45.7%). Les mesures objectives de la fonction physique les plus fréquemment utilisées ont été l'amplitude de mouvement de l'épaule, la force musculaire et les signes de lymphœdème, tandis que la qualité de vie, la fonction du membre supérieur et la douleur ont représenté les principales mesures de résultats rapportées par les patientes (PROMS). La majorité des études éligibles n'ont pas décrit les raisons ayant influencé l'engagement et l'observance thérapeutique des participantes. La survenue d'une autre chirurgie mammaire, le décès et la récidive du cancer furent les principaux motifs justifiant l'abandon des participantes.

Conclusion : Cette revue intégrative de la littérature fait état de l'hétérogénéité et du nombre important d'interventions conservatrices et de mesures des résultats cliniques utilisées dans la réadaptation physique des patientes atteintes d'un cancer du sein. Les interventions multimodales supervisées, combinant l'exercice avec l'éducation du patient,

le drainage lymphatique ou la thérapie manuelle ont été les plus fréquemment étudiées. Ces interventions ont majoritairement été initiées après la chirurgie. Des études supplémentaires sont nécessaires afin d'identifier les obstacles et les facteurs motivant ces patientes à s'engager et à compléter une intervention de réadaptation. Il serait également d'intérêt de s'attarder aux besoins et aux attentes des femmes atteintes d'un cancer du sein, notamment dans la phase préopératoire.

Mots clés *: Cancer du sein, Mastectomie, Réadaptation, Mesures de résultats*

ABSTRACT

Background: Mastectomy represents the first-line treatment approach for more than 90% of breast cancer patients. Physical impairments associated with this surgical procedure are numerous, which negatively impacts the patient's quality of life. Despite evidence supporting the benefits of rehabilitation interventions to reduce shoulder functional deficits in women undergoing mastectomy, there are limited rehabilitation resources available for this population within the institutions affiliated to the Centre intégré universitaire de santé et de services sociaux de la Mauricie-et-du-Centre du Québec (CIUSSS-MCQ). To promote the development of interventions whose modalities will meet patients' needs and reflect the particularities of breast cancer care pathways, we must first establish a comprehensive portrait of rehabilitation strategies and clinical outcome measures that have already been used for this population.

Objective: (1) Identify and describe the conservative interventions and the clinical outcome measures used as part of the perioperative physical rehabilitation of women with breast cancer who are awaiting or have undergone mastectomy; (2) Report on the barriers and facilitators to participation and completion of these rehabilitation programs.

Methods: A scoping review was conducted, which included systematic searches of relevant databases from database inception to January 2021. We included peer-reviewed English and French literature with quantitative designs, describing conservative interventions and clinical outcome measures used within rehabilitation programs designed for women who were awaiting or had undergone mastectomy. Paired reviewers

independently reviewed all citations and articles using a two-phase screening process. Data extracted from eligible studies were descriptively reported.

Results: The literature search yielded 5605 articles and 12 additional articles were retrieved from other data sources. Of the 46 eligible studies, most interventions were multimodal (60.9%), which combined exercise with one or more of the following: [1] patient education (45.7%); [2] manual therapy (23.9%); or [3] lymphatic drainage (17.4%). Rehabilitation programs were initiated a few days following surgery (84.8%) and performed under supervision until hospital discharge (45.7%). Objective measures of physical function most frequently used were shoulder range of motion, muscle strength and signs of lymphedema, whereas quality of life, shoulder function and pain were the primary patient-reported outcome measures. Most studies did not discuss study compliance and reasons to decline research participation. Undergoing another breast surgery, death, and cancer recurrence were the most reported barriers to study completion.

Conclusion: This scoping review reports on the heterogeneity and wide range of conservative interventions and clinical outcome measures used in physical rehabilitation for breast cancer patients who had undergone or were scheduled to undergo mastectomy. Supervised multimodal interventions combining exercise with patient education, lymphatic drainage, or manual therapy were the most frequently reported. These interventions were predominantly initiated following breast surgery. Further research is needed to identify barriers and facilitators to study participation and completion, as well as breast cancer patients' needs and expectations, particularly in the preoperative period.

Keywords: *Breast cancer, Mastectomy, Rehabilitation, Outcome Measures*

TABLE DES MATIÈRES

LISTE DES TABLEAUX

LISTE DES FIGURES

LISTE DES ABRÉVIATIONS

ACS: American Cancer Society

AJCC: American Joint Committee on Cancer

ASTRO: American Society of Radiation Oncology

ASCO: American Society of Clinical Oncology

AVD : Activités de la vie domestique

AVQ : Activités de la vie quotidienne

CCM: Chirurgie conservatrice mammaire

CIF : Classification internationale du fonctionnement, du handicap et de de la santé

ER : Récepteur(s) oestrogénique(s)

ERAS: Enhanced Recovery After Surgery

GMI: Ganglions mammaires internes

HER-2 : Récepteur 2 du facteur de croissance épidermique humain

IMC : Indice de masse corporelle

INSPQ : Institut national de santé publique du Québec

IRM : Imagerie par résonnance magnétique

OMS : Organisation mondiale de la santé

PQDCS : Programme québécois de dépistage du cancer du sein

PR : Récepteur(s) de progestérone

PROMS: Patient reported outcome measures

PRT: Progressive resistance training

SSO: Society of Surgical Oncology

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INTRODUCTION

Le cancer du sein est la forme de cancer la plus fréquente chez la femme à l'échelle mondiale (1). Au Canada, en moyenne une femme sur huit sera confrontée aux défis d'un tel diagnostic au cours de sa vie (1). Le Québec figure parmi les six provinces canadiennes ayant le plus haut taux d'incidence annuelle du cancer du sein, comptant plus de 115 cas par 100 000 femmes (2). Heureusement, grâce à l'amélioration des techniques de soins et la mise sur pied, en 1998, de programmes organisés de dépistage par mammographie (3), le taux de mortalité lié au cancer du sein enregistre une baisse de 49% depuis son sommet atteint en 1986 (3). Bien que ces femmes puissent désormais bénéficier d'une plus grande espérance de vie, le continuum de soins spécifique au traitement du cancer du sein n'est pas sans conséquence pour ces patientes, alors qu'elles devront notamment se soumettre à une série d'interventions thérapeutiques aux effets physiques, psychologiques et sociaux-économiques considérables (4).

La mastectomie représente l'intervention thérapeutique primaire pour plus de 90% des patientes atteintes d'un cancer du sein (5). Les conséquences physiques découlant de cette procédure chirurgicale sont nombreuses (ex., diminution des amplitudes de mouvement de l'épaule, douleur, lymphœdème et faiblesses musculaires) (6), celles-ci pouvant significativement complexifier la réalisation des activités quotidiennes et diminuer la qualité de vie (7).

Les interventions de réadaptation ayant pour objectif la diminution des effets secondaires de la mastectomie ont fait l'objet de plusieurs études scientifiques, dont la majorité montre qu'une approche multimodale, composée principalement d'exercices et de thérapie physique réduit les déficits fonctionnels de l'épaule en phase post-opératoire. (8, 9). Ces interventions se déclinent toutefois en plusieurs composantes dont les modalités d'exécution (c.-à-d. durée, fréquence, moment d'initiation, etc.) s'avèrent très variables. Dans l'objectif éventuel de développer un programme de réadaptation adapté aux patientes atteintes du cancer du sein subissant une mastectomie, connaitre l'étendue des connaissances actuelles dans ce domaine de recherche s'avère une étape préparatoire essentielle.

Ce mémoire se divise en cinq sections principales. La première consistera en une revue de la littérature, où les différents concepts relatifs à l'épidémiologie, le diagnostic et le traitement du cancer du sein seront définis. Un accent particulier sera également mis sur les répercussions physiques associées à la mastectomie, ainsi que sur la pertinence clinique d'intégrer une stratégie de réadaptation dans la trajectoire de soins des patientes atteintes d'un cancer du sein. Ensuite, la problématique liée à la mise en œuvre d'un programme de réadaptation pour cette population sera décrite et les objectifs de ce projet de recherche seront précisés. Enfin, les dernières sections seront constituées de la présentation de l'article scientifique, suivi de la discussion et de l'interprétation des résultats obtenus, pour conclure sur une description des retombées cliniques et des perspectives de recherche.

CANCER DU SEIN

Épidémiologie

Le cancer du sein est le cancer féminin le plus diagnostiqué à travers le monde (1). Cette maladie se classe au troisième rang de tous les diagnostics de cancer, derrière le cancer du poumon et le cancer du côlon (1). En excluant les cancers de la peau non mélanique, le cancer du sein de la femme possède également le plus haut taux d'incidence parmi les tumeurs malignes (2). Au Canada, cela représente en moyenne une femme sur huit qui devra composer avec les défis d'un tel diagnostic au cours de sa vie (1).

L'équipe de Lagacé et al. (2) s'est intéressée au portrait épidémiologique du cancer du sein, s'attardant plus précisément à l'évolution temporelle des taux d'incidence et de mortalité de ce cancer, et identifiant au passage les caractéristiques démographiques des patientes atteintes. Cette analyse, regroupant des données allant de 1992 à 2010, révèle que les femmes caucasiennes, âgées entre 40 et 79 ans, constituent le groupe le plus touché par cette maladie, totalisant plus de 85% des cas au Canada (2). Le taux d'incidence annuelle du cancer du sein a également connu une hausse significative de 22% au cours de la même période, se chiffrant à 115 cas par 100 000 femmes au Québec (2). Toutefois, cette hausse coïncide avec l'implantation, en 1998, des programmes canadiens de dépistage organisés (3). Heureusement, grâce à l'efficacité de ces programmes et l'amélioration des traitements proposés, le taux de mortalité lié au cancer du sein a été

estimé à 22 pour 100 000 Canadiennes en 2020, soit une baisse de 49% depuis le sommet atteint en 1986 de 43 pour 100 000 (3).

Carcinogenèse et classification des tumeurs

Plusieurs mécanismes distincts expliquent le processus de carcinogenèse affectant les cellules de la glande mammaire. En effet, cette glande est l'hôte de nombreux récepteurs, accueillant pour la plupart des ligands hormonaux (10). Les récepteurs d'œstrogènes (ER) et de progestérone (PR) sont largement exprimés à la surface et au sein du noyau des cellules mammaires (11). Ce faisant, le fonctionnement et le développement des cellules mammaires normales et cancéreuses dépendent étroitement du système endocrinien et évoluent, pour la plupart, en parallèle de la production cyclique des hormones ovariennes et pituitaires (12). Ainsi, en fonction de la réponse physiologique des cellules cancéreuses et le statut des récepteurs hormonaux, la tumeur peut être classifiée «hormono-dépendante» ou «non hormono-dépendante » (12).

Tel qu'illustré dans la figure 1, les variétés de tumeurs malignes affectant la glande mammaire peuvent également être catégorisées selon le type de récepteurs qu'elles expriment ou par la présence de certains biomarqueurs comme le récepteur 2 du facteur de croissance épidermique humain (HER-2) (1).

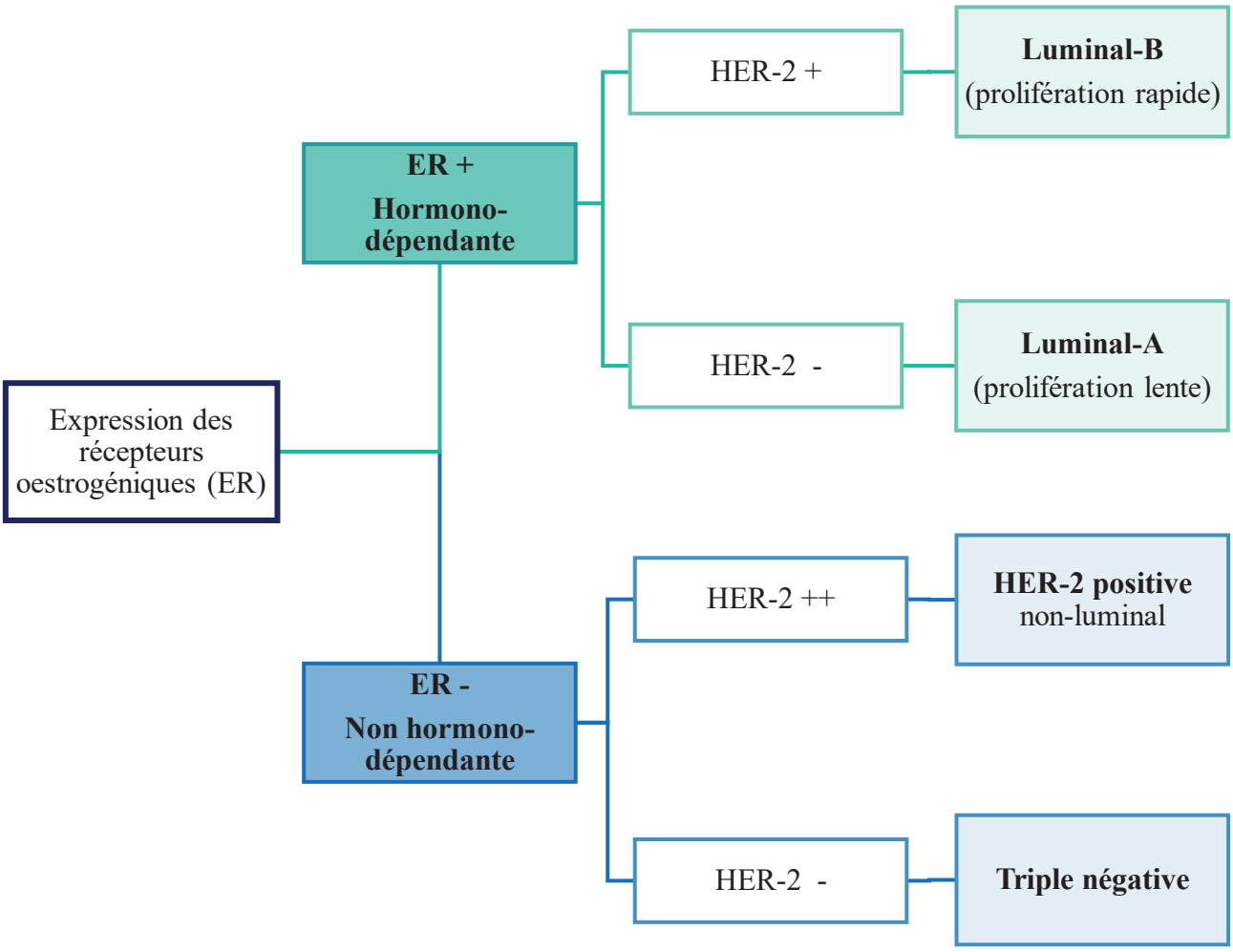


Figure 1: Classification des tumeurs mammaires en fonction de l'expression de récepteurs hormonaux et de biomarqueurs

Adaptée de Senkus et al. (2015)

Ce facteur a notamment un impact sur la vitesse de prolifération de la tumeur (1). Parmi les sous-types de tumeurs malignes affectant la glande mammaire, le cancer du sein «triple négatif» réfère à une tumeur dont le développement n'est pas influencé par l'une ou l'autre

des hormones sexuelles et cette tumeur n'exprime aucun biomarqueur précis (c.-à-d., *ER - / PR- / HER-2 -)* (1).

La classification selon le stade, aussi appelée stadification, représente une autre façon de classifier les tumeurs malignes de la glande mammaire. Le stade de la tumeur est déterminé selon la morphologie de la tumeur primaire, ainsi que par son caractère infiltrant ou non infiltrant (11). Une tumeur non infiltrante est dite «*in situ*», signifiant que les cellules cancéreuses sont circonscrites aux tissus où elles ont initialement pris naissance. Cette tumeur peut toutefois progresser en une tumeur invasive, où les cellules pathologiques peuvent migrer au réseau lymphatique axillaire ou vers le tissu mammaire voisin (11). L'approche *TNM* (tumeur, nodules axillaires, métastases) (13) est l'approche de stadification privilégiée par l'American Joint Committee on Cancer (AJCC) et son utilisation est maintenant répandue mondialement. Les caractéristiques définissant chacun des stades d'un cancer du sein sont détaillées dans le tableau 1.

Tableau 1: Classification des tumeurs mammaires selon leur stade

Adapté de Senkus et al. (2015)

STADE	Critères			
	Sous-classe	**Caractéristiques**	**Implication des nodules axillaires**	**Métastases distales**
0	-	In-situ	Non	Non
I	IA	0-20 mm	Non	Non
	IB	0-20 mm ou absence de T	Mi[a], 1-3 nodules	Non
II	IIA	0-50 mm ou absence de T	M[b] (niveaux I, II) 1-3 nodules	Non
	IIB	20-50 mm	M (I, II), 1-3 nodules	Non
		> 50 mm	Non	
III	IIIA	0-50 mm	M (I, II), 3-9 nodules **ou** Implication des GMI	Non
		> 50 mm	M (I, II) 3-9 nodules **ou** Implication des GMI **et** 1-3 nodules	Non
	IIIB	Extension aux parois thoraciques, à l'exclusion du grand pectoral **et/ou** à la peau	Absence **ou** M (I, II) 3-9 nodules **ou** Implication des GMI **et** 1-3 nodules	Non
	IIIC	Tout type	M (III) > 10 nodules **ou** M (I, II) 3-9 nodules **et** implication des GMI	Non
IV	IV	Tout type	Tout type	Oui

GMI : *Ganglions mammaires internes;* ***M*** *: Métastases;* ***Mi*** *: Micrométastases;* ***mm :*** *millimètres;* ***T*** *: Tumeur primaire*

[a]***Mi*** *: 0,2-2,0 mm de diamètre;* [b]***M*** *: > 2,0 mm de diamètre*

Facteurs de risque

Non modifiables

Le cancer du sein résulte de l'interaction entre plusieurs facteurs de risque, ceux-ci pouvant être scindés en deux catégories distinctes (2). Les facteurs de risque non

modifiables, associés aux changements physiologiques et aux caractéristiques génétiques d'un individu, expliquent plus des deux tiers des diagnostics de cancer du sein (12). Ces facteurs sont intimement liés aux variations hormonales dictant le développement normal de la femme (10). L'âge avancé et le sexe féminin sont les facteurs de risque non modifiables les plus fortement associés à l'incidence du cancer du sein (10). Alors qu'une augmentation du risque au début de la quatrième décennie s'explique par un plus haut niveau d'hormones sexuelles circulant, c'est plutôt l'exposition prolongée à ces hormones qui justifie la hausse de ce risque chez les ainées (10). Ainsi, la puberté précoce, la ménopause tardive, l'absence de grossesse ou une grossesse à un âge avancé sont toutes des facteurs de risque appartenant à cette catégorie (10, 14). Pour les mêmes raisons, une augmentation de la sécrétion de l'hormone de croissance par l'hypophyse antérieure favorise aussi la prolifération des cellules mammaires cancéreuses (12).

D'autre part, le cancer du sein peut être la conséquence d'une mutation génétique affectant les gènes régulateurs de la prolifération des cellules mammaires, *BRCA1* et *BRCA2* (15). Une femme portant cette mutation a un risque 60% plus élevé d'être diagnostiquée d'un cancer du sein au cours de sa vie (16). Enfin, il existe une association positive entre le taux d'incidence du cancer du sein et l'histoire familiale de la patiente (15). Une femme dont un parent du premier degré a reçu un diagnostic de cancer du sein double son risque d'en être elle aussi atteinte au cours de sa vie (17).

Modifiables

Certains facteurs de risque sont dits modifiables, puisqu'ils relèvent des habitudes de vie et des habitudes de consommation d'un individu (16). Il est estimé qu'entre 25 à 33% des diagnostics de cancer du sein sont attribuables à des facteurs modifiables (2). Parmi ces facteurs, un indice de masse corporelle (IMC) indicateur d'obésité (>30 kg/m^2) et l'hyperinsulinémie ont tous deux une association positive avec le taux d'incidence du cancer du sein, chez les femmes post-ménopausées (10, 16). Un faible niveau d'activité physique, la consommation d'alcool quotidienne (>10 g ou plus d'un verre), le tabagisme et l'exposition à la fumée secondaire ou aux radiations ionisantes font également partie de cette catégorie (16). L'hormonothérapie substitutive chez les femmes post-ménopausées et la prise de contraceptifs oraux qui contiennent de l'œstrogène ou de la progestérone contribuent également à hausser ce risque (18).

Dépistage et diagnostic du cancer du sein

Le dépistage du cancer du sein repose principalement sur deux outils cliniques. Le premier, l'examen clinique des seins sera conduit à la suite de la localisation d'une masse palpable ou en présence d'un sein douloureux (5). La mammographie est le second outil diagnostique utilisé dans le dépistage du cancer du sein (5). Instauré en 1998 par le ministère de la Santé et des Services sociaux du Québec, le programme québécois de dépistage du cancer du sein (PQDCS) a permis une réduction significative des taux de

mortalité associés au cancer du sein au cours des vingt dernières années (19, 20), en recommandant un suivi par mammographie tous les deux ans chez les femmes âgées de 50 à 69 ans sans risque accru de cancer du sein (ex., absence d'historique familial ou personnel de cancer du sein ou d'une mutation génétique du gène BRCA1 ou BRCA2) (5).

Les lignes directrices du groupe d'étude canadien sur les soins de santé préventifs réitèrent cette recommandation, en plus d'encourager le dépistage par mammographie biennal chez les femmes âgées de 70 à 74 ans (21). Le dépistage par mammographie n'est pas recommandé pour les femmes âgées entre 30 à 49 ans puisqu'elles présentent notamment un risque absolu plus faible et une probabilité plus grande d'obtenir des résultats faussement positifs, pouvant entre autres mener au surdiagnostic et à des interventions subséquentes inappropriées (21). Les femmes âgées de 30 ans et plus présentant un risque plus élevé de cancer du sein font toutefois partie d'une catégorie distincte pour laquelle la mammographie peut être recommandée annuellement, de manière isolée ou combinée à l'imagerie par résonnance magnétique (IRM) de la glande mammaire (22, 23). L'IRM mammaire annuelle est l'examen privilégié chez les femmes âgées entre 25 à 29 ans porteuses d'une mutation génétique (23).

L'analyse par biopsie est également nécessaire pour obtenir le portrait pathologique et clinique complet de la tumeur mammaire (1). Cet examen, réalisé avant l'initiation de toute approche thérapeutique, est d'abord effectué au site où la tumeur primaire a pris

naissance, afin d'en déterminer le statut pathologique (6). Ce statut pathologique sera défini par l'identification des caractéristiques histologiques de la tumeur, ainsi que par la détermination de son stade et l'expression de certains récepteurs et biomarqueurs (c.-à-d., ER, PR, HER-2, Ki67) (6)

Biopsie et dissection des ganglions axillaires

La région mammaire est entourée d'un réseau de ganglions lymphatiques, disposés de part et d'autre de la clavicule, ainsi qu'à la région axillaire. À l'aspect médial du sein, les ganglions mammaires internes (GMI) s'alignent en périphérie du sternum (11). Les ganglions lymphatiques axillaires forment une chaine entourant le muscle petit pectoral et peuvent être scindés en trois niveaux distincts (voir figure 2). Les ganglions lymphatiques situés à la région axillaire inférieure forment le premier niveau de la chaine, lieu où la lymphe sera initialement drainée. Les ganglions de la région axillaire centrale et supérieure (niveau II et III) recueilleront ensuite la lymphe et complèteront le drainage. En principe, les ganglions des niveaux supérieurs (II et III) sont considérés indemnes en l'absence de cellules tumorales répertoriées au niveau inférieur (I) (11).

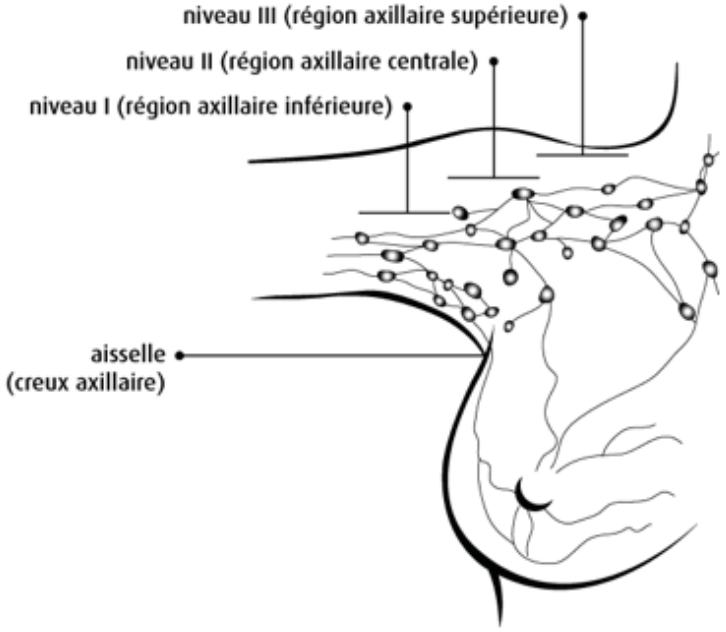


Figure 2: Ganglions axillaires et propagation des cellules cancéreuses

Tirée de la Société canadienne du cancer (11)

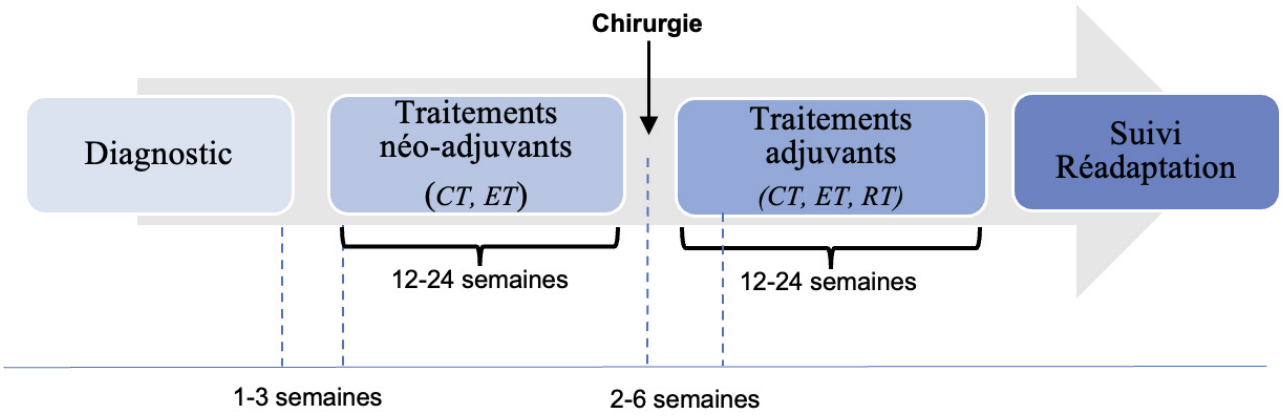
L'analyse par biopsie des ganglions axillaires est réalisée afin de déterminer la présence et l'étendue de la dissémination des cellules cancéreuses. La biopsie ganglionnaire est préférée à la dissection axillaire en première instance, due au caractère invasif de cette dernière. En l'absence de métastases ou en présence de micrométastases (0,2 à 2 mm) à la biopsie, la dissection axillaire n'est pas requise (6, 22). La dissection axillaire partielle ou totale sera toutefois effectuée en présence de métastases plus nombreuses ou si la tumeur possède un haut potentiel de récidive (22). Cette procédure chirurgicale peut s'accompagner de déficits fonctionnels importants au niveau du membre supérieur, tels qu'une diminution des amplitudes de mouvement, du lymphœdème, des paresthésies et

une infection de la plaie. La gravité et la prévalence de ces manifestations cliniques varieront selon les modalités caractérisant la dissection axillaire (ex., résection d'un seul niveau de la chaine ou de plusieurs niveaux) (24).

Traitements du cancer du sein et effets indésirables

Déterminer l'approche thérapeutique appropriée

Il existe une variété d'interventions disponibles ciblant la destruction des cellules mammaires malignes. Celles-ci peuvent être scindées en trois catégories distinctes, selon leur moment d'administration. Un traitement est dit néoadjuvant lorsqu'il précède le traitement principal (5, 6). Dans le continuum de soins d'une patiente atteinte d'un cancer du sein, le traitement néoadjuvant, si indiqué, sera administré avant la chirurgie. Cette approche pré-chirurgicale a pour objectif la modification de la morphologie de la tumeur primaire afin de permettre l'utilisation d'une approche chirurgicale moins invasive (5, 6). D'autre part, le traitement adjuvant sera administré après la chirurgie, dans le but d'éliminer toutes traces de cellules malignes et ainsi réduire le potentiel de récidive (5). La radiothérapie, la thérapie endocrine ainsi que la chimiothérapie sont toutes des modalités thérapeutiques pouvant faire l'objet d'un traitement néoadjuvant ou adjuvant (6). La figure 3 illustre le continuum de soins spécifique au cancer du sein. Les délais entre le diagnostic et le début des traitements néoadjuvants, et entre la chirurgie et l'initiation des traitements adjuvants peuvent varier selon les particularités du milieu de soins.



CT : Chimiothérapie, ET : Thérapie endocrine, RT : Radiothérapie

Figure 3: Séquence des interventions associées au traitement du cancer du sein

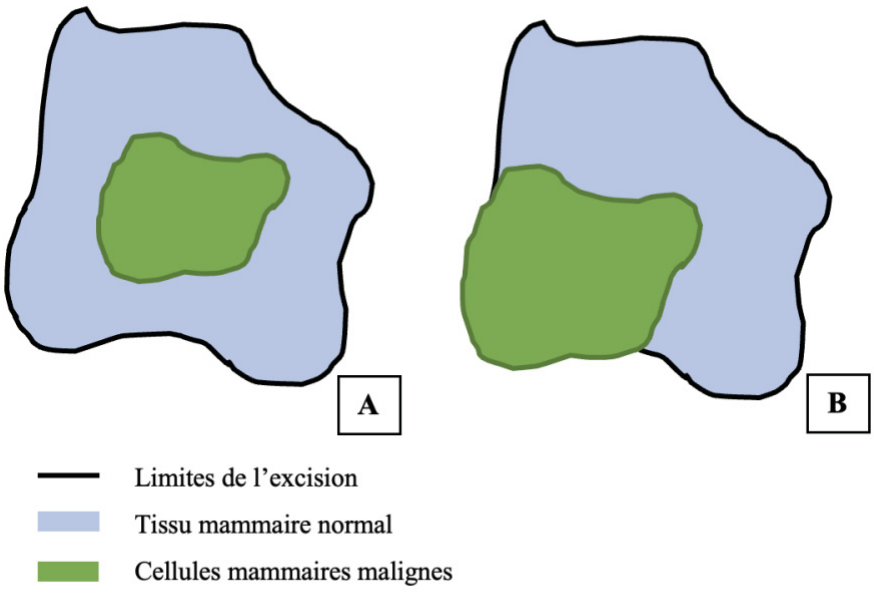
Le choix de l'une ou de plusieurs de ces interventions sera influencé par de multiples facteurs, tels l'âge de la patiente, son statut hormonal, les caractéristiques histologiques et la taille de la tumeur, la présence de facteurs génétiques ou d'un potentiel de récidive, ainsi que l'état de santé général de la patiente (25). Le stade de la tumeur (voir tableau 1) représente un référentiel décisionnel important, celui-ci étant étroitement associé au pronostic de la patiente. En effet, des données publiées en 2011 par l'Institut national de santé publique du Québec (INSPQ) indique que la survie relative à 5 ans des patientes atteintes d'un cancer du sein de bas grade, I ou II, est de respectivement 97,5% et 87,9%, alors que celle-ci chute à 10,5% pour les patientes souffrant d'un cancer du sein de stade IV. L'expression des récepteurs hormonaux influencera également la thérapie privilégiée. Par exemple, seules les tumeurs dites hormono-positives répondront favorablement à la

thérapie endocrine (6). Certains types de tumeurs nécessiteront aussi la tenue d'un protocole de chimiothérapie néoadjuvante (6). Ainsi, cette procédure offre une opportunité clinique intéressante pour la mise en place d'une stratégie de soins préopératoire. Enfin, le choix définitif de la stratégie de soins devra également prendre en considération les préférences et les objectifs des patientes (6).

Intervention chirurgicale

La chirurgie mammaire est l'intervention thérapeutique primaire pour la majorité des patientes atteintes d'un cancer du sein (5). D'une part, la chirurgie conservatrice mammaire (CCM), aussi définie sous le terme *mastectomie partielle*, est la procédure chirurgicale initialement recommandée dans les contextes cliniques suivants : [1] en présence d'une tumeur non infiltrante de taille inférieure à 20 mm chez des patientes à faible risque de récidive et [2] en présence d'une tumeur invasive de bas grade (0, I, II) (6, 26). La CCM consiste en l'excision de la tumeur primaire et d'une marge de tissu sain périphérique (26). L'obtention de marges chirurgicales saines, aussi dites négatives (voir figure 4), caractérisée par l'absence de cellules mammaires malignes en périphérie de la tumeur excisée, est nécessaire au succès de cette approche. En effet, en présence de marges chirurgicales positives, le risque de récidive ipsilatérale est doublé, et ce, même si des traitements succèdent à la chirurgie (26).

Les lignes directrices de *l'American Society for Radiation Oncology* (ASTRO) et de la *Society of Surgical Oncology* (SSO) recommandent que la CCM soit combinée à un régime de radiothérapie post-opératoire, principalement chez les patientes souffrant d'une tumeur invasive de grade I ou II ou d'un carcinome *in situ* à haut potentiel de récidive (c.-à-d., tumeur de taille importante, inhabilité à obtenir des marches chirurgicales saines, âge avancé) (26, 27). Cette combinaison thérapeutique est de plus en plus préférée à la mastectomie totale, puisqu'elle affiche un taux de récidive comparable à la mastectomie (26), tout en minimisant les répercussions physiques et cosmétiques post-chirurgicales (28).

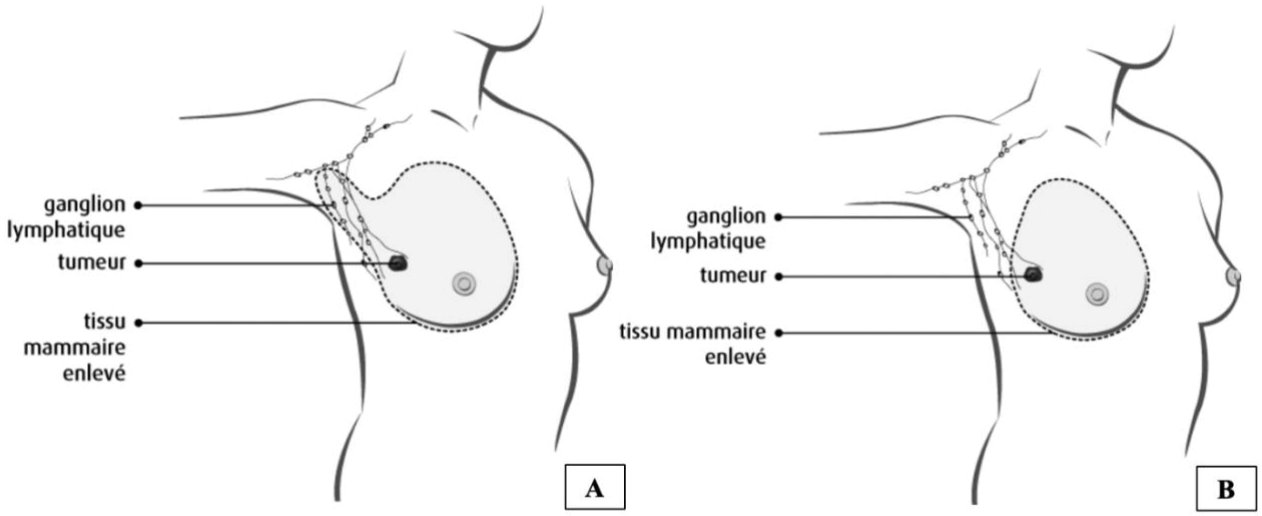


A : Marges chirurgicales négatives (saines); **B** Marges chirurgicales positives

Figure 4 : Statut des marges chirurgicales

Adaptée de Lee et al. (2012)

D’autre part, en l’absence des critères énoncés ci-haut, la mastectomie totale (c.-à-d., résection complète du sein) sera la procédure chirurgicale indiquée (6). En présence d’une mutation génétique, conférant un risque de récidive controlatéral de 25%, certaines patientes peuvent également envisager la mastectomie préventive, soit la résection du sein, en l’absence de cellules mammaires malignes répertoriées (6). De plus, même si elles sont éligibles à l’approche conservatrice, certaines patientes vont tout de même choisir de recourir à la mastectomie totale. Néanmoins, les dernières données relatives à cette pratique et datant des années 2000 révèlent qu’un peu moins de 30% des Québécoises souffrant d’un cancer du sein invasif de grade I ou II ont eu recourt à la mastectomie totale (19). Il existe plusieurs types de mastectomie totale, chacune de ces techniques ayant considérablement évolué au cours des dernières années (28). Selon les caractéristiques de la tumeur, sa localisation et son potentiel de récidive, la mastectomie simple ou radicale-modifiée pourront être réalisées (voir figure 5). Celles-ci ont pour points communs la résection du tissu mammaire et épithélial périphérique, ainsi que le fascia des muscles pectoraux. Le réseau neurovasculaire composé du nerf thoracique long, du nerf thoraco-dorsal, ainsi que des veines et artères thoraco-dorsales est en général épargné, bien qu’à risque de résection (28). La conservation de l’enveloppe cutanée, de l’aréole et du mamelon peut également être envisagée dans certaines situations.



A : Mastectomie radicale-modifiée ; **B** : Mastectomie simple

Figure 5: Types de mastectomie

Adaptée de la Société canadienne du cancer (2021)

Ce type de chirurgie conservatrice permet une approche chirurgicale moins invasive, se caractérisant généralement par une incision plus locale, aux abords de l'aréole ou du mamelon (28). Les différents types de chirurgie mammaire ainsi que leurs principales indications cliniques sont résumés dans le tableau 2.

Tableau 2: Les différents types de mastectomie totale et leurs indications cliniques

Informations tirées de Jones et al. (28)

Type de mastectomie	Caractéristiques distinctives	Indications cliniques
Mastectomie radicale-modifiée	• Résection de la glande mammaire, incluant : NAC, peau, fascia des muscles pectoraux • Dissection des ganglions axillaires (I, II) • Préservation du muscle pectoral majeur (et mineur lorsque possible)	• Tumeur localement avancée avec dissémination aux ganglions lymphatiques • Cancer inflammatoire du sein (IIIB)
Mastectomie simple	• Résection de la glande mammaire, incluant : NAC, peau, fascia des muscles pectoraux • Préservation des ganglions axillaires • Préservation du muscle pectoral majeur et mineur	• Tumeur invasive sans implication des ganglions axillaires
Mastectomie avec conservation de l'enveloppe cutanée	• Résection de la glande mammaire, incluant : NAC, fascia des muscles pectoraux • Préservation de l'enveloppe cutanée • Préservation ou dissection des ganglions axillaires	• Tumeur invasive intra-ductal • Carcinome ductal *in situ* ou tumeur invasive, ne correspondant pas aux critères de la chirurgie conservatrice mammaire
Mastectomie avec conservation du complexe aréolo-mamelonnaire (NAC)	• Résection de la glande mammaire, incluant le fascia des muscles pectoraux • Préservation du NAC • Préservation de l'enveloppe cutanée	• Tumeur suffisamment en périphérie du NAC • Absence d'implication de la peau

Les déficits fonctionnels associés à la mastectomie

La mastectomie, qu'elle soit partielle ou totale, implique des effets secondaires importants, notamment la diminution des amplitudes de mouvement, une augmentation de la douleur, du lymphœdème et des faiblesses musculaires considérables, causant une diminution des capacités fonctionnelles de l'épaule (7). L'Organisation mondiale de la

Santé (OMS) utilise la Classification internationale du fonctionnement, du handicap et de de la santé (CIF) pour définir les composantes nécessaires au fonctionnement des individus (voir figure 6). Selon ce cadre théorique, l'état de fonctionnement humain est le résultat de l'interaction dynamique entre l'état de santé d'un individu et plusieurs facteurs contextuels (c.-à-d. facteurs personnels et environnementaux) (29). Ainsi, un problème de santé, une maladie, un traumatisme ou une blessure qui vient troubler l'équilibre entre ces composantes laisse place à un *handicap*, plus communément appelé *incapacité* (29). En d'autres termes, la CIF reconnait qu'un individu étant atteint d'un trouble de santé peut souffrir d'une incapacité sous sa forme physique, mais que celle-ci peut également s'étendre sur les plans psychologique, social et économique (29). Les travaux de l'OMS ont également permis l'élaboration de listes sélectives de mesures de résultats cliniques destinées à évaluer les besoins particuliers des patients souffrant de pathologies spécifiques (29). Aussi appelées *ICF Core Sets*, ces listes sont le résultat d'une recherche systématique et d'un consensus d'experts ayant permis d'identifier le large spectre de limitations attribuables à diverses conditions de santé.

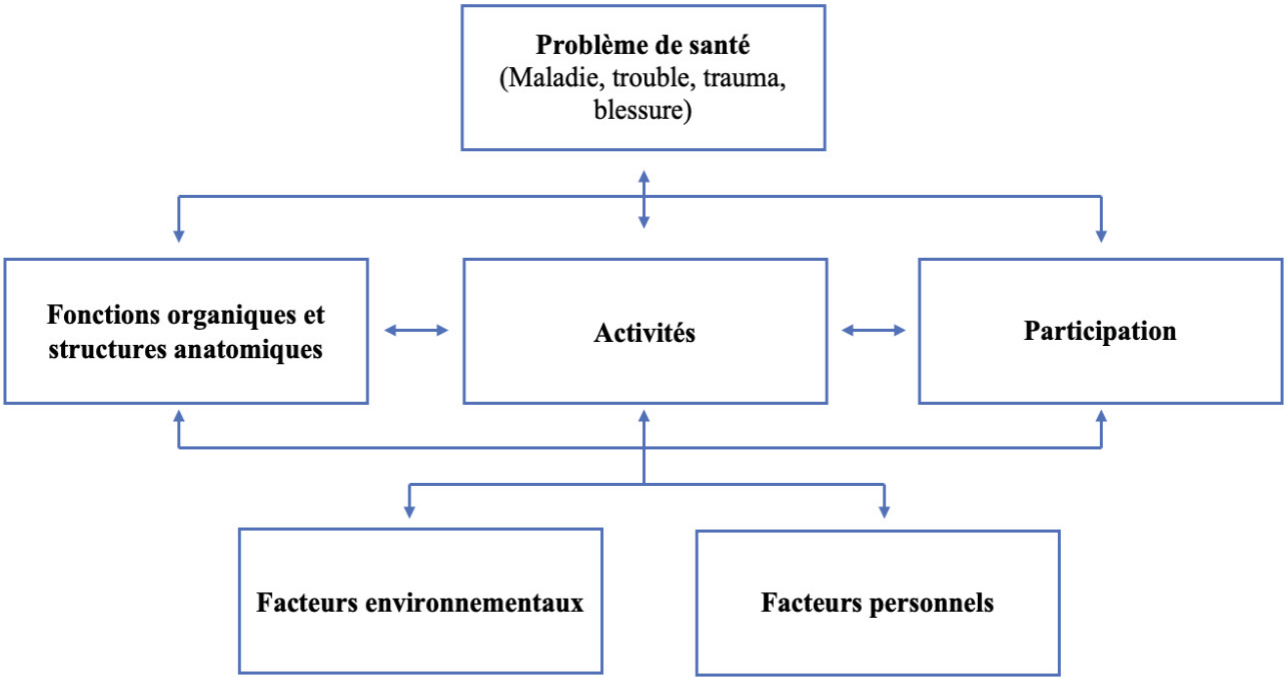


Figure 6 : Classification internationale du fonctionnement, du handicap et de la santé (CIF)

Adaptée de Stucki, 2005

Le tableau 3 présente le *Bref ICF Core Set* développé spécifiquement pour les patientes atteintes d'un cancer du sein. En plus des déficits fonctionnels de l'épaule mentionnés précédemment, les difficultés de sommeil, la fatigue et les troubles émotionnels et des fonctions sexuelles sont communément rencontrés chez les patientes subissant cette intervention chirurgicale (30). Ce déclin fonctionnel des structures anatomiques et de divers systèmes du corps peut également affecter la capacité de ces femmes à effectuer des activités de la vie quotidienne, telles les soins personnels, la réalisation des tâches ménagères ou le soulèvement d'objets (30).

Tableau 3: Description des composantes du Brief ICF Core Set développé pour les patientes atteintes d'un cancer du sein

Adapté de Brach et al., 2004

Composantes de la CIF	Catégories	Exemples
Fonctions organiques	Fonctions de l'énergie et des pulsions	Niveau d'énergie, motivation, appétit, besoins de consommer
	Fonctions du sommeil	Quantité et qualité de sommeil, insomnie, hypersomnie
	Fonctions émotionnelles	Pertinence de l'émotion, maîtrise des émotions, labilité de l'émotion
	Expérience de soi-même et fonctions du temps	Prise de conscience de sa propre identité et de son corps, de son image
	Sensation de douleur	-
	Fonctions du système immunitaire	Réponse immunitaire, fonction des vaisseaux et ganglions lymphatiques
	Fonctions sexuelles	Fonctions mentales et physiques associées à l'acte sexuel et à l'intérêt sexuel
	Mobilité de l'articulation	-
Structures anatomiques	Structures du système immunitaire	-
	Structures de l'appareil reproducteur	-
	Structures associées aux articulations des épaules	-
Activités et participation	Effectuer la routine quotidienne	Planifier, gérer, s'acquitter des tâches quotidiennes, gérer son temps, gérer son niveau d'activité
	Gérer le stress et autres exigences psychologiques	Gestion du stress, assumer ses responsabilités, gestion des distractions
	Soulever et porter des objets	-
	Utilisation des mains et des bras	Tirer et pousser des objets, chercher à prendre, tordre, lancer, attraper
	Faire le ménage	-
	Relations familiales	Relations parents-enfants, avec les frères et sœurs et la famille élargie
	Relations intimes	Relations amoureuses, maritales ou sexuelles
	Emploi rémunéré	S'investir dans les aspects d'un travail à temps partiel ou à temps complet
Facteurs environnementaux	Produits et systèmes techniques à usage personnel dans la vie quotidienne	Aides techniques à usage personnel
	Présence/disponibilité de membres de la famille proche et leurs attitudes individuelles	Conjoints, partenaires, parents, frères et sœurs, enfants

	Présence/disponibilité d'amis et leurs attitudes individuelles	-
	Présence/disponibilité de professionnels de la santé et leurs attitudes individuelles	-
	Services, systèmes et politiques relatifs à la sécurité sociale	Services, systèmes et politiques visant à assurer un revenu
	Services, systèmes et politiques relatifs à la santé	Services, systèmes et politiques visant à prévenir et traiter les problèmes de santé, assurer la réadaptation médicale et promouvoir des modes de vie sains.
	Services, systèmes et politiques relatifs au travail et à l'emploi	Services, systèmes et politiques relatifs à la mise au travail pour les personnes qui sont à la recherche d'un emploi ou voudraient en changer, ou pour appuyer les personnes ayant déjà un travail

Ces patientes peuvent également rencontrer certains défis lors de la participation aux activités sociales, comme des difficultés lors du retour au travail, dans les relations interpersonnelles et lorsqu'elles sont appelées à gérer une situation stressante (30). Enfin, l'accès aux services de santé et de transport, l'implication des membres de la famille et les défis relatifs à l'image corporelle et à l'estime de soi complètent la liste des enjeux majeurs auxquels pourront faire face les femmes atteintes d'un cancer du sein à la suite d'une mastectomie (30).

Traitements adjuvants et néoadjuvants

En plus de subir les répercussions de l'intervention chirurgicale, une patiente atteinte d'un cancer doit fréquemment se soumettre à une série de traitements adjuvants ou néoadjuvants. Les critères pouvant guider la sélection de la thérapie adjuvante ou néoadjuvante appropriée sont résumés dans le tableau 4.

Tableau 4: Choix de la thérapie adjuvante ou néoadjuvante appropriée en fonction des caractéristiques de la tumeur primaire

Adapté de Senkus et al. 2015

Traitement	Critères/Situation clinique appropriée
Radiothérapie	**a)** Obligatoire à la suite d'une CCM **b)** Post-mastectomie totale ou en séquence avec la CT si : • Implication des nodules axillaires **et/ou** • Tumeur de haut grade (III, IV) **et/ou** • Haut risque de récidive (diagnostic en bas âge, luminal-B HER-2)
Thérapie endocrine	*Seule* : **c)** Tumeur luminal-A (ER +/ HER-2-) de bas grade **d)** Tumeur luminal-B (ER +/ HER-2 -) faible prolifération *En combinaison* : **e)** Tumeur luminal-B (ER+/HER-2-) haute prolifération **c) ou d)** avec implication des nodules axillaires
Chimiothérapie adjuvante (CT)	**f)** Tumeur triple négative ou HER-2+, ne répondant pas aux critères de la NA **et/ou** **g)** Implication des nodules axillaires **et/ou** **h)** Tumeur de haut grade (III, IV) ou à haut risque
Chimiothérapie néoadjuvante (NA)	**i)** Tumeur triple négative ou HER-2 + ou tumeur > 20 mm unifocale **j)** Tumeur triple négative ou HER-2 +, avec un ratio tumeur/sein élevé **k)** Tumeur localement avancé, avec extension à la cage thoracique **l)** Cancer du sein de type inflammatoire

Radiothérapie

Tel qu'énoncé précédemment, les lignes directrices de l'ASTRO et de la SSO recommandent que la CCM soit combinée à un régime de radiothérapie post-opératoire (26). La radiothérapie peut également être effectuée à la suite d'une mastectomie totale ou avant l'intervention chirurgicale, dans le but de réduire la taille de la tumeur à exciser. Les caractéristiques du régime de radiation peuvent différer par l'étendue de la région irradiée (ex. région mammaire entière ou partielle, région axillaire ou cage thoracique), le dosage du régime (conventionnel ou hypofractionné), ainsi que par la technique utilisée.

Les recommandations de l'ASTRO varient en fonction de plusieurs paramètres, dont le stade de la tumeur, la dissémination des cellules cancéreuses aux nodules axillaires et au réseau vasculaire à proximité, ainsi qu'en fonction du niveau de risque de récidive (27). Chez les patientes subissant une CCM, la radiothérapie hypofractionnée du sein complet, sans implication de la région axillaire, est l'approche recommandée. Le régime est administré par séquence, aussi dite par «fraction», généralement à raison d'une dose par jour. Contrairement aux régimes conventionnels, les régimes hypofractionnés se caractérisent par un nombre inférieur de fractions, dont les dosages sont toutefois plus élevés. Les fractions sont généralement administrées à raison de cinq jours par semaine, sur une durée moyenne de 3 à 4 semaines (22, 27). Un complément de radiation, effectué localement au site d'excision de la tumeur, peut également être ajouté à ce régime en présence de facteurs de risque défavorables tels un jeune âge au moment du diagnostic (< 50 ans), un stade histologique élevé (III, IV) chez des patientes âgées entre 51 et 70 ans ou en présence de marges chirurgicales positives (voir figure 4) (22). Ces mêmes facteurs de risque dicteront la nécessité de débuter un protocole de radiothérapie après une mastectomie totale (30). Étant administrée d'emblée après la mastectomie chez les patientes à haut risque de récidive, la radiothérapie fait également partie du protocole de soins chez les patientes dont la tumeur s'est disséminée aux ganglions axillaires, si celles-ci n'ont pas subi de dissection axillaire auparavant (22). Bien qu'efficace et sécuritaire, la radiothérapie peut être associée à de multiples effets secondaires locaux et systémiques, tels des irritations cutanées, une diminution des amplitudes de mouvement de l'épaule et une augmentation de l'intensité de la douleur. Les effets secondaires

musculosquelettiques peuvent également être amplifiés par les particularités ergonomiques requises lors de l'administration de la radiothérapie, soit le maintien prolongé de l'épaule dans une position contraignante (c.-à-d. en abduction et rotation externe). (31)

Thérapie endocrine

La thérapie endocrine, soit l'administration orale de bloqueurs hormonaux, peut être utilisée seule ou combinée à la chimiothérapie, principalement à la suite d'une chirurgie mammaire (1). Seuls les cancers hormono-positifs de bas grades sont susceptibles de générer une réponse pathologique complète et favorable à cette thérapie (1). Le choix de la molécule utilisée est réalisé en fonction du statut hormonal de la patiente (6). Ainsi, le tamoxifène sera privilégié chez les femmes préménopausées, alors que les inhibiteurs de l'aromatase seront généralement priorisés après la ménopause (1). Chacune de ces thérapies hormonales devra être administrée sur une période de cinq à dix ans (1). En conséquence du profil d'expression étendu des récepteurs hormonaux, les bloqueurs hormonaux peuvent générer des effets secondaires multi-systémiques (32). Les douleurs articulaires, l'atrophie musculaire et l'ostéopénie sont des exemples d'effets secondaires affectant le système musculosquelettique (32).

Chimiothérapie

La chimiothérapie systémique est également une intervention thérapeutique possible dans le contexte périchirurgical. Les patientes porteuses d'une tumeur dite HER-2 positive ou

triple négative sont les plus susceptibles de retirer des bénéfices de cette thérapie (5). La chimiothérapie peut également être indiquée en présence d'une tumeur à dissémination active, de haut grade ou qui ne répond pas adéquatement à la radiothérapie (5). La chimiothérapie adjuvante devrait être débutée au plus tard deux à six semaines après la chirurgie, afin de ne pas diminuer l'efficacité du protocole de soins (5, 6). La chimiothérapie néoadjuvante, effectuée dans un contexte pré-chirurgical (voir figure 3 p.14), peut être indiquée pour un cancer du sein de type inflammatoire ou en présence d'une tumeur de haut diamètre, dans le but d'en réduire la taille et ainsi permettre une chirurgie conservatrice mammaire (5). La chimiothérapie systémique, peu importe son contexte d'utilisation, consiste principalement en l'administration cyclique d'anthracyclines et de taxanes, des inhibiteurs de la fonction cellulaire, sur une période de 12 à 24 semaines. En l'absence d'une réponse pathologique tumorale adéquate dans un contexte pré-chirurgical, cette thérapie sera interrompue en faveur de la chirurgie, et complétée par de la radiothérapie ou de la chimiothérapie adjuvante (33). Bien qu'efficace, la chimiothérapie systémique génère des effets secondaires variés. Critiquée pour ses effets cardiotoxiques, elle contribue également au lymphœdème local, à la diminution de la densité osseuse (34) ainsi qu'à l'augmentation de la fréquence des nausées, à la perte de cheveux, à une fatigue persistante et à la neuropathie périphérique (4).

RÉADAPTATION

De nombreuses études ont été réalisées dans le but de développer des approches favorisant une récupération optimale des patients après une chirurgie, connues sous le nom d'interventions de réadaptation. La Société internationale à but non lucratif ERAS (*Enhanced Recovery After Surgery*) est reconnue depuis plus de 30 ans pour le développement et la mise en œuvre de programmes de réadaptation périopératoires et multidisciplinaires (35). Les programmes ERAS ont pour objectif commun le maintien de l'homéostasie cellulaire, en proposant des stratégies qui visent à minimiser les stress occasionnés par l'intervention chirurgicale et également à améliorer la réponse du corps face à ceux-ci (35). Le maintien de l'homéostasie prévient alors l'activation des mécanismes cataboliques associés à la chirurgie qui contribuent à la perte protéique, à la fonte de la masse musculaire et aux dysfonctions cellulaires (36). Les programmes ERAS engendrent des retombées cliniques positives et non négligeables pour les patients subissant différents types de chirurgie, notamment par le biais d'une diminution de la durée des séjours hospitaliers et des complications postopératoires, ainsi qu'en favorisant un retour plus rapide aux activités de la vie quotidienne (35).

Chirurgie mammaire et l'approche *ERAS*

Les programmes ERAS ont également été étudiés dans un contexte de chirurgie reconstructrice mammaire chez des patientes atteintes d'un cancer du sein (37). Bien que la majorité des programmes offerts se déclinent sous des modalités de nature

pharmacologique (c.-à-d. stratégies de gestion de la consommation d'analgésiques opioïdes et analgésiques non-opioïdes, prévention et traitements des nausées et vomissements, etc.), ceux-ci proposent également un soutien nutritionnel et des recommandations en termes d'activité physique et de retour aux activités normales, notamment en encourageant la mobilisation du membre supérieur peu après la chirurgie. Une méta-analyse publiée en 2018 (37) confirme l'efficacité de l'approche ERAS chez les patientes atteintes d'un cancer du sein ayant subi une chirurgie reconstructrice. Ces programmes ont contribué à réduire de manière significative la consommation d'analgésiques opioïdes et la durée des hospitalisations, sans accentuer les complications post-opératoires chez ces patientes (37).

Autres interventions de réadaptation

Il n'existe à ce jour aucun programme ERAS pour les patientes atteintes d'un cancer du sein subissant la mastectomie comme chirurgie unique. Toutefois, au cours des dernières années, plusieurs études ont cherché à évaluer l'efficacité des interventions de réadaptation pour soutenir les patientes atteintes d'un cancer du sein confrontées aux répercussions physiques de la mastectomie. Une revue systématique publiée en 2015 par De Groef et al. (8), incluant 18 essais contrôlés randomisés, a confirmé l'efficacité d'une thérapie physique multimodale (c.-à-d. des exercices d'étirement combinés à des exercices actifs généraux) pour amoindrir les incapacités du membre supérieur après une mastectomie. Plus récemment, une seconde revue systématique publiée par Ribeiro et al.

(9) a montré l'efficacité des exercices d'amplitude de mouvement et de renforcement du membre supérieur pour améliorer les amplitudes de mouvement de l'épaule chez les patientes atteintes d'un cancer du sein. Il est intéressant de noter que parmi les 15 études contrôlées randomisées incluses dans cette revue, seules neuf d'entre elles ont pris en compte des mesures de résultats autorapportées par les patientes (PROMS) (9). De plus, les interventions de réadaptation identifiées dans cette étude se sont avérées très hétérogènes en termes de durée, de fréquence et d'outils d'évaluation utilisés (9). À titre d'exemple, certaines études ont favorisé une approche de réadaptation débutant quelques heures seulement après la chirurgie, alors que d'autres ont débuté celle-ci après le retrait des drains chirurgicaux, soit quelques semaines après l'intervention chirurgicale.

Bien que les interventions de réadaptation montrent des résultats favorables chez les patientes atteintes d'un cancer du sein subissant une mastectomie, elles ne sont pas pour autant faciles à mettre en œuvre dans un contexte post-chirurgical. En effet, cette période est souvent chargée en émotions pour ces femmes, qui fréquemment se retrouvent en attente d'un autre traitement, subissent les effets secondaires du traitement précédent ou craignent les effets négatifs d'un protocole de remise en forme sur leur guérison (38). Bien qu'important et nécessaire, l'engagement à un protocole de réadaptation peut s'avérer complexe et difficile (38), d'où l'intérêt de s'intéresser également aux stratégies pouvant être mises en place en phase préopératoire.

Préadaptation

Une intervention chirurgicale représente un stress métabolique important pour un individu, se traduisant par une diminution de la masse musculaire, un déséquilibre homéostatique, ainsi qu'un déclin des capacités aérobies (39). Une chirurgie majeure peut réduire de 40% la réserve physiologique d'un individu et ainsi induire un excès de fatigue, des douleurs résiduelles, une perte d'appétit et une perturbation des habitudes de sommeil, et ce, jusqu'à plus de neuf semaines après l'intervention (39). Ainsi, un patient ayant une condition physique et psychologique amoindrie dans un contexte préopératoire s'expose à des complications post-chirurgicales plus importantes et plus fréquentes (40).

Pertinence clinique de la préadaptation

La préadaptation est définie comme toute stratégie mise en place avant une intervention chirurgicale, afin de potentialiser les réserves fonctionnelles du patient et ainsi mieux le préparer aux stress occasionnés par celle-ci (38). Cette stratégie s'appuie sur le principe que chaque individu possède une réserve fonctionnelle limitée, qui peut se voir négativement affectée par de multiples facteurs contextuels, telle une chirurgie (41). Ainsi, afin de maintenir cette réserve à un niveau optimal et donc de minimiser la perte de fonction en période post-opératoire, des efforts devraient être déployés afin d'optimiser cette réserve avant la chirurgie (41). La période préopératoire s'avère également un moment plus opportun pour les patients, puisque ceux-ci disposent généralement de meilleures capacités physiques et émotionnelles (42). Ce contexte offre donc un

environnement plus favorable à la mise en place d'une stratégie de soins, telle la préadaptation (42).

Préadaptation et cancer du sein

Le concept de préadaptation en cancérologie s'inscrit dans un continuum de soins (voir figure 7), se définissant par les interventions physiques et psychologiques posées entre le moment du diagnostic et l'intervention chirurgicale (4). Ces interventions sont introduites dans le but de prévenir d'éventuelles incapacités et de préparer les patients aux défis des traitements invasifs (4). Cette stratégie s'applique d'autant plus en prévention des effets indésirables associés à la mastectomie chez des patientes atteintes d'un cancer du sein (4).

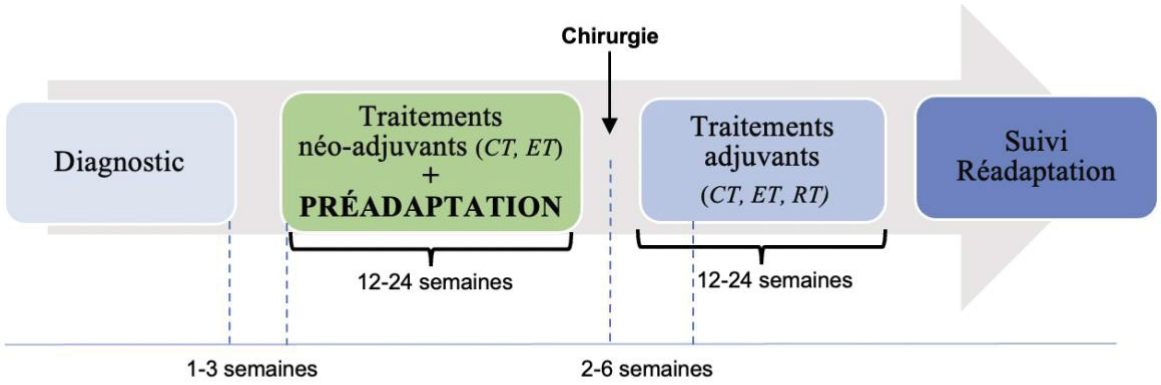


Figure 7: Préadaptation au sein de la stratégie de soins pour les patientes subissant une mastectomie

Telle que présenté par l'équipe de Yang et al. dans une revue systématique publiée en 2018, la pratique d'activité physique régulière et la participation à un programme d'exercices de mobilité et de stabilisation gléno-humérale constituent la pierre angulaire des programmes de préadaptation chez des patientes atteintes d'un cancer du sein devant subir une mastectomie (43). En plus de contrecarrer les effets cardiotoxiques et de favoriser la tolérance à la chimiothérapie par l'optimisation des capacités aérobies, un niveau supérieur d'activité physique préopératoire est associé à une probabilité 85% plus élevée d'avoir une récupération physique complète, trois semaines après la mastectomie (44).

La composante psychologique constitue également un élément important du programme de préadaptation pour les femmes atteintes d'un cancer du sein, puisque ce diagnostic peut provoquer un sentiment d'impuissance, générer de l'anxiété et soulever des inquiétudes existentielles (4). Le soutien psychologique devient alors nécessaire afin que ces patientes puissent assimiler adéquatement l'information partagée et poser un regard éclairé sur le processus de décision clinique auquel elles prendront part (4). Le soutien nutritionnel et la promotion de la cessation tabagique complètent généralement la stratégie de préadaptation chez ces patientes (4) .

PROBLÉMATIQUE DE RECHERCHE

La mise en place en 1998 de programmes organisés de dépistage, parallèlement à l'amélioration des techniques chirurgicales, eurent un impact significatif sur le portrait épidémiologique du cancer du sein au Canada (3). Le dernier rapport de l'INSPQ publié en 2011 appuie cette tendance (19). En effet, plus de 90% des Québécoises atteintes d'un cancer du sein sont maintenant diagnostiquées à un stade précoce de la maladie (3), permettant une prise en charge plus rapide et efficace. Affichant un taux de survie à 5 ans de près de 90% (19), ces femmes devront néanmoins faire face à de multiples défis, incluant se soumettre à une série d'interventions thérapeutiques dont les répercussions physiques et psychologiques sont considérables (4).

Les approches chirurgicales associées au traitement du cancer du sein, telle la mastectomie, ont pour conséquences d'importants déficits fonctionnels du membre supérieur, notamment une diminution des amplitudes de mouvement, du lymphœdème, des faiblesses musculaires et une augmentation de la douleur (7). Combinés aux défis psychosociaux d'un tel diagnostic, ces déficits affectent la qualité de vie de ces femmes, notamment en complexifiant la réalisation de leurs activités quotidiennes (7).

Les interventions de réadaptation conçues pour réduire les effets secondaires de la mastectomie ont fait l'objet de plusieurs études scientifiques (8, 9). Toutefois, malgré qu'elles se soient montrées efficaces et sécuritaires, celles-ci se déclinent sous des

modalités d'exécution (c.-à-d. moment d'initiation, durée, fréquence, etc.) hétérogènes. Cette particularité complexifie significativement l'identification et la sélection des paramètres qui optimiseront la récupération post-opératoire chez cette population (9).

À ce jour, les institutions du Centre intégré universitaire de santé et de services sociaux de la Mauricie-et-du-Centre du Québec (CIUSSS-MCQ) offrent des services limités en matière de réadaptation pour les femmes devant subir une mastectomie. Malgré le besoin impératif de soutenir ces patientes en matière de réadaptation périopératoire, il est d'abord essentiel d'établir un portrait global de la nature des interventions conservatrices et des mesures de résultats cliniques ayant déjà utilisé pour cette population. Ces connaissances sont nécessaires afin de favoriser le développement d'interventions dont les modalités répondront aux besoins et aux attentes spécifiques de cette population.

OBJECTIFS DE RECHERCHE

L'objectif primaire de cette étude est d'identifier les interventions conservatrices et les mesures de résultats cliniques utilisées dans le cadre de la réadaptation périchirurgicale des femmes atteintes d'un cancer du sein devant subir ou ayant subi une mastectomie. En second lieu, nous souhaitons rendre compte des barrières et des facteurs ayant facilité la participation à ces programmes de réadaptation, en plus des bienfaits et des limites de ceux-ci, du point de vue des femmes ayant fait face à cette réalité.

ARTICLE SCIENTIFIQUE

Title: Conservative interventions and clinical outcome measures used in the perioperative rehabilitation of breast cancer patients undergoing mastectomy: a scoping review.

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Abstract

Background: Mastectomy represents the first-line treatment approach for more than 90% of breast cancer patients. Physical impairments associated with this surgical procedure are numerous, which negatively impacts the patient's quality of life. Despite evidence supporting the benefits of rehabilitation interventions to reduce shoulder functional deficits in women undergoing mastectomy, there are limited rehabilitation resources available for this population within the institutions affiliated to the Centre intégré universitaire de santé et de services sociaux de la Mauricie-et-du-Centre du Québec (CIUSSS-MCQ). To promote the development of interventions whose modalities will meet patients' needs and reflect the particularities of breast cancer care pathways, we must first establish a comprehensive portrait of rehabilitation strategies and clinical outcome measures that have already been used for this population.

Objective: (1) Identify and describe the conservative interventions and the clinical outcome measures used as part of the perioperative physical rehabilitation of women with breast cancer who are awaiting or have undergone mastectomy; (2) Report on the barriers and facilitators to participation and completion of these rehabilitation programs.

Methods: A scoping review was conducted, which included systematic searches of relevant databases from database inception to January 2021. We included peer-reviewed English and French literature with quantitative designs, describing conservative interventions and clinical outcome measures used within rehabilitation programs designed for women who were awaiting or had undergone mastectomy. Paired reviewers

independently reviewed all citations and articles using a two-phase screening process. Data extracted from eligible studies were descriptively reported.

Results: The literature search yielded 5605 articles and 12 additional articles were retrieved from other data sources. Of the 46 eligible studies, most interventions were multimodal (60.9%), which combined exercise with one or more of the following: [1] patient education (45.7%); [2] manual therapy (23.9%); or [3] lymphatic drainage (17.4%). Rehabilitation programs were initiated a few days following surgery (84.8%) and performed under supervision until hospital discharge (45.7%). Objective measures of physical function most frequently used were shoulder range of motion, muscle strength and signs of lymphedema, whereas quality of life, shoulder function and pain were the primary patient-reported outcome measures. Most studies did not discuss study compliance and reasons to decline research participation. Undergoing another breast surgery, death, and cancer recurrence were the most reported barriers to study completion.

Conclusion: This scoping review reports on the heterogeneity and wide range of conservative interventions and clinical outcome measures used in physical rehabilitation for breast cancer patients who had undergone or were scheduled to undergo mastectomy. Supervised multimodal interventions combining exercise with patient education, lymphatic drainage, or manual therapy were the most frequently reported. These interventions were predominantly initiated following breast surgery. Further research is needed to identify barriers and facilitators to study participation and completion, as well as breast cancer patients' needs and expectations, particularly in the preoperative period.

Keywords: *Breast cancer, Mastectomy, Rehabilitation, Outcome Measures*

Background

Breast cancer is the malignant tumor with the second highest incidence rate among females worldwide, after non-melanoma skin cancers (2). In 2020, breast cancer cases accounted for one in four new cancer diagnosis among Canadian women (2). Implementation of a biennial population-based mammography screening program in 1998 (3) along with the improvement of surgical techniques (28), has fortunately contributed to a significant decrease in breast cancer mortality rates in Canada over the last twenty years (20). Specifically in Quebec, over 90% of breast cancer patients in the early 2000s were diagnosed with an *in situ* breast tumor (stage 0) or a stage I or II disease. (19). Early detection of lower histological grade cancer significantly improves breast cancer patients prognosis, allowing treatment strategies to be initiated sooner, thus reducing the risk of disease progression (19). In 2003, patients diagnosed with a stage I or II breast tumor showed a 5-year survival rate of 98.1% and 89.2% respectively, while this number dropped to 10.5% for patients with a stage IV disease (19). Although breast cancer patients may now benefit from a longer life expectancy, this is not without consequences for those women, who will still need to undergo a series of therapeutic interventions whose physical, psychological, and socio-economic effects are substantial (4).

Mastectomy (i.e., surgery to remove part of or all the breast) represents the first-line treatment approach for more than 90% of breast cancer patients (5). Physical impairments associated with this surgical procedure are numerous (e.g., loss of shoulder range of

motion, pain, lymphedema, and muscle weakness) (6), leading to limitations in activities of daily living (ADL), which negatively impacts the patient's quality of life (7, 31).

Several studies aimed to develop effective interventions to support breast cancer patients dealing with musculoskeletal adverse events resulting from mastectomy. A systematic review published in 2015 by De Groef et al. (8) confirmed the effectiveness of multimodal physical therapy (i.e., stretching exercises combined with general active exercises) to treat upper limb impairments after breast cancer treatments. Another systematic review published in 2019 by Ribeiro et al. (9) concluded that range of motion (ROM) and upper extremity strengthening exercises were effective in improving shoulder ROM in patients who had undergone breast surgery. However, when comparing the 15 randomized controlled studies included in this review, the rehabilitation interventions described were found to be highly heterogeneous, especially in terms of initiation time, duration, intensity and frequency (9), preventing any conclusions as to which parameters should be chosen to promote optimal postoperative recovery for this population.

To date, there are limited rehabilitation resources available for breast cancer patients undergoing mastectomy within the institutions of the Centre intégré universitaire de santé et de services sociaux de la Mauricie-et-du-Centre du Québec (CIUSSS-MCQ). Although there is a critical need to support these patients in the perioperative period, we must first establish a comprehensive portrait of rehabilitation interventions and clinical outcome measures currently used. It stands to reason that such understanding represents a

prerequisite for the development of interventions whose modalities will reflect patients' needs and expectations and which will also consider the particularities of breast cancer care pathways.

Therefore, the aim of this study was to identify the conservative interventions and the clinical outcome measures used as part of the perioperative physical rehabilitation of women diagnosed with breast cancer who plan to or have undergone mastectomy. As a secondary objective, we aimed to report on the barriers and facilitators to participation and completion of these rehabilitation programs.

Methods

To address our broad research question, a scoping review was conducted. This type of study allows to report on the current state of knowledge in a research field and captures the breadth of information on a topic that has been widely studied and for which the available data are both numerous and heterogeneous (45). This scoping review was based on the framework from Arksey & O'Malley (46) and Levac et al. (47), using a 5-step method review. Consistent with this framework, we did not appraise the methodological quality of the included studies.

Step 1: Identifying the research question

Our scoping review was guided by the following research question: *What are the conservative interventions and clinical outcome measures used as part of the*

perioperative physical rehabilitation of women diagnosed with a stage 0-III breast cancer who are awaiting or have undergone mastectomy?

Step 2: Identifying relevant studies

Our search strategy was developed by one of the authors (J.M.) and two coauthors (A.A.M., M.D.) subsequently cross-validated the search to ensure completeness of results. The search strategy was first developed in MEDLINE and then adapted to other bibliographic databases. Search terms included controlled vocabulary for each database and free text words for the key concepts of breast cancer, mastectomy and rehabilitation (see Appendix A for full search strategy). In addition, reference lists from relevant articles and from previously published systematic reviews were hand searched for any additional relevant studies. We searched MEDLINE, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and Cochrane databases from database inception to January 24, 2021. EndNote X9 was used to de-duplicate references electronically across all databases.

Step 3: Study selection

Eligibility criteria

To be included, studies had to meet the following criteria: 1) be written in the English or French language; 2) were randomized controlled trials, quasi-randomized trials, cohort studies, secondary analysis, exploratory studies or systematic reviews (for reference purposes only); 3) focused on adult women (aged ≥ 18 years) who engaged in a physical rehabilitation intervention before or following any type of mastectomy (e.g., partial

mastectomy or breast conserving surgery (BCS), lumpectomy, quadrantectomy, wide local excision (WLE), segmental mastectomy) for a stage 0-III breast cancer. Studies including participants that underwent a mastectomy combined with an axillary staging procedure (i.e., axillary sampling or sentinel lymph node biopsy) or a lymph node dissection (ALDN) were also included, considering that these surgical interventions are in line with the Society of Surgical Oncology-American Society of Clinical Oncology (SSO-ASTRO) clinical practice guideline recommendations (48). All included studies also had to match the following characteristics for physical rehabilitation interventions:

1. Initiated within 3 months preceding or following the surgical intervention.
2. Involved at least one active physical modality (i.e., the patient physically contributed to its own treatment), including but not limited to exercises, conditioning, yoga, Tai Chi and Pilates.
3. Provided alone or in combination with other types of conservative interventions (e.g., patient education, manual therapy, manual lymphatic drainage (MLD), nutritional or psychological interventions).

Study exclusion criteria included: cross-sectional studies, case report and case series designs, study protocol, practice guidelines, letters, editorials, commentaries, unpublished manuscripts, books and book chapters, conference proceedings, cost analyses, meeting and conference abstracts, thesis and dissertations, non-systematic reviews, qualitative studies, laboratory studies, study not reporting on methodology and cadaveric or animal

studies. Studies focusing solely on patients with a stage IV disease, not providing sufficient detail on interventions' procedures (e.g., initiation, frequency, duration, etc.) or whose objective was to manage or prevent the adverse events of systemic treatments (i.e., chemotherapy, radiation, or hormonal therapy) rather than surgery were also excluded.

Screening and agreement

A two-phase screening process was used to select eligible studies. An Excel spreadsheet was used in both phases to manage search results. In phase I screening, a pair of independent reviewers (J.M., C.D.) screened citation titles and abstracts to determine the eligibility of studies (categorizing studies as possibly relevant or irrelevant). In instances where eligibility could not be ensured due to limited information in the title/abstract, the citation was considered "possibly relevant'' until a final decision could be made upon full text review. A pair of independent reviewers (J.M., N.L.) screened possibly relevant studies in full text during phase II screening to determine eligibility and reasons for exclusion were documented. Reviewers met to discuss disagreements and to reach consensus in both phases. An additional reviewer (A.A.M.) was involved if consensus could not be reached.

Step 4: Data charting

Data extraction forms were drafted, and pilot tested, using a random sample of fifteen articles. Both reviewers (J.M., N.L.) extracted the following data (when available) from half of the eligible studies: 1) study description (first author, publication year and country

of origin); 2) study population (sample size, cancer stage, surgery type and systemic treatment administered); 3) rehabilitation interventions provided (e.g., type, initiation, duration, frequency); 4) outcome measures and outcome validation information and 5) patients' experience data (e.g., reasons for not completing the study or for declining to participate, adherence outcomes, postoperative complications, adverse events). An evidence table was built (see Appendix B), using a Microsoft Word document. Details of the intervention components were extracted using the TIDieR checklist and guide (49) and are provided in Appendix C. A third reviewer (M.D.) independently verified the extracted data to minimize error.

Step 5: Collating, summarizing, and reporting the results

A descriptive synthesis was conducted to provide details with regards to the total number of studies kept for analysis, their authors and year of publication, country where they were conducted, study design and study population. The summary of evidence table includes a brief description of conservative rehabilitation interventions identified as well as outcome measures used for each of them. Interventions' procedures and data pertaining to barriers and facilitators to engagement in these interventions were summarized separately in Appendix B and C. In order to answer our research question, our review findings were sorted by themes of interest: "conservative rehabilitation interventions", "clinical outcome measures" or "patients' experience''.

Results

Descriptive synthesis

A total of 5605 articles were identified from the literature search. Following the removal of duplicates (n=848), 4723 articles were excluded (see Fig. 8). Twelve articles were retrieved from additional data sources and added to the final result, bringing the total count to 46 papers, including 44 original studies.

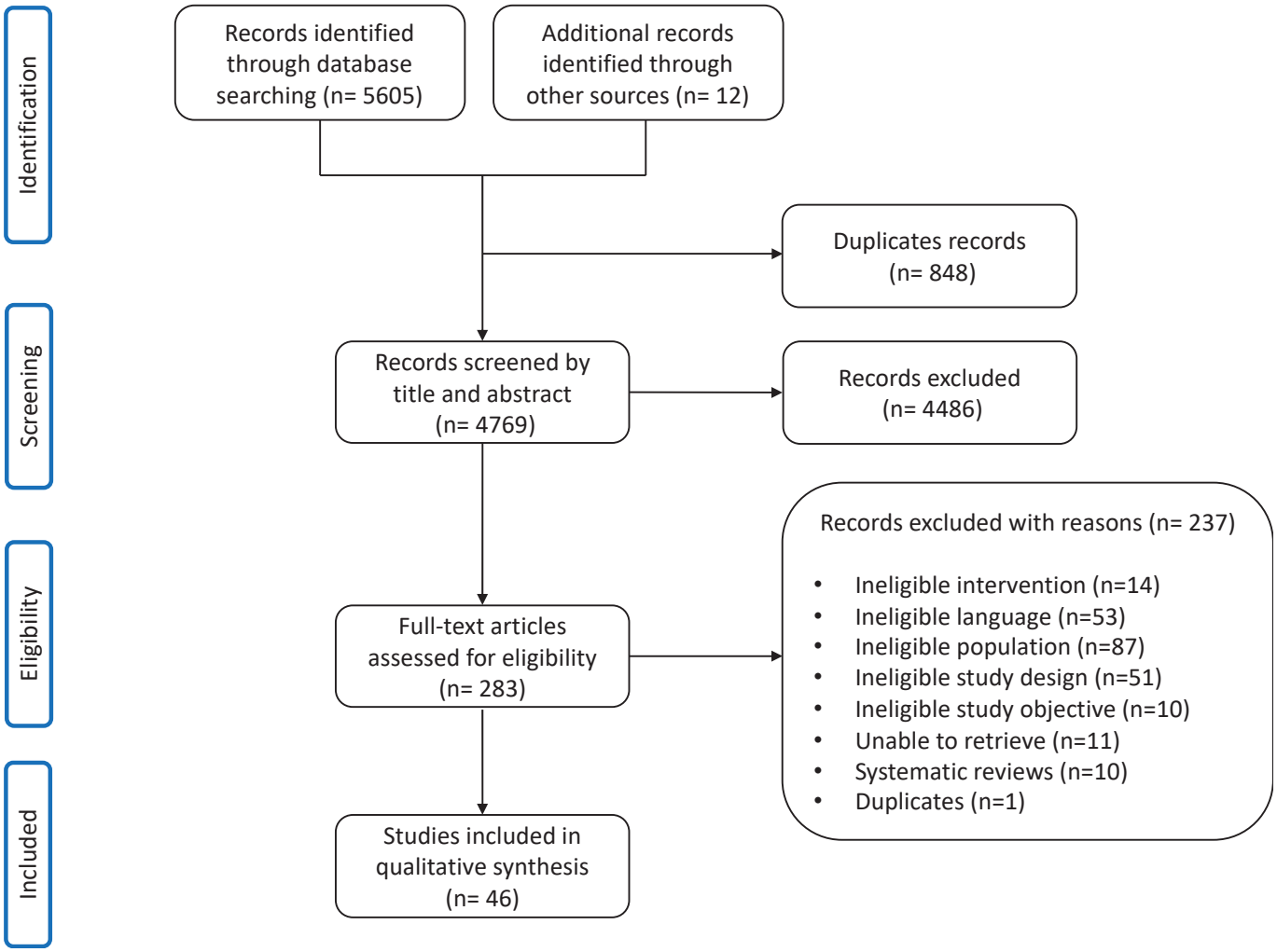


Figure 8: Flowchart

Table 5 summarizes the key findings from the included articles. Most studies (32 of 46) were RCT (50-81), three were controlled non randomized clinical trials (82-84), three were prospective observational studies (85-87), one was a retrospective cohort study (88), one was a case-control study (89), four were quasi-experimental (90-93), one was a pilot study (94) and one was a feasibility study (95). The studies originated from 19 countries distributed across 4 continents (i.e., Americas, Europe, Asia and Oceania), most of which were high income countries (50-57, 60, 62, 64-67, 70-72, 75-78, 81, 83, 85-89, 91, 93-95) or upper-middle income countries (58, 59, 61, 63, 68, 69, 73, 74, 79, 80, 82, 84, 92), with only one study conducted in India, a lower-middle income country (90). The body of literature on this topic turned out to be quite recent, with 65.2% (30 of 46) of studies having been published between 2010 and 2020 and 28.2% (13 of 46) between 2000 and 2009.

Participants

Studies' sample size varied between 22 to 1217 participants, with participants mean age ranging from 45.6 to 63.4 years old. Most studies (29 out of 46) included women diagnosed with different breast cancer stages (i.e., 0-III), who underwent breast surgery combined with either an axillary staging procedure or ALDN, and systemic treatments (i.e., chemotherapy, hormonotherapy, or radiotherapy). In 86.9% of the studies (40 out of 46), the study groups included both patients who underwent BCS and those who underwent total mastectomy. Therefore, no conclusions could be drawn as to whether the type of surgery might have an impact on clinical outcomes and on breast cancer patients' motivation to engage in and complete a rehabilitation intervention.

Table 5: Summary Table of Evidence

First Author (Year) Country	Study design	Participants	Intervention	Outcome measures
Ammitzbøll[50] (2019) Denmark	RCT	N= 158 **Exercise IG; n= 82** *Age, mean ± SD*: 53 ± 10 *Stage, n (%):* I: 12 (15)/II: 48 (59)/III: 15 (18)/N/A: 7 (9) *Sx type, n (%):* LUMP +ALDN: 43(52)/MX + ALDN:39(48) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 48 (59) Neoadj Ch: 25 (30)/HT: 64 (78) **Usual-care CG; n = 76** *Stage, n (%):* I: 16 (21)/II: 35 (46)/III: 18 (24)/N/A: 7 (9) *Sx type, n (%):* LUMP + ALDN: 41(54) MX +ALDN: 35(46) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 45 (59) Neoadj Ch: 21 (28)/HT: 51 (67)	**Exercise intervention group** Resistance exercises program (covered all major muscles groups of the UL and lower limbs, and core strength and stability) *Phase 1 (w1-w20)* Initiation: 3rd post-op w Frequency: 3 days/w *Phase 2 (w21-w50)* Initiation: after phase 1 Frequency: 3 days/w *Exercise sessions duration*: 50-55 min (10-15-min warm-up, 40 min of resistance training) **Usual-care control group** No intervention provided but were allowed to participate in municipality-led rehabilitation programs without restrictions	-Arm VOL-*ILVD* (water displacement) -LE-related symptoms: heaviness, tightness and swelling (NRS-11) -Muscle strength (7RM-test and dynamometer) -Shoulder movement (goniometer) -Interlimb mass difference-*ILMD* (DXA and arm scan) -Clinical examination- LE (Stanton & al. criteria) -Clinically relevant LE (> 3% increased ILVD, NRS-11 ≥ 2 and 2 or more clinical criteria)
Ammitzbøll[51] (2019) Denmark	RCT	N= 158 **Exercise IG; n= 82** *Age, mean ± SD*: 53 ± 10 *Stage, n (%):* I: 12 (15)/II: 48 (59)/III: 15 (18) N/A: 7 (9) *Sx type, n (%):* LUMP +ALDN: 43(52)/MX + ALDN:39(48) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 48 (59) Neoadj Ch: 25 (30)/HT: 64 (78) **Usual-care CG; n = 76** *Stage, n (%):* I: 16 (21)/II: 35 (46)/III: 18 (24)/N/A: 7 (9) *Sx type, n (%):* LUMP + ALDN: 41(54)/MX +ALDN: 35(46) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 45 (59) Neoadj Ch: 21 (28)/HT: 51 (67)	**Exercise intervention group** Resistance exercises program (covered all major muscles groups of the UL and lower limbs, and core strength and stability) *Phase 1 (w1-w20)* Initiation: 3rd post-op w Frequency: 3 days/w *Phase 2 (w21-w50)* Initiation: after phase 1 Frequency: 3 days/w Exercise sessions duration: 50-55 min (10-15-min warm-up, 40 min of resistance training) **Usual-care control group** No intervention provided but were allowed to participate in municipality-led rehabilitation programs without restrictions	-HRQOL (EORTC QLQ C-30 v3; FACIT-f) -Symptom clustered: pain-sleep-fatigue (EORTC QLQ-C30 v3)

Anderson[52] (2012) USA	RCT	N= 104 **Intervention arm; n= 52** *Age group, n (%):* *< 50:* 21 (40)/*50-64:* 23 (44) *65-74:* 4 (8)/ *>75:* 4 (8) *Stage, n (%):* I: 25 (48)/II: 19 (37)/III: 8 (15)/N/A: 1(2) *Sx type, n (%):* LUMP: 23 (44)/MX: 28 (54)/ N/A: 1 (2) *Type of node dissection, n (%):* SND only: 10 (19)/AND: 39 (75) Neither: 1 (2)/N/A: 2 (4) *Systemic treatment, n (%):* *Ch:* 31(60)/*HT:* 26(50)/*RT:* 31(60) **Comparison arm; n=52** *Age group, n (%)* *< 50:* 23 (44)/*50-64:* 19 (37) *65-74:* 7 (13)/ *>75:* 3 (6) *Stage, n (%):* I: 26 (50)/II: 21 (40)/III: 4 (8)/N/A: 1(2) *Sx type, n (%):* LUMP: 25 (48)/MX: 24 (46)/ N/A: 3 (6) *Type of node dissection, n (%):* SND only: 9 (17)/ALND: 40 (77) Neither: 0/ N/A: 3 (6) *Systemic treatment, n (%):* Ch: 31(60)/HT: 23(44)/RT: 36(69)	**Intervention arm** Comprehensive program consisting of tailored exercises and LE prevention module *Initiation*: 4-12w post-op *Intensive phase (m1-3)* Frequency: 2 days/w *Phase 2 (m4-6):* Transition to HB exercises (Supervised exercises 1 day/w) *Phase 3 (m7-12):* HB exercises *Exercise sessions duration*: 65 min (5-min warm-up, 30-min of walking, 20 min of strengthening exercises and 10 min of stretching) **Comparison arm** Usual care consisting of patient ED (LE awareness, tips about PA and nutrition, recommendations for improving function and strength)	-Arm VOL (Water displacement) -Function (6MWT) -HRQOL (FACT-B)
Bendz[53] (2002) Sweden	RCT	N= 230 **Group A; n= 115** *Age, mean ± SD*: 58 ± 11 *Stage*: N/A *Sx type, n (%):* MX: 31 (31) /MX + RT: 5 (5) QT: 20 (20) / QT + RT: 45 (44) **Group B; n = 115** *Age, mean ± SD*: 58 ± 11 *Stage:* N/A *Sx type, n (%):* MX: 22 (21) / MX + RT: 7 (7) QT: 23 (22) /QT + RT: 52 (50)	**Group A** Early shoulder exercises (to be started on the 1st pod) Day 1-13: Early shoulder exercises including intermittent hand contractions and basic ROM exercises/ From Day 14: Comprehensive ROM exercise program **Group B; n = 115** Delayed shoulder exercises Day 1-13: No further information was provided/From Day 14: Comprehensive ROM exercise program Frequency: 3 times daily 5 times in every set	-Arm VOL (Water displacement) -Shoulder ROM (Myrin goniometer) -Grip strength (vigorimeter) -Patient-reported measures of pain, heaviness and tension (VAS scale)

Beurskens[54] (2007) Netherlands	RCT	N= 30 **Physiotherapy group; n= 15** *Age, mean ± SD*: 53.7 ± 13.0 *Stage:* N/A *Sx type, n (%):* BCS + ALDN: 3 (20)/MX+ ALDN: 12 (60) *Systemic treatment, n (%):* Ch: 2 (13)/HT: 1 (7)/RT+ Ch: 6 (40) Ch+ HT: 1 (7)/RT+ HT: 1 (7) RT + HT + Ch: 1 (7) **Control group; n=15** *Age, mean ± SD*: 55.4 ± 9.3 *Stage*: N/A *Sx type, n (%):* BCS + ALDN: 4 (27)/MX + ALDN: 11 (73) *Systemic treatment, n (%):* RT: 2 (13)/Ch: 2 (13)/HT: 1 (7) RT+ Ch: 8 (53)/Ch + HT: 1 (7) RT + HT: 1 (7)	**Physiotherapy group** PT sessions (advice and exercises for arm/shoulder, posture correction, coordination exercises, exercises for muscular strength, improvement of general physical condition, exercises to prevent LE and instruction for ST massage of the scar if required Initiation: 2w following surgery Duration: 3 months Frequency: 1-2/w for the first 3w and then once a fortnight or less + 10 min of home exercises daily **Control group** Leaflet flyer with advice and exercises for the arm/shoulder and had no further contact with the physiotherapist Initiation: 1st w following surgery	-Arm/shoulder pain (VAS) -Shoulder mobility (Digital inclinometer) -Disabilities in daily life (DASH) -Arm edema (Water displacement) -Grip strength (hand-held dynamometer) -Quality of life (SIP questionnaire short version)
Box[55] (2002) Australia	RCT	N= 65 **Treatment group; n= 33** *Age, mean ± SD*: 53.03 ± 9.49 Stage: N/A *Sx type (%):* BCS + ALND: 46.9/ MRM: 53.1 **Control group; n = 32** *Age, mean ± SD*: 59.00 ± 10.95 Stage: N/A *Sx type (%):* BCS + ALND: 51.5/MRM: 48.5	**Treatment group** *Physiotherapy Management Care Plan (PMCP)* Included a thorough preop assessment and explanation with postop reviews to monitor shoulder ROM, progress exercise program, LE awareness ED and individualized intervention as required. **Control group** Exercise instruction booklet	-Shoulder ROM (goniometer) -Function (12-items functional questionnaire)
Box[56] (2002) Australia	RCT	N= 65 **Treatment group; n= 33** *Age, mean ± SD*: 53.03 ± 9.49 *Stage*: N/A *Sx type (%):* BCS + ALND: 46.9/ MRM: 53.1 **Control group; n = 32** *Age, mean ± SD*: 59.00 ± 10.95 *Stage*: N/A *Sx type* (%): BCS + ALND: 51.5/MRM: 48.5	**Treatment group; n = 33** *Physiotherapy Management Care Plan (PMCP)* Included a thorough preop assessment and explanation with postop reviews to monitor shoulder ROM, progress exercise program, LE awareness ED and individualized intervention as required. **Control group; n = 32** Exercise instruction booklet	-Arm size- *CIRC* -Arm VOL (Water displacement) -Multi-frequency bioimpedance-*MFBIA* (spectroscopy) -Incidence of secondary LE (based on preop CIRC, preop VOL and MFBIA ratio)

Cho[57] (2016) South Korea	RCT	N= 48 BC patients with AWS **PTMLD group; n= 24** *Age, mean ± SD*: 50.7 ± 9.6 *Stage, n (%):* I: 5 (24)/III: 16 (76) *Sx type, n (%):* MX: 12 (57)/ LUMP: 7 (33) Breast recons: 2 (10) *Systemic treatment, n (%):* *Ch:* 9 (43)/*RT:* 21(100)/*HT:* 14 (67) **PT group; n = 24** *Age, mean ± SD*: 46.6 ± 6.8 *Stage, n (%):* I: 12 (60)/III: 8 (40) *Sx type, n (%):* MX: 16 (80) / LUMP: 3 (15) Breast recons: 1 (5) *Systemic treatment, n (%):* *Ch:* 11 (55)/*RT:* 19(95)/*HT:* 12 (60)	**PTMLD group** PT program combined with MLD *Supervised PT program* UE strengthening and stretching exercises combined with MT session (ST mobs and stretching, shoulder stretching exercises, shoulder girdle mobs and PROM exercises *Initiation*: At least 4w after BSx *Duration*: 4w *Frequency*: 3 times/w *MLD* Frequency: 5 days/w for 4w MLD sessions duration: 30 min **PT group; n = 24** PT program solely	-Arm VOL (CIRC tape measurements) -Muscular strength (dynamometer) -Active ROM (inclinometer) -Pain (NRS-11) -Arm disability (DASH) -QoL (EORTC QLQ-C30 v3, EORTC QLQ-BR23) Visible cording (Subjective assessment by a rehab doctor)
Cinar[58] (2008) Turkey	RCT	N = 57 **Treatment group; n = 27** *Age, mean ± SD*: 51.1 ± 13.0 *Stage, n (%):* N/A *Sx type*: *MRM* *Systemic treatment, n (%):* Ch: 29 (97)/RT: 14 (47) **HB exercise program; n= 30** *Age, mean ± SD*: 52.6 ± 12.2 *Stage, n (%):* N/A *Sx type*: *MRM* *Systemic treatment, n(%):* Ch:23(85)/RT:10(4)	**Treatment group** Early shoulder ROM exercises (to be started on the 1st post-op day) and PT program *PT program* Included ROM, stretching and strengthening exercises *Initiation*: Following drains removal *Duration*: 15 supervised sessions and 8w self-A **HB exercise program group** Postoperative exercise forms to perform at home	-ROM (Myrin goniometer) -Arm VOL (CIRC tape measurements) Function (10-item functional questionnaire)
de Almeida Rizzi[59] (2020) Brazil	RCT	N= 62 **Free ROM group; n = 31** *Age, mean ± SD*: 49.90 ± 10.11 *Stage, n (%):*0: 10 (33)/ I: 4 (13)/ II: 3 (10) IIB: 7 (23)/III: 5 (17)/ IIIB: 1(3)/IV: 0 (0) *Sx type, n (%):* Breast sparing Sx: 14 (47) MX: 16 (53)/Breast recons: 30(97) *Type of node dissection, n (%):* SNB: 15 (50)/ALND: 14 (47)	**Both groups** Exercise protocol consisting of neck and UL stretching exercises and shoulder ROM exercises *Initiation*: 1st pod Day1-14: Exercises 1-6 From Day15: Exercises 1-8 **Free ROM group** Were allowed to perform the protocol exercises and ADL in free amplitude	Dehiscence (Inspection, palpation and tape measure) Seroma (Inspection and palpation, medical record) Infection

		Systemic treatment, n (%): Neoadj Ch: 13 (43) **Limited ROM group; n = 31** *Age, mean ± SD*: 54.46 ± 10.68 *Stage, n (%):* 0: 11 (37)/ I: 4 (13)/ II: 7 (23) IIB: 5 (17)/ III: 2 (7)/ IIIB: 0 (0)/IV: 1 (3) *Sx type, n (%):* Breast sparing Sx: 10 (33) MX: 20 (67)/Breast recons: 30(97) *Type of node dissection, n (%):* SNB: 21 (70)/ ALND: 7 (23) *Systemic treatment, n (%):* Neoadj Ch: 10 (33)	**Limited ROM group** Had ROM maintenance limited to 90° until the 30th post-op day, then started free ROM exercises	(Inspection and palpation, medical record) Necrosis (Inspection and medical record) Shoulder ROM (Goniometer) Pain (VAS) Upper limb function (DASH)
De Groef[60] (2017) Belgium	RCT	N= 147 **Intervention group; n= 72** *Age, mean ± SD* :53.9 ± 11.5 *Stage, n (%):* 0: 7 (10)/ I: 16 (22) /II: 36 (50)/ III: 13 (18) IV: 0 (0) *Sx type, n (%):* MX: 46 (64)/ BCS: 26 (36) *Systemic treatment, n (%):* RT, IMC and medial supraclavicular:72(100) RT, axilla: 8(11)/Ch: 60(83) Neoadj Ch:29(40) Target therapy: 22(31)/HT: 57(79) **Control group; n = 75** *Age, mean ± SD*: 54.7 ± 11.9 *Stage, n (%):*0: 2 (3)/ I: 20 (27)/ II: 37(48)/ III:14(19)/ IV:2 (3) *Sx type, n (%):* MX: 50 (67)/ BCS: 25 (33) *Systemic treatment, n (%):* RT, IMC and medial supraclavicular:75(100) RT, axilla: 9(12)/Ch:55(73) Neoadj Ch:21(28) Target therapy: 9 (12)/HT: 62 (83)	**Both groups** Individual standard PT program consisting passive mobs, stretching and transverse strain of pectoral muscles, scar tissue massage, exercises schemes, posture and movement control and shoulder AROM *Initiation*: after surgery *Duration:* 4 months *Exercise sessions duration*: 30 min *Frequency*: 2 session/w, reducing to once/w after the first 2 months **Intervention group** Individual standard PT program + MT *Initiation*: 2 months post-surgery *Duration* (MT): 2 months *Freq of MT sessions*: once/w **Control group** Individual standard PT program + placebo t_x consisting of static bilateral hand t_x at the upper body and arm *Initiation:* 2 months post-surgery *Duration* (placebo): 2 months *Frequency*: once/w *Placebo t_x duration*: 30 min	-Point prevalence of pain (Yes/No question) -Pain intensity (VAS) -Pressure hypersensitivity (Digital algometer) Pain quality (McGill Pain Questionnaire) Point prevalence of impaired shoulder function (DASH score of more than 15%) -Shoulder function (DASH) -Quality of life (SF-36)
De Rezende[61] (2006) Brazil	RCT	N= 60 **Directed exercises group; n = 30** *Age, mean ±SD*: 54.00 ± 10.11 *Stage, n (%):* I: 5 (17)/ IIA: 4 (13)/ IIB: 5 (16)	**Directed exercises group** 19 ROM-exercises program performed in groups of 5 to 20 women and supervised by a team of PT and students *Initiation*: 1st post-op day	-Shoulder ROM (Manual goniometer) -Lymphatic disturbance (Drainage VOL)

		IIIA: 4 (13)/ IIIB: 8 (27)/ IIIC: 2 (7)/ IV: 2(7) *Sx type, n (%):* Halsted RMX: 5(17)/MRM: 16 (53)/QT: 9(30) *Systemic treatment, n (%):* Previous Ch: 8 (27) **Free exercises group; n = 30** *Age, mean ± SD*: 55.40 ± 11.24 *Stage, n (%):* I: 6 (20)/ IIA: 10 (33)/ IIB: 6 (20) IIIA: 3 (10)/ IIIB: 3 (10)/ IIIC: 0 (0)/IV: 2 (7) *Sx type, n (%):* Halsted RMX: 1(3)/ MRM: 21(70)/QT:8 (27) *Systemic treatment, n (%):* Previous Ch: 9 (30)	*Duration*: 3 days/w for 42 days *Exercise sessions duration*: 40 min **Free exercises group** Same ROM exercises program without a previously defined sequence or number of repetitions	-Arm CIRC (tape measure)
Devoogdt[62] (2018) Belgium	RCT	N= 160 **Experimental group; n = 79** *Age, mean ± SD*: 56 ± 13 *Stage, n (%):* 0: 1 (1)/ I: 21 (27)/ II: 38 (48)/III: 13 (17) IV: 6 (8) *Sx type, n (%):* MX + ALDN: 52 (66)/BCS + ALDN: 27(34) *Systemic treatment, n (%):* Ch: 50 (63)/Target therapy:14(18)/HT:55(70) **Control group; n = 81** *Age, mean ± SD:* 55 ± 11 *Stage, n (%):* 0: 0 (0)/ I: 26 (32)/ II: 39 (48)/III: 12 (15) IV: 4 (5) *Sx type, n (%):* MX + ALDN: 56 (69)/BCS + ALDN: 25(31) *Systemic treatment, n (%):* Ch: 58 (72)/ Target therapy: 7 (9)/HT: 66 (82)	**Both groups** *During hospitalization:* Received information about the prevention of LE + exercise therapy (mobilizing exercises) *After hospitalization:* 30-min individual exercise sessions *Duration*: 6 months *Frequency*: 2 times/ w, gradually diminished to 1/ 2w **Experimental group** Protocol described above + MLD Initiation: one week after removal of axillary drains *Duration of MLD*: 20 weeks Frequency of exercise sessions during this period: one to 3 times/ w and then gradually decreased to once/w **Control group** Protocol described above without MLD	-Incidence of arm LE (Water displacement, arm CIRC) -Point prevalence of arm LE (water displacement, arm CIRC) -Point prevalence of subjective arm and trunk LE (Questioned at interview) -Arm VOL difference (water displacement) -Shoulder ROM-abd, flexion, ext and int rotation (Goniometer, tape measure) -HRQoL (SF-36) -Problems in functioning (Lymph-ICF)
Feyzioğlu[63] (2020) Turkey	RCT	N= 40 **Kinect-based rehabilitation group; n =20** *Age, mean ± SD*: 50.84 ± 8.53 Stage, n (%): N/A	**Both groups** Breathing, ROM and pumping exercises, limitations for shoulder ROM amplitudes, weightlifting, jumping and running up to 6w post-op	-Pain intensity (VAS) -Shoulder ROM (Digital goniometer)

		Sx type: Unilateral BSx + ALND *Systemic treatment, n (%):* Ch: 4 (21)/ RT: 13 (68)/ HT: 2 (11) **Standardized physiotherapy group; n = 20** *Age, mean ± SD*: 51.00 ± 7.06 *Stage, n (%):* N/A *Sx type*: Unilateral BSx + ALND *Systemic treatment, n (%):* Ch: 2 (12)/ RT: 13 (77)/ HT: 2 (12)	*Initiation*: 1st post-op day *Duration*: 2w **KBR group** Xbox 360 Kinect video game program combined with tissue massage and passive mobs **SPT group** Standard UE PT program including scar tissue massage and mobilizations *Initiation*: 2nd post-op w *Duration:* 2 days/w for 6 w *Program sessions duration:* 45 min	-Shoulder muscle strength (Handheld dynamometer) -Handgrip strength (Hydraulic hand dynamometer) -Upper extremity function (DASH) -Fear of movement (TKS)
Kilbreath[65] (2012) Australia	RCT	N= 160 **Exercise group; n = 81** *Age, mean ± SD*: 53.5 ± 12.1 Stage, %: I: 17 / II: 44 / III: 38 *Sx type, %:* MX + SNB: 48/ ALDN: 62 *Systemic treatment, %:* Ch: 68/ RT: 79 **Control group; n = 79** *Age, mean ± SD*: 51.6 ± 11.0 *Stage, n (%):* I: 19/ II: 37/ III: 44 *Sx type, %:* MX: 47/ ALDN: 58 *Systemic treatment, %:* Ch: 71/ RT: 76	**Both groups** Postop care including information outlining arm exercises and prevention of LE *Initiation*: 4-6w post-surgery *Duration*: 8 w **Exercise group:** Resistance training and passive stretching for shoulder muscles + home program of resistance training and stretching +HB program *Initiation*: 4-6 w post-surgery *Duration*: 8w *Frequency*: once/w **Control group** No exercises or advice was provided.	-Self-reported arm symptoms (EORTC- BR23) -Breast symptoms (EORTC-BR23) -Shoulder ROM (Digital inclinometer) -Upper shoulder muscle strength (hand-held dynamometer) -Presence of LE (Bioimpedance spectroscopy)
Kilbreath[64] (2006) Australia	RCT	N= 22 **Exercise group; n = 14** *Age, mean ± SD*: 52.7 ± 14.0 *Stage*: N/A *Sx type, n (%):* MX + ALDN: 8 (57)/ WLE + ALDN: 6 (43) *Systemic treatment, n (%):* RT: 9(64)/ Ch: 7(50) **Control group; n = 8** *Age, mean ± SD*: 51.5 ± 10.2 *Stage*: N/A *Sx type, n (%):* MX + ALDN: 4 (50)/ WLE + ALDN: 4 (50) *Systemic treatment, n (%):* RT:7(88)/ Ch:6 (75)	**Exercise group** Usual care + shoulder ROM, strengthening and stretching exercises *Initiation:* 4 to 5w post-surgery *Frequency:* performed daily and supervised once/w by a PT **Control group** Usual care (monitoring by a breast care nurse, may be seen by a PT to review UL exercises and by an OT who discussed prevention of lymphedema) provided at the hospital, were discharged 2 to 7 days post-surgery	-Quality of life (EORTC-QLC-C30, EORTC-QLC-BR23) -Presence of LE (Arm CIRC measurements) -Shoulder ROM (inclinometer) -Maximal isometric shoulder strength (dynamometer)

Lauridsen[66] (2005) Denmark	RCT	N= 139 **Group A; n = 72** *Age (age range):* MRM + RT: 49 (40-70)/MRM: 60 (37-74) BCS: 54 (31-79) *Stage*: N/A *Sx type, n (%):* MRM + RT:20(28)/MRM: 21(29)/BCS: 31(43) *Systemic treatment, n (%):* Ch: 26 (36)/ RT: 23(32)/ HT:25(35) **Group B; n = 67** *Age (age range):* MRM + RT: 51 (29-70)/MRM: 63 (32-77) BCS: 54 (32-69) *Stage*: N/A *Sx type, n (%):* MRM + RT: 23 (34)/MRM: 13(19)/ BCS: 31(46) *Systemic treatment, n (%):* *Ch:* 21 (31)/ RT: 17(25)/HT: 17(25)	**Group A** Team instructed PT program consisting of relaxation and strengthening exercises, combined to vein pump therapy and stretching of scar tissue *Initiation*: 6th to 8th post-op w *Duration:* 2 days/w for 6w *Exercise sessions duration*: 60 min **Group B** ''Standard treatment of the ward'' and were offered the same PT program after the 26th post-op w	-Shoulder function (Constant Shoulder Score) -Presence of ''strings'' in the axilla (Physical assessment)
Majed[67] (2020) USA	RCT	N= 69 BC women undergoing MRM **Intervention group; n=35** *Age group, n (%):* 35-42: 14 (47)/43-48: 10 (33) 49-55: 6 (20) **Control group; n=34** Age group, n (%): 35-42: 14 (47)/43-48: 10 (33) 49-55: 6 (20)	**Intervention group** *Phase 1 and 2* Measurements: QoL-BC survey and shoulder ROM Intervention: one-to-one ED in addition to routine hospital care. Demonstration of the exercises by the researcher with a return demonstration by the patient was done. *Phase 3 (post-surgery)* Deep breathing + shoulder exercises. Shoulder flexion was limited to 90° of assisted AROM until the drains were removed, gradually increased after the 3rd pod **Control group** Routine hospital care that did not include any exercise training or ED. Routine hospital care included explanation by the surgeon on the surgical procedure.	Quality of life (Breast Cancer Patient Version (QoL-BC)) Shoulder ROM (Goniometer)
Pace do Amaral[68] (2012)	RCT	N= 131 **MT+UL exercises group; n = 65** *Age, mean ± SD*: 55.0 ± 11.4	**Both groups** Initiated PT on the 1st pod **MT+UL exercises group**	-Shoulder ROM (goniometer) -Upper limb function

Brazil		*Stage, n (%):* I/II: 46 (72)/ III/IV: 18 (28) *Sx type, n (%):* BCS: 15 (23)/ RM: 50 (77) *Systemic treatment, n (%):* Ch: 22(88)/ RT: 13(52)/ HT: 15(60) **UL exercises group; n = 66** *Age, mean ±SD:* 56.7 ± 11.7 *Stage, n (%):* I/II: 38 (58)/ III/IV: 28 (42) *Sx type, n (%):* BCS: 13 (20)/ RM: 53 (80) *Systemic treatment, n (%):* Ch: 27 (90)/ RT: 24(80)/HT: 18(60)	UL exercises sessions, followed by an MT protocol consisting of scapular and glenohumeral joint mobs and therapeutic massage *Duration*: 1 month *Frequency*: twice a week *MT sessions duration*: 20 min **UL exercises group** Outpatient physical therapy program combining UL exercises to precautions to prevent LE *Initiation*: 3rd post-op day *Duration*: 1 month *Frequency*: 3 times a week *Exercise sessions duration*: 45 min	(Modified-University of California at Los Angeles Shoulder Rating Scale) -Postoperative complications (Observations made by the main investigator)
Petito[69] (2014) Brazil	RCT	N=77 **Early group; n=40** *Age, mean ± SD*: 55 ± 8 *Sx type, n (%):* MX: 24 (59)/QT: 17 (42) **Late group; n=40** *Age, mean ± SD*: 53 ± 12 *Sx type, n (%):* MX: 21 (57)/ QT: 16 (43)	**Exercise program (both groups)** 9 exercises outside hospital with illustrated manual *Duration*: 105 post-operative days *Frequency*: daily at home **Early group** *Initiation*: 1st post op day **Late group** *Initiation*: After drain removal (postoperative day 7-10, mean postoperative day: 9)	-Evaluation incision (presence of seroma formation and dehiscence) -ROM (goniometer)
Sagen[70] (2009) Norway	RCT	N= 207 **No activity restriction group (NAR); n=104** *Age, mean ± SD*: 54 ± 90.6 *Sx type, n (%):* BSx: 46 (44)/ BCS: 57 (55) *Systemic treatment, n (%):* RT, nodes: 47 (45)/RT, breast: 78 (75) Ch: 42 (40)/ HT: 48 (46) **Activity restriction group; n=100** *Age, mean ± SD*: 55 ± 90.6 *Sx type, n (%):* BSx: 51 (51)/ BCS: 49 (49) *Systemic treatment, n (%):* RT, nodes: 40 (40)/ RT, breast: 73 (73) Ch: 38 (38)/ HT: 50 (50)	**NAR group** Supervised physical therapy program which emphasized moderate progressive resistance exercise training *Duration*: 6 months *Frequency*: 2-3 times a week *Exercise duration*: 45 min **AR group** Physical therapy program with restricted activities of the OA avoiding heavy (>3kg) and strenuous activity. *Program*: 6 different passive manual techniques emphasizing flexibility and light massage of the affected shoulder, arm and scar. *Duration:* 6 months *Frequency*: 1/ week *Program duration*: 45 min	-Development of arm LE (VOL diff in mL) -Pain and sensation of heaviness (VAS)

Schultz[71] (1997) Sweden	RCT	N=163 with MRM **Early postoperative shoulder exercise group; n=89** Age, median (range): 59 (35-83) **Delayed postoperative shoulder exercise group; n=74** Age, median (range): 62 (41-84)	**Early postoperative shoulder exercise group** Active shoulder exercise (anteflexion, abduction, rotation) *Initiation:* 1st postop day *Frequency:* 3 times/day **Delayed postoperative shoulder exercise group** Active shoulder exercise (anteflexion, abduction, rotation) *Initiation*: 1st postop w *Frequency:* 3 times/day	Shoulder mobility (abduction and anteflexion) Volume of seroma aspirations and number of aspirations
Siedentopf[72] (2013) Germany	RCT	N=93 **Intervention group; n=48** *Age, mean ± SD*: 55.82 ± 10.72 *Sx type, n (%):* BCS: 29 (62)/RM: 18 (38) SND: 37 (71)/ ALND: 15 (29) *Systemic treatment, n (%):* Ch: 17 (53)/ RT: 23 (70) **Control group; n=41** *Age, mean ± SD*: 58.41 ± 9.91 *Sx type, n (%):* BCS: 24 (60)/ RM: 16 (40) SND: 32 (78)/ ALND: 9 (22) *Systemic treatment, n (%):* Ch: 7 (30)/ RT: 16 (64)	**Intervention group** Yoga classes *Initiation*: Immediately after Sx *Duration*: 5 w *Frequency*: 2 times /w *Class duration*: 75 minutes 10 classes over 5 w **Control group** *Yoga classes* *Initiation*: 5 weeks after surgery Duration: 5 w *Frequency:* 2 times / w, 10 classes over 5 w *Class duration*: 75 minutes Yoga classes: started with lying postures and the gradual mobilization of arms and legs + breathing exercises + dynamic exercises	Quality of life (German version of the European Organization of Research and Treatment of Cancer Quality of Life questionnaire (EORTC QLQ-C30) and its breast-cancer-specific module EORTC QLQ-BR23)
Temur[73] (2019) Turkey	RCT	N= 72 **Intervention group; n = 36** *Age, mean ±SD*: 46.7 ± 9.96 *Stage, n (%):* I: 2 (7)/ II: 16 (53)/ III: 12 (40) *Sx type, n (%):* MRM: 22 (73)/ BCS: 8 (27) **Control group; n= 36** *Age, mean ±SD*: 45.6 ± 9.03 *Stage, n (%):* I: 2 (7)/ II: 16 (52)/ III: 13 (12) *Sx type, n (%):* MRM: 17 (55)/ BCS: 14 (45)	**Intervention group** Self-management of LE program (SMLP) + exercising program + simple LD *SMLP program:* Training booklet containing information about mechanisms and risk factors of LE and about prevention interventions" *Exercising program:* Hand squeezing exercises, active and passive arm exercises *Frequency:* 3-6 times/day at first and gradually increased to 10 *Exercise sessions duration*: 30-60 min *Duration*: 6 months	Upper extremity function (DASH) Presence of LE- upper extremity CIRC (Measuring tape) Quality of life (EORTC QLQ-30 and EORTC QLQ-BR23)

			Simple lymphatic drainage: Deep diaphragmatic breathing exercises, neck drainage, axillary drainage and UE drainage. *Frequency of breathing exercises*: 3 times a day *Frequency of self-massage*: 2 times a day **Control group** Usual post-op care	
Teodózio[74] **(2020)** **Brazil**	RCT	N=572 **Free ROM group, n=254** *Age, mean ± SD*: 52.54 ± 12.03 *Sx type, n (%):* Segmentectomy: 107 (42) MX: 147 (58) **Restricted ROM group, n=211** *Age, mean ± SD*: 54.53 ± 10.95 *Sx type, n (%):* Segmentectomy: 94 (45) MX: 117 (56)	**Free ROM group** Active UL movements with ROM over 90° (leaflet + home guide) **Restricted ROM group** Active UL movements with ROM restricted to 90° from 1st pod until removal of all surgical stitches (leaflet + home guide) *Initiation*: 1st postop day *Frequency*: 3 times/day (at least once a day)	Presence of seroma Necrosis Dehiscence Hematoma Infection Bruise
Testa[75] **(2014)** **Italy**	RCT	N=70 **Treated group, n=35** *Age, mean ± SD*: 54.3 ± 8.02 *Stage*: N/A *Sx type, n (%):* Maddens' MRM: 19 (54) Segmental MX + ALDN: 16 (45) *Systemic treatment, n (%):* Ch: 24 (69)/ RT: 30 (86) **Control group, n=35** *Age, mean ± SD*: 55.3 ± 8.5 *Stage*: N/A *Sx type, n (%):* Maddens' MRM: 21 (60) Segmental MX + ALDN: 14 (40) *Systemic treatment, n (%):* Ch: 25 (71)/ RT: 27 (77)	**Treated group** Early physical rehabilitation program from latest guidelines for rehabilitation in BC *Initiation*: 2nd postop day *Program duration*: 40 min *Frequency*: 5 times / w during all the duration of axillary drainage Once drainage removed (approximatively postoperative day 7): 20 PT sessions *Frequency*: 5 times / w *Duration*: 60 min / session **Control group:** *N*o early physical rehabilitation program with no instructions of a PT. Rehabilitation program from the old rehabilitation guidelines	Mobility of the glenohumeral joint (goniometer) Grade of pain perceived (VAS) Quality of life (EORTC QLQ30 and QLQ-BR23)
Todd[76] **(2008)** **UK**	RCT	N= 116 **Delayed shoulder mobs; n=58** *Age, mean ± SD*: 56.5 ± 12.4 *Stage, n (%):*	**Delayed shoulder mobs** Exercise program that limited arm movements < 90° in all planes, followed by a full shoulder ROM program	Incidence of LE-limb VOL difference (Water displacement)

		I: 8 (14)/ II: 24 (41)/ III: 26 (45) *Sx type, n (%):* WLE: 36 (57)/ MX: 24 (43) *Systemic treatment, n (%):* RT: 39 (67)/Ch: 30(52)/HT: 34 (59) **Early full shoulder mobs; n= 58** *Age, mean ± SD:* 57 ± 14 *Stage, n (%):* I: 8 (14)/ II: 27 (48)/III: 23 (38) *Sx type, n (%):* WLE: 29 (50)/ MX: 29 (50) *Systemic treatment, n (%):* RT: 41 (71)/Ch: 26(45)/ HT: 41(71)	**Early full shoulder mobs** Full shoulder mobilization (i.e., movement > 90°) and shoulder ROM exercises *Initiation:* *Limited ROM program*: 2nd pod *Full ROM program:* 2nd post op w *Exercise sessions duration*: 10 minutes *Frequency*: 4 times/day until full shoulder ROM was restored and then once/day for the 1st postop year	Shoulder ROM (Manual goniometer) Grip strength (hand-held dynamometer) Health-related QoL (FACT-B+4 and SDQ)
Torres[77] (2010) Spain	RCT	N= 120 **Early physiotherapy group; n = 60** *Age, mean ± SD*: 52.9 ± 10.7 *Stage*: N/A *Sx type, n (%):* QT: 24 (40)/Modified MX: 23 (38)/ LUMP:13 (22) *Systemic treatment, n (%):* RT: 44 (75)/Ch: 50(85)/HT: 39 (66) **ED strategy group; n = 60** Age, mean ± SD: 52.9 ± 12.5 *Stage*: N/A *Sx type, n (%):* QT: 26 (43)/ Modified MX: 20 (34)/LUMP:14(23) *Systemic treatment, n (%):* *RT*: 49 (86)/*Ch*: 45(79)/*HT:* 33 (58)	**Early physiotherapy group** MLD + progressive massage of the scar, stretching exercises and progressive active and action assisted shoulder exercises, combined with functional activities and proprioceptive neuromuscular exercises + ED strategy **ED strategy only group** Instruction with printed materials about the lymphatic system, concepts of normal load vs overload, source of 2ndary LE, precipitating factors and 4 preventive interventions *Initiation*: 3 to 5 days after hospital discharge *Duration of both programs*: 3 w *Frequency of both programs*: 3 times/ w	Incidence of secondary LE (Arm CIRC)
Wingate[78] (1989) USA	RCT	N= 115 **Treated group, n=61** *Age, mean*: 56.26 **Control group, n=54** *Age, mean:* 58.27	**Treated group:** Physical therapy: active hand, wrist, elbow and postural exercises, active and active assisted shoulder exercises, functional activities and PNF After drain removal: HB program with progressive restrictive exercises and PNF *Initiation:* 1st postop day *Duration:* 8 w minimum *Frequency:* 2 session / day Exercise sessions duration: 30 min **Control group** Untreated group with no physical therapy	-Psychopathologic self-report inventory (SCL-90-R) -Shoulder ROM for flexion and abduction (goniometer) -Functional evaluation of the ipsilateral shoulder (Scale of difficulty) -Upper extremity CIRC measurement

Zhang[79] (2016) China	RCT	N= 1000 **Physical exercise group; n=500** *Age group, n (%):* <50: 272 (54)/ ≥50: 228 (46) *Stage, n (%):* I/II: 211 (42)/ III: 289 (58) *Sx type, n (%):* MRM: 500 (100) **MLD group; n=500** *Age group, n (%):* <50: 266 (53)/ ≥50: 234 (47) *Stage, n (%):* I/II: 197 (39)/ III: 303 (61) *Sx type, n (%):* MRM: 500 (100)	**Physical exercise group** Physical exercise alone *Initiation*: 24h before surgery with patient ED *Frequency*: pod 1, 2, 3 and day of discharge *Session duration*: 20-30 min Postop day1-7: Passive exercises *Frequency*: 3 times / day *Session duration*: 15 min. Postop day7-30: (after drain removal to sutures removal): Exercises progressed to localized exercises on the affected UL After removal sutures to 6 months: Extensive active exercises involving affected shoulder *Frequency*: 3 times / day *Session duration*: 15 min. **MLD group** Physical exercises + Self MLD *Initiation*: after sutures removal *Frequency:* 3 sessions / day *Session duration:* 30 min	Stage of upper limb LE (Observation and tape-measuring) Scar formation (Vancouver Scare Scale) Shoulder function (max. shoulder abduction)
Zhou[80] (2019) China	RCT	N=92 **Intervention group; n=46** *Age, mean ± SD*: 49.94 ± 8.88 *Stage, n (%):* I: 18 (35)/ II: 27 (53)/ III: 6 (12) *Sx type, n (%):* MX + SND: 24 (47)/MX + ALND: 15 (29) BCS + SND:10(20)/BCS +ALND:2(4) *Systemic treatment, n (%):* Ch: 41 (80) **Control group; n=46** *Age, mean ± SD*: 49.40 ± 9.88 *Stage, n (%):* I: 14 (28)/II: 29 (57)/III: 8 (16) *Sx type, n (%):* MX + SND: 25 (49)/MX + ALND: 17 (33) BCS + SND: 6(12)/BCS +ALND: 3(6) *Systemic treatment, n (%):* Ch: 43 (84)	**Intervention group** Progressive UL exercises and muscle relaxation training by nurses *Initiation*: before surgery *Duration*: 6 months *Frequency:* 1 session/ day at hospital and 1 session/ week at home after discharge **Control group** Routine nursing care (surgery district nursing, drainage tube nursing, routine health ED, physical exercises, vital sign monitoring and post-surgery complications)	Quality of function (Constant-Murley Score) HRQOL (FACT-Bv4.0)
Zimmermann[81] (2012) Germany	RCT	N=67 **MLD group; n=33** *Age, mean ± SD*: 60.3 ± 8.2 Stage, n (%): I: 12 (36)/ II: 15 (46)/ III: 6 (18)	**Both groups** Exercises of limb and chest physiotherapy *Initiation*: 2nd postop day **MLD group** *Manual lymph drainage*	VOL of both arms (water displacement With glass cylinder with water) VOL of LE

		Sx type, n (%): BCS: 20 (61)/ MRM: 13 (39) SND:14 (42)/ ALND: 19 (58) *Systemic treatment, n (%):* Ch: 13 (39)/RT: 22 (67) **Control group; n=34** *Age, mean ± SD*: 58.6 ± 12.2 *Stage, n (%):* I: 11 (32)/II: 16 (47)/III: 7 (21) *Sx type, n (%):* BCS: 20 (59)/ MRM: 14 (41) SND: 18 (53)/ ALND: 16 (47) *Systemic treatment, n (%):* Ch: 15 (44)/RT: 25 (74)	*Initiation:* 14th postop day *Duration*: 6 months *Frequency:* 5 sessions/ week **Control group** Applied self-drainage from modification of the method described by Földi and Strönbenreuher	
de Oliveira[82] (2014) Brazil	Controlled non-randomized clinical trial	N= 96 **Exercise group; n = 48** *Age, mean ± SD*: 56.7 ± 15.1 *Stage, n (%):* I: 1 (2)/ II: 17 (37)/ III/IV: 28 (61) *Sx type, n (%): MRM:* 48 (100) *Systemic treatment, n (%):* *Neoadj Ch:* 22 (48) **MLD group; n = 48** *Age, mean ±SD*: 55.6 ± 11.9 *Stage, n (%):* I: 0 (0)/ II: 9 (20)/III/IV: 34 (79) *Sx type, n (%):* MRM: 42 (62)/Halsted RM: 1 (2) *Systemic treatment, n (%):* Neoadj Ch: 29 (67)	**Both groups** *ED strategy:* Information leaflets about proper care for the OA and lectures delivered by a multi-D team *Initiation*: 1st post-op day **Exercise group** 19-exercise supervised program including neck and rotator cuff muscles stretching and active assisted and free AROM exercises *Initiation*: 3rd post-op day *Duration:* 2 days/w for 30 days *Exercise sessions duration:* 40 min **MLD group** MLD applied by 3 experienced PT *Initiation*: 3rd post-op day *Duration*: 2 days/w for 30 days *MLD sessions duration*: 40 min	Upper limb CIRC (Measuring tape) Shoulder ROM (Goniometer) Scarring complications (Signs of wound dehiscence, infection, seroma and puncture)
Na[83] (1999) South Korea	Controlled non-randomized clinical trial	N= 33 **Rehabilitation group; n = 20** *Age, mean ±SD*: 43.8 ± 2.1 *Stage*: N/A *Sx type, n (%):* MRM: 15 (75)/Partial MX: 5 (25) **Control group; n = 13** Age, mean ± SD: 46.9 ± 9.8 Stage: N/A *Sx type*, n (%): MRM: 7 (54)/Partial MX: 6 (46)	**Rehabilitation group** Early postmastectomy rehabilitation program *Initiation*: 1st post-op day *Duration*: 4w (40 min of PT and 30 min of exercises) *Frequency*: 4 times/day *1st postop day:* Postural exercises, AROM of the shoulder, elbow, wrist, and hands with active use of the involved arm *From the 3rd postop day:* Physical modalities for pain relief and therapeutic exercises	Symptoms Checklist (SCL-90-R) Shoulder ROM (Goniometer) Shoulder function (10 items provided by Wingate) Upper limb circumference (Tape measurement)

			After drains removal: Progressive resistance exercises with an increase in functional activities **Control group** Instructions alone for ROM exercises pertaining to the affected shoulder and postural exercises	
Oliveira[84] (2018) Brazil	Controlled non-randomized clinical trial	N=116 **Active exercise group; n=58** *Age group, n (%): <55:* 22 (42)/ *≥55:* 31(59) *Stage, n (%):* I: 1 (20)/II: 17 (34)/III/IV: 32 (64) *Sx type, n (%):* MRM Patey: 29 (55)/MRM Madden: 24 (45) RM Halsted: 0 (0) *Systemic treatment, n (%):* Neoadj Ch: 24 (45)/Adj Ch: 8 (36) RT: 16 (73)/ HT: 14 (64)/ IT: 3(14) **MLD group; n=58** *Age group, n (%): <55:* 24 (45)/*≥55:* 29 (55) *Stage, n (%):* I: 0 (0)/II: 9 (18)/III/ IV: 43 (82) *Sx type, n (%):* MRM Patey: 19 (36)/MRM Madden: 33 (62) RM Halsted: 1 (2) *Systemic treatment, n (%):* Neoadj Ch: 36 (68)/Adj Ch: 18 (62) RT: 26 (87)/HT:18 (60)/ IT: 5 (17)	**Both groups** Educational strategy: Information leaflets about proper care for the OA and daily active exercises to do at home) + lectures delivered by the multidisciplinary team during the first month after surgery. *Initiation:* 1st postop day **Active exercise group** *Initiation*: 48h after surgery *Duration:* 30 days *Frequency:* 40 min group session, 2/w **MLD group** Manual lymphatic drainage *Initiation*: 48h after surgery *Duration*: 30 days *Frequency:* 40 min individual session, 2/w	Velocity visualization of axillary lymph nodes and degree uptake in axillary lymph nodes (Lymphoscintigraphy) ROM Upper limb CIRC
Kim[89] (2019) South Korea	Retrospective case-control study	N= 115 **Early rehabilitation group; n = 49** *Age (age range):* 43 (34-61) *Stage*: N/A *Sx type*: Skin-sparing total MX and immediate Brecons with tissue expander *Type of node dissection, n (%):* SNB: 41 (84)/ ALND: 8 (16) *Systemic treatment, n (%):*Neoadj Ch: 3 (6) **Conventional protocol; n = 66** *Age (age range):* 42 (24-61) *Stage*: N/A *Sx type*: Skin-sparing total MX and immediate Brecons with tissue expander *Type of node dissection, n (%):* SNB: 46 (70)/ ALND: 20 (30) *Systemic treatment, n (%):* Neoadj Ch: 7 (11)	**Both groups** Self-exercise ED *Initiation*: 1st post-op w **Early rehabilitation group** Short term immobilization period (2w) followed by a self-exercise program including progressive shoulder stretch exercises and strengthening exercises *Initiation*: 3rd post-op w *Frequency*: 4 times a day/ 7 days per w **Conventional protocol** Were asked to immobilize the OA for more than 4w and engaged themselves in the same self-exercise program after the immobilization period *Initiation:* From the 5th post-op w *Frequency*: 4 times a day/ 7 days per w	Shoulder ROM (goniometer) Pain (NRS-11) QoL (SF-36) Upper limb function (DASH) Postoperative complications (Plastic surgeon assessment)

Lu[88] (2015) Taiwan	Retrospective cohort study	N= 1217 **Group A; n= 415** *Age, mean ± SD*: 51.79 ± 11.97 *Stage, n (%):*0-2: 326 (79)/ 3: 89 (21) *Sx type, n (%):* BCS: 123 (30)/Simple MX: 25 (6) MRM: 267 (64) *Systemic treatment, n (%):* RT: 182 (44)/ Ch: 342 (82) **Group B; n = 672** *Age, mean ± SD*: 52.67 ± 11.01 *Stage, n (%):*0-2: 503 (75)/ 3: 169 (25) *Sx type, n (%):* BCS: 152(23)/ Simple MX:11(2)/ MRM: 509(76) *Systemic treatment, n (%):* RT: 297 (44)/ Ch: 549 (82) **Group C; n = 130** *Age, mean ± SD*: 51.88 ± 10.08 *Stage, n (%):* 0-2: 92 (71)/ 3: 38 (29) *Sx type, n (%):* BCS: 303(25) Simple MX: 41(3)/MRM: 873(72) *Systemic treatment, n (%):* RT: 66 (51)/ Ch: 111 (85)	**Group A** No ED or PT provided **Group B** ED only which provided information on the lymphatic system, the symptoms and signs of LE, suggestions for preventing LE. **Group C** ED + PT sessions which included the following treatments: breathing exercise, postsurgical positioning, massaging of scar tissue, mobs of the shoulders and UE exercises, passive and active stretching of the major and minor pectoral muscles *Initiation*: 1st postop w in the hospital and was continued at outpatient clinics post discharge *Frequency*: 2 times/w PT sessions duration: 30 min	Occurrence of LE (Limb-to-limb CIRC difference) LE severity (Criteria defined by the International Society of Lymphology)
Morimoto[87] (2003) Japan	Prospective observational study	N=72 BC women stage I or II **PCM group; n=33** *Age, mean ± SD*: 50.0 ± 11.0 *Stage*: N/A *Sx type*: PCM **BCS group; n=38** *Age, mean ± SD*: 50.8 ± 8.8 *Stage*: N/A *Sx type*: BCS	**Both groups** Initiation: postoperative day 1 Duration: After hospital discharge, was entrusted to the patient's own initiative *Postoperative day 1:* Prevention of development of rigidity of shoulder joint on the OA: Lateral and forward arm raising on the affected side in the dorsal sitting positions *Postoperative day 2:* Training for force releasing through exercise of shoulder joint *Postoperative day 3:* Exercise to approximate preoperative life *Postoperative day 4:* Exercise to reduce functional differences between the normal and affected sides	Shoulder joint ROM (goniometer) Grip strength Pain after surgery Movement associated chest pain Operative wound pain ADL (Ability to sleep on the affected side, ability to tie an apron, ability to air the futon in the sun)

Scaffidi[86] (2012) Italy	Prospective observational study	N=83 **Group A; n=25** *Age, mean ± SD*: 49.6 ± 8.8 *Sx type, n:* *LUMP:* 10 with 7 SND and 3 ALND *RM:* 15 with 2 SND and 13 ALND **Group B; n=58** *Age, mean ± SD*: 52.1 ± 11.9 *Sx type, n:* *LUMP:* 35 with 26 SND and 9 ALND *RM:* 23 with 6 SND and 17 ALND	**Group A** Preoperative information orally + home rehabilitation program **Group B** Preoperative information orally + information materials + PT treatment at hospital + home rehabilitation program PT at hospital: 1 per day, 30-40 min Home rehab program: 3 times/ day	Shoulder arm mobility (goniometer) Upper limb function (Constant and Murley Score) Presence of LE (Universal level meter)
Springer[85] (2010) USA	Prospective observational study	N=94 Age, mean ± SD: 53.39 ± 11.80 *Stage, n (%):* 0: 11 (12)/ I: 40 (43)/ II: 30 (32)/III: 13 (14) *Sx type, n (%):* BCT: 41(44)/MRM: 50(53)/Simple MX: 3(3) Lymph nodes dissection, n (%): None: 8 (9)/SND: 20 (21)/ALND: 66 (70) *Systemic treatment, n (%):* Ch: 57 (61)/RT: 64 (66)/HT: 67 (7)	**Upper Limb ROM program** Flexion, abduction, internal and external rotation Pre-operative examination: subjects were instructed in a post-operative UL ROM exercise program, and were educated regarding UL LE precautions and physical exercise initiation and progression *Initiation*: post-surgery Reviewed at 1 month	Pain (NRS) Bilateral shoulder ROM (Goniometer) Bilateral shoulder strength (Break testing of upper limbs) Volume and girth measurements for both upper limbs in standard position (Optoelectronic volumeter, Perometer®) Upper limb function and disability (Upper Limb Disability Questionnaire)
Hsieh[91] (2008) USA	Pretest and post-test quasi-experimental study	N= 96 Women referred by local oncologists for rehabilitative exercises *Sx type:* N/A *Stage*: N/A **Surgery alone; n = 22** *Age, mean ±SD*: 55.6 ± 11.3 **Surgery and Ch; n = 30** *Age, mean ±SD*: 55.6 ± 11.0 **Surgery and RT; n= 17** *Age, mean ±SD*: 57.2 ± 9.4 **Surgery, Ch and RT; n = 27** *Age, mean ±SD*: 63.1 ± 9.8	**All groups** Individualized exercise intervention based on the results of the medical and cancer history, physical examination, and the initial physiologic and psychological assessments *Initiation*: immediately following treatment for BC *Exercise sessions duration* 10-min warm-up, 40-min of aerobic exercises, resistance training and stretching and concluded with a 10-min cooldown *Intensity*: 40-65% of HR reserve (based on the treadmill assessment results)	Cardiovascular endurance (Bruce Treadmill Protocol; HR, BP, predicted VO_{2max}, time on treadmill and oxygen saturation) Pulmonary function- FVC, FEV_1 (Flowmate™ spirometer) Cancer-related fatigue (Piper Fatigue Scale)

Petito[92] (2012) Brazil	Quasi-experimental, before and after study	N=64 **Mastectomy group; n=43** *Age, mean ± SD*: 52.2 ± 9.6 *Sx type, n (%):* MRM: 37(86)/ Simple MX:4 (9)/ RMX:2 (5) **QT group; n=21** *Age, mean ± SD*: 63.4 ± 9.0	**Exercise program** *Initiation*: 1st post-op day *Duration*: 105 post-op days *Frequency*: daily *Phase 1 (until drain removal):* Two stretches for the cervical region, two exercises for movement of the scapular girdle, one for shoulder flexion and one for extension beyond the midline *Phase 2 (after drain removal)* Three additional exercises: one exercise for flexion and two for abduction of the shoulder.	Shoulder ROM: flexion, extension, abduction (goniometer)
Singh[93] (2013) Canada	Quasi-experimental pretest post-test study	N= 73 **Experimental group; n = 42** *Age, mean ± SD*: 55.1 ± 14.8 *Stage, n (%):*0 or I: 2 (5)/ II: 14 (34) III: 19 (46)/ N/A: 6 (15) *Sx type, n (%):* MRM: 22 (54)/ Simple MX: 7 (17) BCS: 12 (29)/B recons: 22 (54) *Systemic treatment, n (%):* RT: 22 (54)/Ch: 16 (39) **Comparison group; n = 31** *Age, mean ± SD:* 62.8 ± 14.1 *Stage, n (%):* 0 or I: 2 (7)/ II: 10 (32) III: 13 (42)/ N/A: 6 (19) *Sx type, n (%):* MRM: 7 (23)/Simple MX: 9 (29) BCS: 15 (48)/ Brecons: 3 (10) *Systemic treatment, n (%):* RT: 14 (45)/Ch: 16 (32)	**Experimental group** Standardized preoperative ED + PT treatment if needed focusing on teaching self-management strategies, scar tissue massage and AROM and assisted shoulder exercises *Standardized preoperative ED program:* -General postop mobility exercises -AROM exercises -ED on LE -Scar management **Comparison group** Standardized preoperative ED alone	Arm mobility-Shoulder ROM (goniometer) Presence of LE (Arm CIRC, tape measure) UE strength (Manual muscle testing) UE function (DASH) Quality of life (FACT-B+4) Postoperative pain (VAS)
Rekha[90] (2020) India	Quasi-experimental study	N= 20 *Age range*: 40-60 *Sx type*: Unilateral BSx (MX or BCS) within a month	**Group A; n= 10** Swiss ball exercises + diaphragmatic breathing exercises (10 repetitions) *Duration:* 4w; 5 days/w **Group B; n= 10**: Stretching exercises + diaphragmatic breathing exercises (10 repetitions) *Duration:* 4 w; 5 days/w	Chest expansion (inch tape) -FEV_1 (computerized spirometer) - Shoulder ROM (goniometer)

Kilgour[94] (2008) Canada	Pilot study	N= 40 **Home-based exercise (HBE) group; n = 20** *Age, mean ± SD*: 50.6 ± 9.3 *Stage, n (%):* N/A *Sx type*: MRM + ALDN **Usual care (UC) group; n = 20** *Age, mean ± SD*: 49.1 ± 5.7 *Stage, n (%):* N/A *Sx type*: MRM + ALDN	**HBE group** HB exercise video program that incorporated the exercises and guidelines described in a brochure from CCS *Initiation*: 3rd postop day *Phase 1 (Day3-9):* Self- adm shoulder ROM and flexibility exercises *Frequency*: 3 set/day *Sets duration*: 5-7 minutes *Phase 2 (Day 10-14):* Same exercises as Phase 1 *Frequency*: 2 sets/day *Sets duration*: 10-15 min **UC group** Received information on diet and skin scare and a 9-page brochure containing stretching and ROM shoulder exercises printed by the CCS, without further instructions	Shoulder ROM (goniometer) Shoulder strength (Manual muscle testing techniques) Grip strength (Hand-grip dynamometer) Forearm CIRC (Tape measurement) Frequency of medication intake, VOL of fluid from the axillary drains and self-perceived pain level (CR-10 Pain Scale) and exertion (Borg Scale)
Baima[95] (2017) USA	Feasibility study	N= 60 *Age, mean, stage and systemic treatment*: N/A *Sx type*: MX or lumpectomy **Gr 1- in person teaching; n= 36** **Gr 2- video-only teaching; n= 24**	**Both groups** Prehabilitation exercise program and postsurgery shoulder ROM exercises restrictions > 90° until drains were removed *Initiation* 1-4w prior to surgery *Frequency*: once daily, suspended postsurgery **Group 1- in person teaching** Physical demonstration and instructions of supervised shoulder ROM exercises **Group 2- video-only teaching** Instruction's sheet of shoulder ROM exercises and optional exercises video without additional supervision	Pain (NRS-11) Shoulder abduction ROM (Goniometer) Postoperative seroma formation

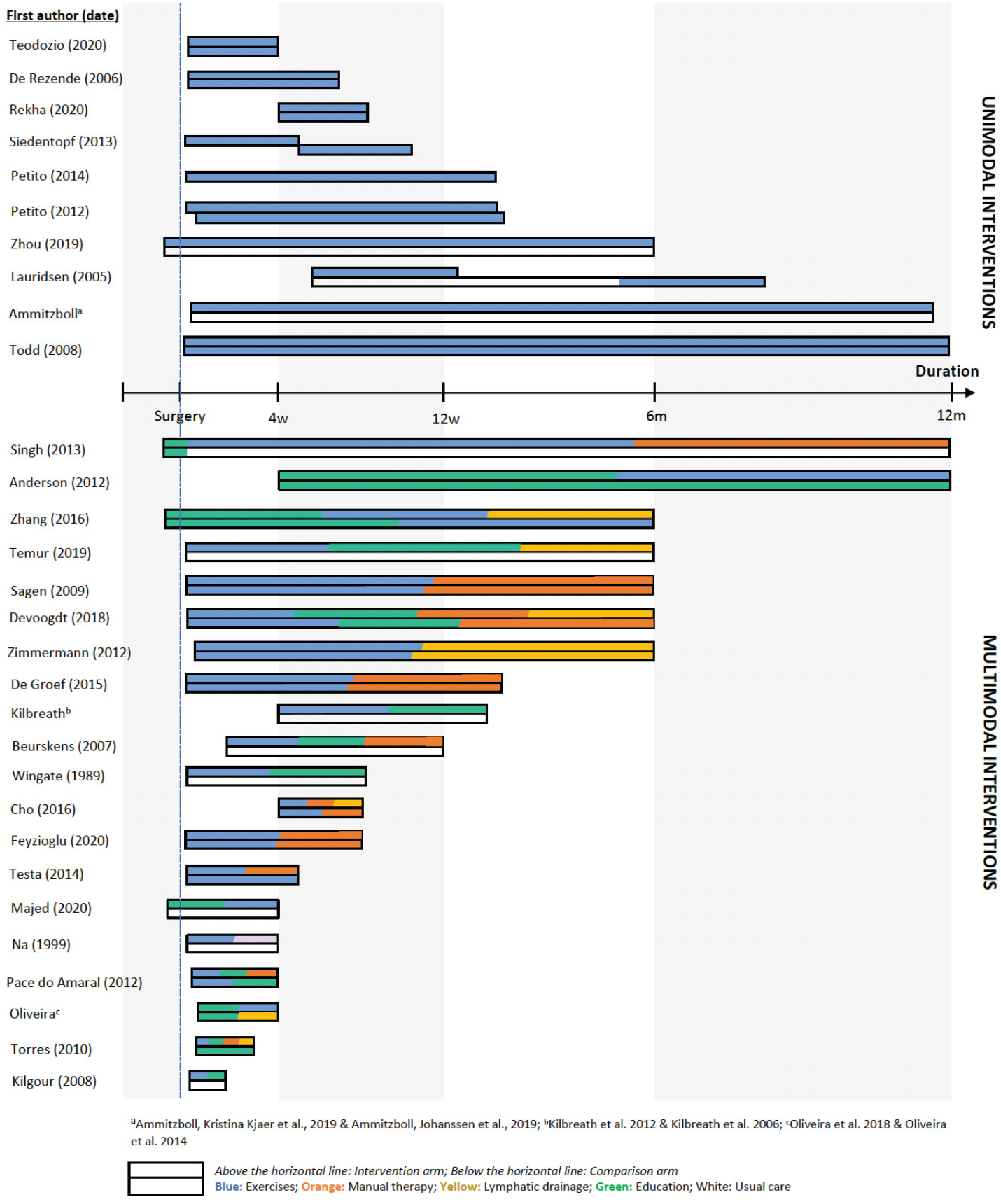
***ADL**: Activities of daily living; **Adj Ch**: Adjuvant chemotherapy; **ALND:** Axillary lymph node dissection; **AROM**: Active range of motion; **AWS**: Axillary web syndrome; **BC**: Breast cancer; **BCS:** Breast conserving surgery; **BP**: Blood pressure; **BSx:** Breast surgery; **B recons**: Breast reconstructive surgery; **CCS**: Canadian Cancer Society; **CIRC**: Circumference; **Ch:** Chemotherapy; **CG**: Control group; **DASH**: Disabilities of the Arm, Shoulder and Hand; **DXA:** Dual-energy X-ray absorptiometry; **ED**: Education; **EORTC QLQ:** European Organization for Research and Treatment of Cancer quality of life questionnaire; **FACT-B**: Functional Assessment of Cancer Therapy-Breast; **FEV_1:** Forced expiratory volume in one second; **FVC:** Forced vital capacity; **HB**: Home-based; **HR**: Heart rate; **HRQOL:** Health-related quality of life; **HT:** Hormonotherapy; **IG**: Intervention group; **IVLD**: Interlimb volume difference; **KBR:** Kinect based rehabilitation; **LE**: lymphedema; **LUMP**: Lumpectomy; **MFBIA**: Multi-frequency bioimpedance; **min**: minutes; **MLD**: Manual lymphatic drainage ; **Mobs:** mobilizations**; MRM**: Modified radical mastectomy; **MT:** Manual therapy; **MX**: Mastectomy; **N/A**: Not available; **Neoadj**: Neoadjuvant; **NRS:** Numeric Rating Scale; **OA**: Operated arm; **OT**: Occupational therapist; **PCM**: Pectoral muscle-conserving mastectomy; **PROM**: Passive range of motion; **PT**: Physical therapy(ist); **QT:** Quadrantectomy; **RCT:** Randomized controlled trial**; RM:** Repetition maximum; **RMX:** Radical mastectomy; **ROM:** Range of motion; **RPE:** Rated Perceived Exertion; **RT:** Radiotherapy; **SD**: Standard deviation; **SDQ**: Shoulder Disability Questionnaire; **SIP**: Sickness Impact Profile; **SNB:** Sentinel lymph node biopsy; **SND**: Sentinel lymph node dissection; **ST**: Soft tissue; **TKS**: Tampa Kinesiophobia Scale; **UE:** Upper extremity; **UL:** Upper limb; **VAS**: Visual Analog Scale; **VOL**: Volume; **w**: week; **WLE**: Wide local excision; **6MWT**: 6-Minute Walk Test*

Conservative rehabilitation interventions

Four main different modalities were identified amongst rehabilitation programs, which were consistent with exercises, patient education, lymphatic drainage, and manual therapy. Exercises were part of every rehabilitation program, with 39.1% (18 out of 46) of these interventions being unimodal. Multimodal interventions were characterized by 2 to 4 modalities, the most common combinations being: (1) exercise and patient education (23.9%); (2) exercise and manual therapy (8.7%); (3) exercise, patient education and manual therapy (8.7%); and (4) exercise, patient education and lymphatic drainage (8.7%). Nearly half of rehabilitation interventions (45.7%) were delivered using a mixed approach, being initially performed under nursing staff or physical therapists' supervision, and in most instances, transitioned to a home-based intervention upon hospital discharge. Home-based only interventions (15.2%) all consisted of exercises, which were either performed alone (69, 74, 89, 92) or combined with patient education (67, 85, 94).

Five studies reported implementing group interventions, consisting solely of supervised exercise programs (61, 72, 80, 84) or of exercises combined with manual therapy (68). Of all the included studies, 7 interventions (67, 79, 80, 85, 86, 93, 95) were initiated prior to surgery, 6 of which consisted of patient education combined with exercises.

Figure 9 illustrates the timing, duration, and modalities characterizing the rehabilitation interventions identified. This graphical representation was constructed only for studies that clearly defined all three components. Looking at these studies (33 out of 46), we noted that 84.8% of interventions were initiated a few days to 4 weeks following surgery and went on for 2 to 24 weeks, while 3 interventions (52, 88, 93) lasted up to 12 months.



[a]Ammitzboll, Kristina Kjaer et al., 2019 & Ammitzboll, Johanssen et al., 2019; [b]Kilbreath et al. 2012 & Kilbreath et al. 2006; [c]Oliveira et al. 2018 & Oliveira et al. 2014

Above the horizontal line: Intervention arm; Below the horizontal line: Comparison arm
Blue: Exercises; **Orange:** Manual therapy; **Yellow:** Lymphatic drainage; **Green:** Education; White: Usual care

Figure 9: Initiation, duration and modalities characterizing rehabilitation interventions

Exercises

Types of exercises included in the rehabilitation programs are detailed in Figure 10. Eleven types of exercises were identified, the most frequently reported being: (1) upper limb ROM exercises (76.1%); (2) stretching of shoulder muscles (41.3%) and (3) upper limb strengthening exercises (34.8%). Although a small proportion of studies (23.9%) suggested a single type of exercise, most built programs that included 2 to 5 different types of exercises. Exercises targeting upper limb tissues and function were predominant, while fewer studies adopted a more global approach, providing aerobic exercises (52, 54, 91) or yoga (72), as well as strengthening or stretching of the lower extremity (50-52) or of neck muscles (59, 75, 82, 84, 86, 92).

Patient education

Educational strategies were included in 45.7% (21 out of 46) of rehabilitation interventions identified. Prevention and lymphedema awareness, skin care routine, risks of postoperative complications, as well as physical activity or nutrition counseling were the cornerstones of these strategies. Patient education was mostly provided postoperatively, while 6 educational strategies were shared prior to surgery, although focusing on similar components. One study (67) explicitly mentioned having the patient informed about the surgical procedure's characteristics in the preoperative period. Five studies also reported prescribing shoulder ROM limitations and activity restrictions (e.g., avoiding lifting, carrying heavier items, running, jumping or other strenuous activities) up to 6 weeks following surgery (53, 63, 70) or upon surgical drains removal (67, 95).

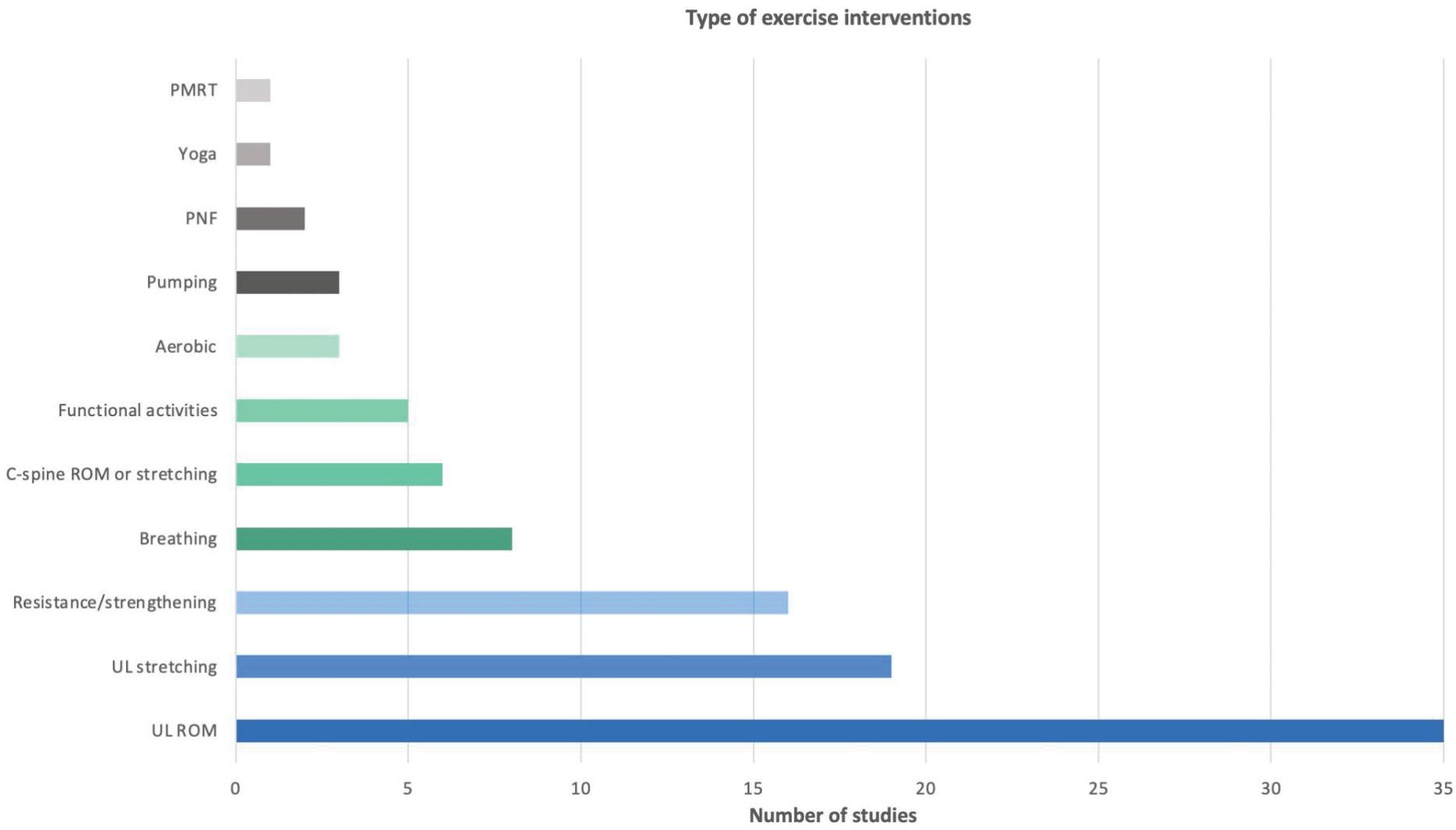


Figure 10: Types of exercise used in rehabilitation interventions

PMRT: *Progressive muscle relaxation training;* ***PNF:*** *Proprioceptive neuromuscular facilitation;* ***C-spine:*** *Cervical spine;* ***ROM:*** *Range of motion;* ***UL:*** *Upper limb*

Lymphatic drainage

Eight studies (57, 62, 73, 77, 79, 81, 82, 84) included lymphatic drainage within their rehabilitation programs. Gentle pressure and circular massage were generally applied along the course of superficial lymph nodes lining in the axillary region, at the lateral aspect of the shoulder, at the base of the neck, in the chest region, and on both the affected and non-affected arm and hand. Lymphatic drainage was performed either by trained physical therapists (PTs) or self-administered following supervised sessions. While most studies reported on initiating this modality a few days following surgery without further indications, two studies (62, 79) described waiting for suture and surgical drains removal before proceeding.

Manual therapy

Eleven studies incorporated manual therapy into their rehabilitation programs. This modality was always paired up with exercises, and in some cases complemented with lymphatic drainage (57, 62, 77). Manual therapy was mainly characterized by passive scapular and shoulder joint mobilizations, scar tissue massage and passive shoulder muscles stretching performed by trained PTs (54, 57, 62, 63, 68, 77, 93). Two studies also included passive mobilizations of the elbow, wrist, and hand on the affected side (62, 75).

Clinical outcome measures

Three categories of outcome measures were used to report the effects of rehabilitation interventions on breast cancer patients undergoing mastectomy, which included objective measures of physiological function, objective measures of physical function, and patient self-reported outcome measures (PROMS). Figure 11 illustrates the outcomes investigated in each category and the measurement tools used for each of them. The most commonly reported outcomes regarding physical function were shoulder ROM, muscle strength and signs of lymphedema. Although these outcomes were reported through a range of measurement tools, the most common ones were, respectively, the goniometer for shoulder ROM, the dynamometer for muscle strength and arm circumference or arm volume for signs of lymphedema. Quality of life, shoulder function and pain were the PROMS most often reported. The European Organization for Research and Treatment of Cancer questionnaire (EORTC QLC C-30/BR23), the Disability of the Arm, Shoulder and Hand questionnaire (DASH) and the Visual Analogue Scale (VAS) were respectively the most frequently used outcome measures for these three domains. Three studies also investigated objective measures of physiological function, such as chest expansion (90), the forced expiratory volume in one second (FEV1) (90, 91) and the forced vital capacity (FVC) (91).

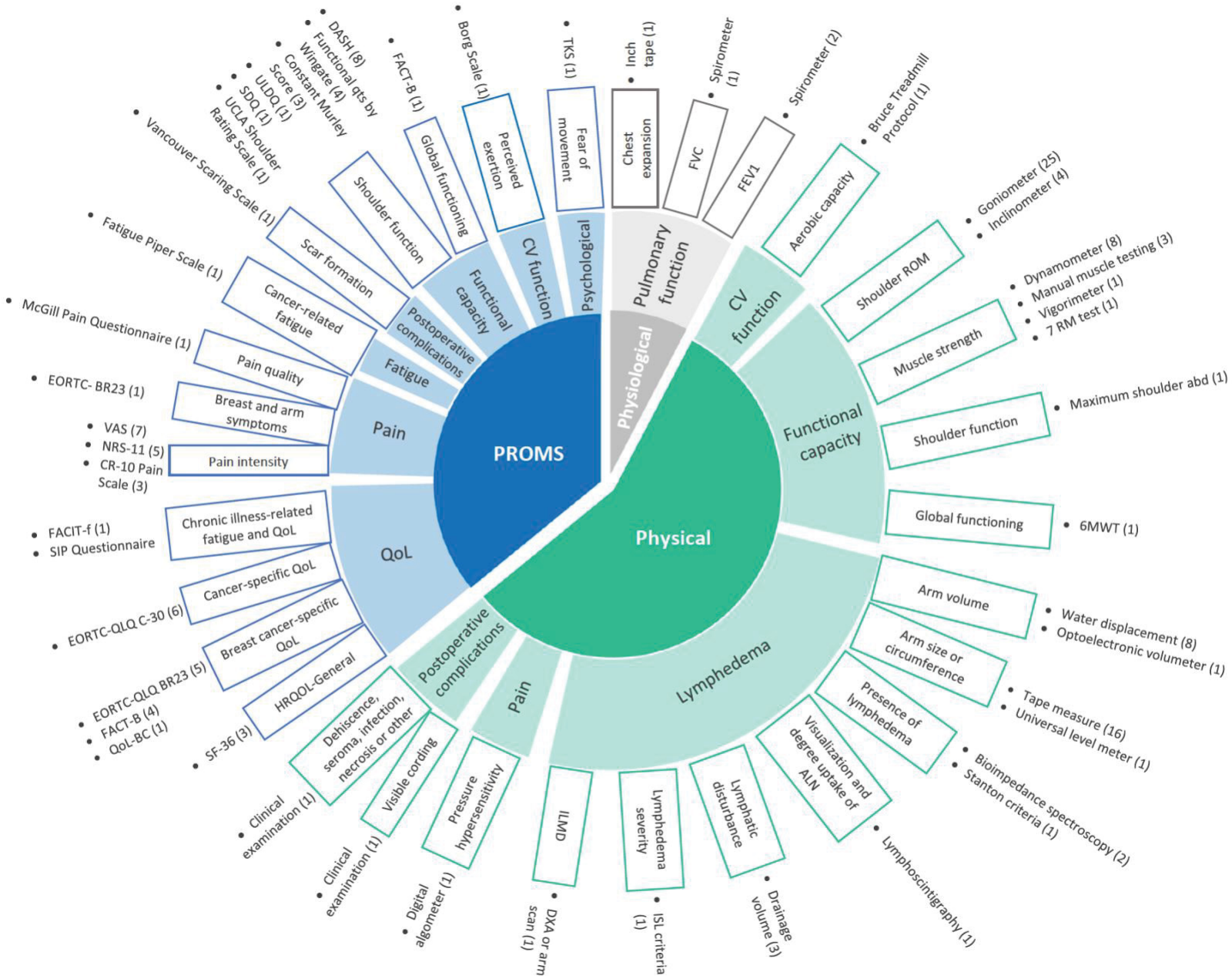


Figure 11: Outcome measures

Abd : *Abduction;* ***ALN:*** *Axillary lymph nodes;* ***BC:*** *Breast Cancer;* ***CV:*** *Cardiovascular;* ***DASH:*** *Disabilities of the Arm, Shoulder and Hand;* ***DXA:*** *Dual-energy X-ray absorptiometry;* ***EORTC QLC:*** *European Organization for Research and Treatment of Cancer quality of life questionnaire;* ***FACT-B:*** *Functional Assessment of Cancer Therapy - Breast;* ***FACIT-f:*** *Functional Assessment of Chronic Illness Therapy – Fatigue;* ***FVC:*** *Forced vital capacity;* ***FEV1:*** *Forced expiratory volume in one second;* ***HRQOL:*** *Health-related quality of life* ***ILMD:*** *Interlimb mass difference;* ***ISL:*** *International Society of Lymphology;* ***NRS:*** *Numeric Rating Scale;* ***PROMS:*** *Patient-reported outcome measures;* ***QoL:*** *Quality of life;* ***RM :*** *Repetition Maximum;* ***ROM:*** *Range of motion;* ***SF-36:*** *36-Item Short Form Health Survey;* ***SIP:*** *Sickness Impact Profile;* ***TKS:*** *Tampa Kinesiophobia Scale;* ***UCLA:*** *University of California at Los Angeles;* ***ULDQ:*** *Upper Limb Disability Questionnaire;* ***VAS:*** *Visual analogue scale;* ***6MWT:*** *6-Minute Walking Test*

Patients' experience

Study participation

The number of patients who chose not to engage in rehabilitation interventions was reported in 21 of the 46 selected articles. Of all individuals assessed for eligibility, 2 to 75% declined to participate in each study. The main reasons cited for refusal were disclosed in only 7 studies and were consistent with transportation issues (52, 60, 66), a preference for another intervention (54, 62, 68) or for their own therapist (60, 62), lack of interest (60, 62) and a desire to minimize hospital appointments in favor of getting back to work and to a normal lifestyle (76).

Compliance with the study protocol

Adherence to rehabilitation interventions was measured in 19.6% of studies (9 out of 46) and deemed reasonable in each case (see Appendix B for details). Coordinating therapy sessions with oncologist appointments (52, 70, 76), follow-up calls and positive reinforcement by physical therapists (55, 56, 73, 94), individualization of interventions based on the patient's needs (91), and support from spouses or family members (94) were identified as factors promoting adherence. Dropout rates were reported in 24 of the 46 included studies and were highly heterogeneous, ranging from 1 to 58%. Main reasons stated for not completing the study were undergoing another breast surgery (50, 51, 53, 59, 69, 70, 73, 74, 92, 95), death (50, 51, 53, 55, 62, 66, 68-70, 76, 84), cancer recurrence or other medical conditions (50, 51, 53, 55, 62, 63, 66), having to deal with systemic treatments-related adverse events (62, 63, 70, 72, 73), moving away (50, 51, 53, 55, 68,

70, 76), lack of interest or time (52, 55, 67) and transportation issues (60, 62). Two studies also identified lack of support from family and friends (94) and hospital anxiety (50) as barriers to completion.

Adverse events

Only six studies included in this review explicitly discussed the occurrence of adverse events. Of these, most studies (5 out of 6) found that the patients' clinical presentation and symptoms were not affected by the intervention. Sagen et al. (70) reported two cases of adhesive capsulitis and one case of supraspinatus tendinopathy. However, the timing of these adverse events was not specified, therefore it is unclear whether these are due to the rehabilitation interventions or related to breast cancer treatments. A significant proportion of studies (22 out of 46) also reported that some participants suffered from postoperative complications. Among these, lymphedema, seroma, wound dehiscence, and scar contracture were the most frequent. Once again, with little or no description of when these complications occurred, it remains unclear whether these were acute or late effects of breast cancer treatments.

Discussion

This scoping review examined the extent and nature of clinical research on perioperative physical rehabilitation for women with breast cancer who were awaiting or had undergone mastectomy. Our main objective was to identify conservative interventions and relevant

clinical outcome measures currently used for this population. As a secondary objective, we aimed to report on barriers and facilitators to participation and completion of these interventions. Over half of the eligible studies included mixed breast cancer stages (0-III) populations, who underwent various types of breast surgery (i.e., total or partial mastectomy), axillary procedures (i.e., biopsy or lymph node resection), and a series of adjuvant treatments. We were also able to determine that most studies identified were randomized controlled trials conducted in high income countries and published within the last 10 years.

Conservative interventions

Four main modalities were identified among rehabilitation programs, which can be categorized as exercises, patient education, manual therapy, and lymphatic drainage. Multimodal rehabilitation interventions were most frequently reported, all of which included exercises primarily focusing on increasing shoulder ROM, as well as stretching and strengthening of shoulder muscles. A few studies also offered aerobic training, yoga classes or exercises targeting lower extremities or neck muscles. Rehabilitation interventions consisted primarily of one-on-one sessions initially performed under supervision in hospital settings until discharge. Modalities' characteristics (e.g., timing, duration, frequency, intensity, etc.) varied significantly across studies, with many of these components being poorly described or not documented. This review also established that rehabilitation interventions were by far most studied after breast surgery, with six studies comparing the effects of an intervention initiated immediately after surgery to those of a

delayed intervention. Only seven interventions were initiated preoperatively, with these consisting primarily of self-management strategies to be implemented in the postoperative period.

The rehabilitation interventions identified in this scoping review reflect, to some extent, the recommendations provided by cancer care guidelines. However, we noted that the eligible studies have placed less emphasis on aerobic training, primarily providing rehabilitation programs that included exercises targeting upper extremity function. Few recommendations concerning rehabilitation strategies to be implemented before surgery were identified, either in the eligible studies or in cancer care guidelines, indicating that further research is needed in this area. In 2017, the World Health Organization (WHO) urged for a coordinated and concerted global action towards improving the accessibility of high-quality rehabilitation services in health systems. Given the systemic effects resulting from cancer and its associated treatments, oncology was designated as a priority area for this initiative (96). Accordingly, a systematic review was conducted to identify and synthesize rehabilitation-specific recommendations provided by most recent cancer care guidelines (97). Of these, the American Cancer Society (ACS)/American Society for Clinical Oncology (ASCO) guideline (98) concluded that there was insufficient evidence to support a specific intervention that would promote optimal postoperative recovery for breast cancer patients. Nevertheless, physical rehabilitation recommendations endorsed by this guideline advised clinicians to encourage their patients to adhere to the ACS's physical activity recommendations (99), which include moderate to vigorous aerobic

exercises and strength training. Returning to normal daily activities as soon as possible after diagnosis, and inclusion of spouses and family members in usual breast cancer care were also both promoted. In turn, to manage breast cancer patients with or at risk for lymphedema, the National Comprehensive Cancer Network (NCCN) Survivorship Guideline (100) recommended a supervised multimodal rehabilitation intervention consisting of progressive resistance training, shoulder ROM exercises, manual lymphatic drainage, education regarding signs and symptoms of postoperative complications and self-care management strategies. This multimodal strategy is also consistent with the recommendations issued from the American College of Sports Medicine guideline (101), which supported the effectiveness of combined moderate-intensity aerobic and progressive resistance training, performed for 8 to 12 weeks, in improving cancer-related health outcomes, including physical functioning, quality of life and fatigue. Interestingly, none of these recommendations provided guidance as to what parameters (i.e., frequency, repetitions, sets, etc.) should characterize shoulder ROM exercises. It should also be stressed that these guidelines were primarily derived from studies performed in breast cancer survivors. Therefore, these recommendations may not be fully applicable to breast cancer patients dealing with the acute effects of mastectomy.

Clinical outcome measures

A significant number of outcome measures were used to report the effects of perioperative rehabilitation in breast cancer patients, each of which was measured through a wide range of questionnaires and measurement tools. Objective measures of physical function were

the most frequently used, focusing primarily on the assessment of shoulder ROM, muscle strength, and on the presence of lymphedema. Quality of life, upper limb function, and pain intensity were the most frequently reported PROMS. Two studies also used objective measures of physiological function, measuring chest expansion, the forced expiratory volume, and the forced vital capacity. Considering the large spectrum of side effects resulting from breast cancer and its treatments, selecting relevant clinical outcome measures for this population can be challenging. The WHO's International Classification of Functioning, Disability and Health (ICF) is a common framework used to describe health and disability worldwide (29). As the ICF was considered hardly practical for research and clinical practice, the WHO developed core sets from this classification, which are lists of predetermined outcome measures that are known to be relevant for specific health conditions (29). The ICF Core Set for breast cancer (30) covers all the factors that may impact breast cancer patients' functioning. Beyond physical and physiological impairments resulting from breast cancer and its treatments, this model acknowledges that these individuals may also experience difficulties in task execution and activities participation, and that they may also be affected by a range of psychological, social and environmental factors. (30). As we have seen in most studies included in this review, measures of physical function were used extensively, whereas quality of life questionnaires were used to account for psychological, social, and environmental domains of patients' functioning. As quality of life is a construct that encompasses many dimensions, the data obtained from these questionnaires may not be as informative. For psychological, social and environmental factors to be adequately measured, it is advisable

to select tools that can provide individual scores for these domains. As an example, the Functional Assessment of Cancer Therapy-Breast Questionnaire (FACT-B) is a questionnaire designed to measure five domains of health-related quality of life in breast cancer patients: physical, social, emotional, functional well-being as well as a breast cancer-specific concerns (102).

Patients' experience

This literature review also revealed that a variable, but significant proportion of breast cancer patients refused to engage in a rehabilitation intervention despite their eligibility. Reasons for refusal were mainly related to transportation issues, preferences for another intervention or therapist, lack of interest, or a desire to minimize hospital appointments in favor of returning to a normal lifestyle. Study withdrawals were attributed to cancer recurrence, undergoing another breast surgery, death, side effects from systemic treatments, and transportation issues. Coordinating rehabilitation sessions with medical appointments, providing positive reinforcement through regular follow-ups, individualizing interventions according to participants' needs and getting support from family and friends were all identified as factors promoting compliance in this clinical setting. This information suggests that implementing supervised rehabilitation interventions in outpatient clinics or community settings may promote patient engagement and treatment completion. In addition, recognizing the positive impact that support from family and friends had on participants' motivation, this raises the possibility that breast cancer patients could also benefit from a group intervention, where they could support

each other as they go through the same challenges. However, given the small number of studies from which these data were obtained, further work is needed to better document these issues.

Limitations

Our scoping review has some limitations. Despite conducting robust systematic searches in multiple relevant databases, we excluded studies that were not published in English or French, which may have resulted in relevant studies being missed. Some studies were also excluded as they focused on breast cancer survivors (i.e., patients who had completed all forms of cancer treatments). However, some organizations, such as the National Cancer Institute (NCI), identify cancer patients as survivors from the day of their diagnosis until the end of their lives (103). Therefore, studies that did not provide a clear definition of survivorship may have been excluded despite their eligibility. Some limitations of this review also lie in the studies' individual flaws. By relying on the revised CONSORT statement and extensions (49, 104, 105) to guide data extraction, we were able to identify several gaps in interventions and harms' reporting. As shown in Appendix B and C, these limitations are such that it remains unclear as to which parameters should be preferred to promote optimal postoperative recovery in breast cancer patients. Improvements in reporting are needed, not only to ensure patient safety, but also replicability of interventions in clinical settings.

A better description of recruitment and compliance issues arising in this clinical context is also warranted to foster the development of interventions that are tailored to breast cancer patients' needs and concerns. However, we must consider that conducting a mixed method scoping review, which would have included qualitative designs, would probably have been better suited to identify barriers and facilitators to study engagement and completion. As for clinical outcome measures, several studies have used measurement tools and questionnaires without mentioning their validity for the population of interest. To ensure the effects of rehabilitation interventions are accurately measured, future studies should focus on better describing these tools, while providing evidence supporting their validity for breast cancer patients.

Conclusion

This review reports on the heterogeneity and wide range of conservative interventions and clinical outcome measures used in physical rehabilitation for breast cancer patients who had undergone or were scheduled to undergo mastectomy. Our findings also highlighted the complexity of breast cancer care pathways. Exercises, patient education, manual therapy and lymphatic drainage were identified as key components characterizing rehabilitations strategies for this population. Although most studies failed to adequately describe interventions' procedures and characteristics, we were able to determine that most interventions were multimodal, initiated a few days following surgery and initially performed in supervised hospital settings. Objective measures of physical function were used more extensively to report the effects of perioperative rehabilitation in breast cancer

patients. More emphasis should be placed on selecting measurement tools and questionnaires that have already been validated for this population. Further studies are needed to improve recommendations for preoperative rehabilitation strategies, as well as to identify the factors that may influence breast cancer patients' decision to engage in rehabilitation interventions. Increasing our knowledge in these areas is essential to promote the development of interventions that will meet patients' needs and reflect breast cancer care pathways.

DISCUSSION

Cette revue intégrative de la littérature avait comme principal objectif l'identification des interventions conservatrices et des mesures de résultats cliniques utilisées dans le cadre de la réadaptation physique des patientes atteintes d'un cancer du sein devant subir ou ayant subi une mastectomie. Nous souhaitions également rendre compte des barrières et des facteurs ayant motivé ces patientes à prendre part à ces interventions dans un contexte périopératoire. Plus de la moitié (63%) des études éligibles ont inclus des femmes atteintes de stades variés de cancer du sein (0-III), ayant subi différents types de chirurgies mammaires (c.-à-d. mastectomie totale ou partielle) et axillaires (c.-à-d. biopsie ou résection ganglionnaire), ainsi qu'une série de traitements adjuvants. Nous avons également pu établir que la majorité des études étaient des essais cliniques contrôlés randomisés menés dans des pays développés et publiées au cours des 10 dernières années.

Interventions conservatrices

Quatre modalités principales ont été identifiées dans les interventions de réadaptation répertoriées, soient l'exercice, l'éducation, le drainage lymphatique, ainsi que la thérapie manuelle. Parmi les études incluses, la majorité ont proposé une intervention multimodale, dont la totalité ont intégré des exercices, combinés à de l'éducation de la thérapie manuelle ou du drainage lymphatique. Ces interventions ont principalement été menées sous la forme de séances individuelles, et près de la moitié d'entre elles ont d'abord été réalisées sous la supervision d'infirmières ou de thérapeutes physiques, puis adaptées de sorte qu'elles puissent être poursuivies à la maison de façon autonome après

l'hospitalisation. Le moment d'initiation, la durée des interventions, ainsi que les caractéristiques propres à chacune des modalités utilisées (c.-à-d. fréquence, intensité, séries, répétitions) ont varié significativement parmi les études incluses, et bon nombre de ces composantes n'ont peu ou pas été décrites. La majorité des interventions proposées ont été initiées après la chirurgie. Six études ont comparé les effets d'une intervention débutée immédiatement après la chirurgie à ceux d'une intervention différée. Parmi toutes les études incluses, seules sept interventions ont été initiées en phase préopératoire, celles-ci étant essentiellement composées de stratégies d'autogestion à mettre en place après la chirurgie.

Le développement d'interventions de réadaptation et l'amélioration de l'accessibilité à ces services de santé constituent une priorité que s'est donnée l'Organisation mondiale de la santé (OMS) afin d'améliorer la qualité de vie des patients souffrant de diverses conditions de santé (97). En 2017, l'OMS a lancé l'initiative *Rehabilitation 2030,* un appel à l'action afin que l'accès aux ressources en réadaptation soit reconnu comme un service de santé essentiel (97). Tenant compte des effets secondaires multi-systémiques associés au traitement du cancer, la création et la mise en œuvre de stratégies de réadaptation adaptées aux patients souffrant de cette maladie ont d'emblée été identifiées comme des enjeux prioritaires. En ce sens, une équipe de chercheurs mandatés par l'OMS s'est d'abord chargée d'identifier et de synthétiser les recommandations en matière de réadaptation contenues dans les plus récents guides de pratiques cliniques portant sur le traitement de divers types de cancers (97). Parmi les guides de pratiques identifiés

correspondants aux critères de qualité préétablis par l'OMS (AGREE II ≥ 45), le *Breast Cancer Survivorship Care Guideline* (98), développé par l'ACS et l'*American Society of Clinical Oncology* (ASCO), ont formulé plusieurs recommandations en matière de réadaptation physique destinées aux patientes atteintes d'un cancer du sein. Ces lignes directrices n'ont toutefois identifié aucune intervention spécifique permettant de favoriser une meilleure récupération post-opératoire chez cette population, encourageant plutôt la reprise rapide des AVD et des AVQ, ainsi que la pratique d'activité physique régulière en concordance avec les critères de l'ACS (c.-à-d. 150 minutes d'intensité modérée par semaine, incluant un entrainement en résistance au moins 2 fois par semaine) (98). De son côté, afin de prendre en charge les patientes souffrant de lymphœdème, le *National Comprehensive Cancer Network (NCCN) Survivorship Guideline* (100) recommande la mise en œuvre d'une intervention de réadaptation multimodale supervisée, composée d'exercices de renforcement musculaire d'intensité progressive, de drainage lymphatique, d'exercices d'amplitude de mouvement de l'épaule et d'éducation en matière d'autogestion des complications post-opératoires. Cette stratégie multimodale s'accorde également avec les lignes directrices émises par l'*American College of Sports Medecine* (ACSM) (101). En effet, celles-ci précisent que la pratique d'activité physique aérobie, combinée à un entrainement en résistance, devrait être privilégiée dans la prise en charge des patients atteints d'un cancer afin d'améliorer leurs fonctions physiques et leur qualité de vie, et également dans le but d'amoindrir les symptômes d'anxiété, de dépression et de fatigue. L'ACSM ajoute également que pour maximiser son efficacité, cette intervention devrait être réalisée à raison de 2 à 3 fois par semaine pour une durée moyenne de 8 à 12

semaines, et prendre la forme d'une séance supervisée, plutôt que d'un programme réalisé à domicile (101). Enfin, bien que la diminution des amplitudes de mouvement de l'épaule ait été identifiée comme un signe clinique justifiant l'initiation d'un programme de réadaptation chez cette population, aucun des guides pratiques précédemment mentionnés n'a émis de recommandations précisant la nature et les paramètres devant caractériser les exercices d'amplitude de mouvement à exécuter. Il est également important de souligner que ces guides pratiques étaient principalement destinés aux survivantes du cancer du sein, soit des patientes ayant terminé toutes formes de traitements adjuvants. Il est donc possible que ces recommandations ne soient pas en tout point applicables à la réalité des patientes aux prises avec les répercussions aigües de la mastectomie. Les interventions de réadaptation identifiées par cette revue de la littérature reflètent, dans une certaine mesure, les recommandations formulées par les plus récents guides de pratiques cliniques. Cependant, nous avons remarqué que les études éligibles ont principalement proposé des programmes de réadaptation comportant des exercices ciblant la fonction du membre supérieur, alors que peu d'entre eux ont aussi intégré un entrainement aérobique. De plus, conformément aux lignes directrices détaillées précédemment, peu d'études ont partagé des recommandations portant sur des stratégies de réadaptation à mettre en œuvre avant la chirurgie, appuyant la nécessité de réaliser des études supplémentaires sur ce sujet.

Mesures de résultats cliniques

Les mesures de résultats cliniques identifiées ont été regroupées en trois catégories : [1] les mesures objectives d'ordre physique; [2] les mesures objectives d'ordre

physiologique; et [3] les mesures autorapportées par le patient (PROMS). Les mesures objectives de la fonction physique ont été les plus fréquemment utilisées, se résumant principalement à l'évaluation des amplitudes de mouvement de l'épaule, aux tests de force musculaire, ainsi qu'à l'évaluation de la présence de lymphœdème. Ces composantes ont été rapportées à l'aide d'un éventail important d'outils de mesure, les plus courants étant, respectivement, le goniomètre pour les amplitudes de mouvement, le dynamomètre pour la force musculaire et la circonférence ou le volume du membre supérieur pour la présence de lymphœdème. La qualité de vie, la fonction du membre supérieur, ainsi que l'intensité de la douleur sont les composantes ayant été les plus fréquemment évaluées par le biais de questionnaires autorapportés. Parmi plus de 20 questionnaires différents, le *European Organization for Research and Treatment of Cancer questionnaire* (EORTC-QLQ C30/BR23) pour la qualité de vie, le *Disability of the Arm, Shoulder and Hand questionnaire* (DASH) pour la fonction du membre supérieur et l'échelle visuelle analogue (VAS) pour l'intensité de la douleur ont été les plus fréquemment utilisés. Enfin, deux études se sont également intéressées à des indicateurs de la fonction physiologique, mesurant chez leurs participantes l'expansion de la cage thoracique, le volume expiratoire maximal et la capacité vitale forcée.

Afin d'uniformiser la description des incapacités causées par certaines conditions de santé, l'OMS a également développé, en 2001, la Classification internationale du fonctionnement, du handicap et de de la santé (CIF) (29). Cette classification permet l'identification et la catégorisation de tous facteurs personnels et contextuels pouvant

porter atteinte au bon fonctionnement d'un individu (voir p. 32). Ce cadre théorique s'accompagne également de listes de mesures de résultats cliniques, aussi appelées *ICF Core Sets,* destinées à évaluer les besoins particuliers des patients souffrant de pathologies spécifiques (29), comme le cancer du sein. Tel qu'en témoigne cette liste (voir Introduction p. 33-34), au-delà des répercussions physiques et psychologiques associées au cancer du sein et à ses traitements, les difficultés rencontrées par ces patientes peuvent également se rapporter au contexte social et à l'environnement dans lequel elles évoluent, en plus d'affecter la réalisation et la participation aux AVD et AVQ. Afin d'obtenir un portrait complet de l'impact d'une intervention de réadaptation sur la récupération post-opératoire des femmes subissant une mastectomie, l'ensemble des composantes de la CIF devraient être considérées.

Expériences des patientes

Cette revue intégrative de la littérature scientifique a également permis de mettre en lumière qu'une proportion variable (2-75%) de femmes atteintes d'un cancer du sein invitées à s'engager dans une intervention de réadaptation ont refusé l'invitation malgré leur éligibilité. Sept études ont détaillé les raisons ayant motivé ces refus, se résumant principalement à des problèmes de transport, à une préférence pour une autre intervention ou pour un autre thérapeute, à un manque d'intérêt, ou au désir de minimiser les rendez-vous afin de favoriser un retour à la vie normale. L'observance aux interventions de réadaptation proposées a été évaluée dans 20% des études éligibles et considérée

appropriée dans chacun des cas. Coordonner les séances de réadaptation avec les rendez-vous médicaux, effectuer du renforcement positif par le biais de suivis téléphoniques réguliers et individualiser les interventions selon les besoins spécifiques de chaque participante ont tous été identifiés comme des facteurs pouvant potentiellement favoriser l'observance thérapeutique dans ce contexte clinique. Pour chacune des interventions proposées, une proportion variable de femmes (1-58%) a également choisi de mettre un terme à leur participation avant la fin de celles-ci. La survenue d'une récidive ou d'une autre chirurgie mammaire, le décès, les effets secondaires causés par les traitements adjuvants, ainsi que les problèmes de transport furent les raisons les plus fréquemment mentionnées pour expliquer ces abandons. Ces informations suggèrent que la mise en œuvre d'interventions de réadaptation hors des milieux hospitaliers, notamment dans des cliniques externes ou en milieux communautaires, serait susceptible de mieux répondre aux besoins des patientes subissant une mastectomie. De plus, il est intéressant de constater que certaines participantes ont manifesté une plus grande motivation à s'engager dans une intervention de réadaptation grâce au soutien de leur entourage. Ceci nous amène à penser que ces patientes pourraient également bénéficier du support d'autres femmes partageant les mêmes défis associés au diagnostic de cancer du sein. Alors que la majorité des interventions identifiées par cette revue ont pris la forme de séances individuelles, il serait pertinent d'évaluer si une intervention de groupe pourrait mieux répondre aux besoins de ces patientes.

Limites

Cette revue intégrative présente certaines limites. Bien que nous ayons effectué une recherche systématique dans plusieurs bases de données pertinentes, les études publiées dans une autre langue que le français ou l'anglais ont été exclues. De plus, certaines études ont également été rejetées puisqu'elles proposaient une intervention dédiée aux femmes survivantes du cancer du sein (c.-à-d. des femmes ayant terminé toutes formes de traitements). Cependant, certaines organisations, comme le National Cancer Institute (NCI), considèrent tous les patients atteints de cancer comme des survivants, et ce, dès le moment de leur diagnostic jusqu'à la fin de leur vie (103). Par conséquent, les études qui n'ont pas défini clairement ce concept ont pu être exclues malgré leur éligibilité. Certaines limites de cette revue intégrative résident également dans les études individuelles qui la composent. En se référant à l'énoncé révisé CONSORT et à ses documents complémentaires (49, 104, 105) pour guider l'extraction des composantes définissant chacune des interventions de réadaptation identifiées, il a été possible de mettre en lumière plusieurs failles dans la description des études originales sélectionnées. En effet, plusieurs lacunes ont été identifiées dans la description des modalités choisies, ainsi que dans les circonstances entourant leur exécution (ex. : moment d'initiation, durée, fréquence, intensité, professionnels impliqués, etc.). Tel que présenté dans les annexes B et C, il est possible de constater qu'à de multiples reprises, une ou plusieurs de ces composantes n'ont peu ou pas été décrites. Ces lacunes se reflètent également dans bon nombre de recommandations contenues dans les plus récents guides de pratiques cliniques. Une meilleure description de ces interventions apparait essentielle pour assurer l'identification

des paramètres favorisant la récupération post-opératoire optimale des patientes atteintes d'un cancer du sein. Ces améliorations sont également souhaitables afin d'assurer la reproductibilité et l'applicabilité des interventions dans les milieux cliniques.

En ce qui concerne les mesures de résultats cliniques identifiées, nous avons notamment pu constater une utilisation plus importante des mesures objectives de la fonction physique, alors que les facteurs psychologiques, sociaux et environnementaux pouvant potentiellement affecter le bon fonctionnement de ces patientes ont été le plus souvent évalués au moyen de questionnaires généraux de qualité de vie. De ce fait, nous croyons que cette approche témoigne plutôt du niveau global de fonctionnalité de ces patientes, et que pour favoriser le développement d'interventions mieux adaptées aux réalités de cette population, il serait d'intérêt de tenir également compte des aspects individuels des composantes sociale, émotionnelle et fonctionnelle. Le questionnaire *Functional Assessment of Cancer Therapy* spécifique au cancer du sein (FACT-B) est un exemple qui propose une appréciation globale de la qualité de vie des patientes, en plus d'évaluer indépendamment ces 3 principaux domaines (102). Enfin, plusieurs études ont utilisé des outils de mesure et des questionnaires sans en mentionner la validité pour la population d'intérêt. Il est souhaitable qu'une meilleure sélection de ces outils soit effectuée, notamment pour s'assurer que ceux-ci mesurent adéquatement les variables à l'étude chez les femmes ayant subi une mastectomie.

Finalement, parmi les études incluses, il a été établi qu'un nombre non négligeable de patientes ont refusé de s'engager dans une intervention de réadaptation malgré leur éligibilité, alors que d'autres ont préféré quitter l'intervention avant la fin de celle-ci. Toutefois, un faible nombre d'études ont décrit les raisons ayant justifié ces décisions. Des efforts supplémentaires sont nécessaires afin de mieux documenter ces enjeux et ainsi favoriser le développement d'interventions prenant davantage en compte les préoccupations et les besoins de ces patientes. De plus, dans le cadre de cette revue, les études qualitatives ont été exclues. L'intégration de ces devis par la réalisation d'une revue intégrative à méthode mixte aurait pu permettre de mieux identifier les facteurs influençant l'engagement à une intervention de réadaptation chez cette population.

Retombées cliniques et perspectives de recherche

Les données présentées dans ce mémoire font état de l'hétérogénéité et du nombre important d'interventions conservatrices et de mesures de résultat cliniques utilisées dans le cadre de la réadaptation physique des patientes atteintes d'un cancer du sein ayant subi ou devant subir une mastectomie. Cette synthèse nous a également permis de prendre conscience de la complexité des diverses trajectoires de soins pouvant être empruntées par les patientes souffrant d'un cancer du sein. Considérant les enjeux relatifs à l'accessibilité et à la disponibilité des ressources en matière de réadaptation au sein des établissements affiliés au CIUSSS-MCQ, ces connaissances représenteront des atouts essentiels dans l'élaboration éventuelle d'interventions adaptées aux réalités des femmes devant subir une mastectomie. Cette étude a également mis en lumière certains défis

susceptibles d'être rencontrés par ces femmes lorsqu'elles s'engagent dans un programme de réadaptation. Tenant compte du devis d'étude utilisé pour ce projet de maîtrise, il est clair que cet aspect se doit d'être approfondi davantage, notamment en questionnant directement les patientes afin de mieux comprendre leurs besoins et leurs attentes en matière de soins de réadaptation périchirurgicaux.

CONCLUSION

Les résultats de ce projet de maîtrise ont permis d'établir que l'exercice, l'éducation, le drainage lymphatique, ainsi que la thérapie manuelle sont au cœur des stratégies de réadaptation proposées pour les patientes atteintes d'un cancer du sein subissant une mastectomie. Bien que les études comportent des lacunes importantes, notamment dans la description des interventions de réadaptation mises en œuvre, nous avons pu déterminer que la majorité des interventions étaient des stratégies multimodales, initiées quelques jours après la chirurgie, et d'abord réalisées dans un environnement supervisé. Les mesures objectives de la fonction physique ont été les plus fréquemment utilisées pour rendre compte des effets de la réadaptation périopératoire chez les patientes atteintes d'un cancer du sein. Une attention particulière devrait être portée à la sélection d'outils de mesure et de questionnaires dont la validité est connue pour cette population. Des études complémentaires sont également nécessaires afin de mieux comprendre les besoins et les attentes des patientes subissant une mastectomie en matière de réadaptation périopératoire, ainsi que les facteurs pouvant influencer leur décision à s'engager ou non

dans ce type d'interventions. Il est essentiel de bonifier nos connaissances en ce sens afin de favoriser le développement d'interventions qui prendront mieux en compte le continuum de soins spécifique au cancer du sein, ainsi que les réalités des femmes aux prises avec les conséquences multidimensionnelles de la mastectomie.

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ANNEXE A

Stratégie de recherche dans la base de données MEDLINE

Dernière recherche effectuée : 24 janvier 2021

1. Breast Neoplasms [Mesh – no exp]
2. Carcinoma, Ductal, Breast [Mesh]
3. Carcinoma, Lobular [Mesh]
4. Breast Carcinoma In Situ [Mesh -no exp]
5. Carcinoma, Intraductal, Noninfiltrating [Mesh]
6. Unilateral Breast Neoplasms [Mesh]
7. Triple Negative Breast Neoplasms [Mesh]
8. breast cancer* [Title/Abstract]
9. breast tumo*
10. breast carcinoma*
11. breast neoplasm*
12. lobular N2 (carcinoma* or neoplasm* or tumo* or cancer*)
13. ductal carcinoma*
14. intraductal carcinoma*
15. breast malignant neoplasm*
16. breast malignant tumo*
17. mammary carcinoma*
18. mammary cancer*
19. mammary tumo*
20. mammary neoplasm*
21. **1-20/ OR**

22. exp Mastectomy [Mesh]
23. mastectom*
24. mammectom*
25. postmastectom*
26. postmammectom*
27. simple mastectomy
28. total mastectomy
29. extended simple mastectomy
30. radical-mastectomy
31. modified radical-mastectomy
32. prophylactic-mastectomy
33. risk-reducing (surgery or mastectomy)
34. preventive mastectomy

35. contralateral mastectomy
36. bilateral mastectomy
37. breast-conserving (surgery or therapy)
38. partial (mastectomy or mammectomy)
39. lumpectomy
40. postlumpectomy
41. segmental (mastectomy or mammectomy)
42. breast segmentectomy
43. quadrantectomy
44. breast tumorectomy
45. breast tumo* (resection or excision)
46. wide local excision
47. limited resection (mastectomy or mammectomy)
48. local excision (mastectomy or mammectomy)
49. sector* resection
50. conservative breast cancer treatment
51. partial-breast treatment
52. breast conservation therapy
53. nipple-sparing-mastectomy
54. aerola-sparing-mastectomy
55. breast-sparing (mastectomy or surgery)
56. subcutaneous mastectomy
57. **22-56/OR**

58. Rehabilitation [Mesh- no exp]
59. Activities of Daily Living [Mesh]
60. Range of Motion, Articular [Mesh]
61. exp Exercise Therapy [Mesh]
62. Physical Therapy Modalities [Mesh- no exp]
63. Complementary Therapies [Mesh- no exp]
64. Tai Ji [Mesh]
65. Yoga [Mesh]
66. Musculoskeletal Manipulations [Mesh-no exp]
67. Manipulation, Chiropractic [Mesh]
68. Manipulation, Osteopathic [Mesh]
69. exp Therapy, Soft Tissue [Mesh]
70. Conservative Treatment [Mesh]
71. exp Exercise Movement Techniques [Mesh]
72. exp Exercise [Mesh]
73. rehabilitation [Title/Abstract]
74. preoperative N2 (rehabilitation or exercise*)
75. postoperative N2 (rehabilitation or exercise*)
76. prehabilitation

77. activit* N3 (daily living or daily life)
78. exercise*
79. training
80. conditioning
81. stretching
82. physical activit*
83. range of motion
84. (shoulder or arm or upper limb or upper extremity) N3 (pain or morbidity or impairment*)
85. manipulation* or mobilization* or mobilisation* or massage or manual therap*
86. osteopath* or chiropractic or physiotherapy or kines*
87. conservative or nonsurgical
88. therap* N3 (exercise* or motion or soft tissue)
89. yoga
90. qigong
91. 58-91/ OR
92. 21 AND 57 AND 91

ANNEXE B

Tableau d'extraction des données complet

First author (Year) Country	Study design	Participants	Intervention	Outcome measures	Outcome validation information	Patients' experience
Ammitzbøll (2019) Denmark	RCT	N= 158 **Exercise IG; n= 82** *Age, mean ± SD*: 53 ± 10 *Stage, n (%):* I: 12 (15)/II: 48 (59)/III: 15(18)/ N/A: 7 (9) *Sx type, n (%):* LUMP +ALDN: 43(52)/ MX + ALDN: 39(48) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 48 (59) Neoadj Ch: 25 (30)/HT: 64 (78) **Usual-care CG; n = 76** *Stage, n (%):* I: 16 (21)/II: 35 (46)/III: 18 (24)/N/A: 7 (9) *Sx type, n (%):* LUMP + ALDN: 41(54) MX +ALDN: 35(46) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 45 (59) Neoadj Ch: 21 (28)/HT: 51 (67)	**Exercise intervention group** Resistance exercises program (covered all major muscles groups of the UL and lower limbs, and core strength and stability) *Phase 1 (w1-w20)* *Initiation*: 3rd post-op w *Frequency*: 3 days/w (supervised in group: 2/w; self-A: 1/w) *Phase 2 (w21-w50)* *Initiation*: after phase 1 *Frequency*: 3 days/w (self-A exercises solely) *Exercise sessions duration*:50-55 min (10-15-min warm-up, 40 min of resistance training) *Rep/Load/Sets:* w1-4 :15-20/25 RM/2-3 sets w5-8: 15-17/20 RM/3 sets w9-12: 10-12/15 RM/3 sets w13-50: 10-12/10-12 RM/3 sets **Usual-care control group** No intervention provided but were allowed to participate in municipality-led rehabilitation programs without restrictions *Follow up:* 12 months	-Arm VOL-*ILVD* (water displacement) LE-related symptoms: heaviness, tightness and swelling (NRS-11) -Muscle strength (7RM-test and dynamometer) -Shoulder movement (goniometer) -Interlimb mass difference-*ILMD* (DXA and arm scan) -Clinical examination-LE (Stanton & al. criteria) -Clinically relevant LE (> 3% increased ILVD, NRS-11 ≥ 2 and 2 or more clinical criteria)	*BC-specific outcomes:* Water displacement *General*: DXA *Undisclosed*: NRS-11 ILMD Clinical criteria 7RM-test Goniometer	Intervention group: 17 participants experienced an increased in symptoms during phase 1 *Lost to follow-up* Intervention group: hospital anxiety (n=1), cancer recurrence (n=1), deaths (n=3) Control group: pain due to scar tissue (n=1), recent breast recons (n=1), no time or resources (n=2), cancer recurrence (n=3)
Ammitzbøll (2019) Denmark	RCT	N= 158 **Exercise IG; n= 82**	**Exercise intervention group** Resistance exercises program (covered all major muscles groups of the UL and	-HRQOL (EORTC QLQ C-30 v3; FACIT-f)	*Cancer-specific outcomes:*	*Lost to follow-up:* IG: death (n=3),

		Age, mean ± SD: 53 ± 10 *Stage, n (%):* I: 12 (15)/II: 48 (59)/III: 15 (18) N/A: 7 (9) *Sx type, n (%):* LUMP +ALDN: 43(52)/MX + ALDN: 39(48) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 48 (59) Neoadj Ch: 25 (30)/HT: 64 (78) **Usual-care CG; n = 76** *Stage, n (%):* I: 16 (21)/II: 35 (46)/III: 18 (24)/N/A: 7 (9) *Sx type, n (%):* LUMP + ALDN: 41(54)/MX +ALDN: 35(46) *Systemic treatment, n (%)* RT: 82 (100)/Adj Ch: 45 (59) Neoadj Ch: 21 (28)/HT: 51 (67)	lower limbs, and core strength and stability) *Phase 1 (w1-w20)* *Initiation*: 3rd post-op w *Frequency:* 20 w; 3 days/w (supervised in group: 2/w; self-A: 1/w) *Phase 2 (w21-w50)* *Initiation:* after phase 1 *Duration*: 30 w; 3 days/w (self-A exercises) *Exercise sessions duration:* 50-55 min (10-15-min warm-up, 40 resistance training) *Rep/Load/Sets:* w1-4 :15-20/25 RM/2-3 sets w5-8: 15-17/20 RM/3 sets w9-12: 10-12/15 RM/3 sets w13-50: 10-12/10-12 RM/3 sets **Usual-care control group** No intervention provided but were allowed to participate in municipality-based PT (heterogeneous offers of MT and mobility exercises) *Follow up:* 20w, 12 months	-Symptom clustered: pain-sleep-fatigue (EORTC QLQ-C30 v3)	EORTC QLQ C-30 FACIT-f *Undisclosed:* Symptom clustered	logistics (n=3), unable to contact (n=1), hospital anxiety (n=1), personal reasons (n=1) and cancer recurrence (n=1) CG: unable to contact (n=3), other Sx (n=1), no time (n=2), personal reasons (n=3), withdrew consent (n=1), pain from scar (n=1), cancer recurrence (n=3)
Anderson (2012) USA	RCT	N= 104 **Intervention arm; n= 52** *Age group, n (%):* *< 50:* 21 (40)/*50-64:* 23 (44) *65-74:* 4 (8)/ *>75:* 4 (8) *Stage, n (%):* I: 25 (48)/II: 19 (37)/III: 8 (15)/N/A: 1(2) *Sx type, n (%):* LUMP: 23 (44)/MX: 28 (54)/ N/A: 1 (2) *Type of node dissection, n (%):* SND only: 10 (19)/AND: 39 (75) Neither: 1 (2)/N/A: 2 (4) *Systemic treatment, n (%):*	**Intervention arm** Comprehensive program consisting of tailored exercises and LE prevention *Initiation*: 4-12w post-op *LE prevention module (LPM)* Included instructions and care for the affected arm and hand, video-taped tutorial of arm strengthening and lymph flow exercises and instructions to wear a compression sleeve *Tailored exercise program*	Arm VOL (Water displacement) -Function (6MWT) -HRQOL (FACT-B)	*BC-specific outcomes:* Water displacement FACT-B *Cancer-specific outcomes* 6MWT	Reasons stated for not completing the study: -Feeling overwhelmed or lack of time to participate (38%) -Lost to follow-up (19%) -Lack of interest (10%) -Family issues (10%)

		Ch: 31(60)/*HT:* 26(50)/*RT:* 31(60) **Comparison arm; n=52** *Age group, n (%)* *< 50:* 23 (44)/*50-64:* 19 (37) *65-74:* 7 (13)/ *>75:* 3 (6) *Stage, n (%):* I: 26 (50)/II: 21 (40)/III: 4 (8)/N/A: 1(2) *Sx type, n (%):* LUMP: 25(48)/MX: 24(46)/N/A: 3(6) *Type of node dissection, n (%):* SND only: 9 (17)/ALND: 40 (77) Neither: 0/ N/A: 3 (6) *Systemic treatment, n (%):* Ch: 31(60)/HT: 23(44)/RT: 36(69)	Included an aerobic warm-up, moderate to hard walking (RPE scale), upper and lower body strength training and stretching exercises *Initiation*: following initiation of LPM *Intensive phase (m1-3)* Frequency: 2 days/w (supervised exercises) *Phase 2 (m4-6)* Transition to HB exercises (supervised exercises 1 day/w) *Phase 3 (m7-12)* HB exercises (supervised exercises not mandatory) *Exercise sessions duration*: 65 min (5-min warm-up, 30-min of walking, 20 min of strengthening exercises and 10 min of stretching) *Load/Repetitions*: 50% 1 RM /up to 12 repetitions (weights were increased weekly) **Comparison arm** Usual care consisting of patient ED (LE awareness, tips about PA and nutrition, recommendations for improving function and strength) *Follow up:* 6, 9, 12 and 18 months post-Sx			-Death (10%) -Other reasons (10%) Adherence: Participants completing 71.2% of all prescribed exercise sessions with a range of 0–97%. Majority (61%) of participants attending more than 75% of prescribed sessions and only 13% of participants attending less than 50% of sessions
Bendz. (2002) Sweden	RCT	N= 230 **Group A; n= 115** *Age, mean ± SD*: 58 ± 11 *Stage*: N/A *Sx type, n (%):* MX: 31 (31) /MX + RT: 5 (5) QT: 20 (20) / QT + RT: 45 (44) **Group B; n = 115** *Age, mean ± SD*: 58 ± 11 *Stage:* N/A *Sx type, n (%):* MX: 22 (21) / MX + RT: 7 (7) QT: 23 (22) /QT + RT: 52 (50)	**Group A** Early shoulder exercises (to be started on the 1st post-op day) Day 1-13: Early shoulder exercises including intermittent hand contractions and basic ROM exercises From Day 14: Comprehensive ROM exercise program **Group B; n = 115** Delayed shoulder exercises Preoperative instructions: were advised to use the arm as much as comfortable	Arm VOL (water displacement) Shoulder ROM (Myrin goniometer) Grip strength (vigorimeter) Patient-reported measures of pain, heaviness and tension (VAS scale)	*BC-specific outcomes:* Water displacement *Disclosed for general population:* Myrin Goniometer	During the study period 25 patients dropped out. The causes were: death (five patients), moving from the area (six patients), other diseases (three patients), Sx on the opposite side (three patients)

			but to avoid lifting and carrying heavier items Day 1-13: No further information was provided From Day 14: Comprehensive ROM exercise program Patients were told to perform each exercise 5 times in every set and repeat the session 3 times daily. *Follow up:* 2w, 1 month, 6 months, 2 years		Vigorimeter VAS scale	and personal reasons (eight patients).
Beurskens (2007) Netherlands	RCT	N= 30 **Physiotherapy group; n= 15** *Age, mean ± SD*: 53.7 ± 13.0 *Stage:* N/A *Sx type, n (%):* BCS + ALDN: 3 (20)/MX+ ALDN: 12 (60) *Systemic treatment, n (%):* Ch: 2 (13)/HT: 1 (7)/RT+ Ch: 6 (40) Ch+ HT: 1 (7)/RT+ HT: 1 (7) RT + HT + Ch: 1 (7) **Control group; n=15** *Age, mean ± SD*: 55.4 ± 9.3 *Stage*: N/A *Sx type, n (%):* BCS + ALDN: 4 (27)/MX + ALDN: 11 (73) *Systemic treatment, n (%):* RT: 2 (13)/Ch: 2 (13)/HT: 1 (7) RT+ Ch: 8 (53)/Ch + HT: 1 (7) RT + HT: 1 (7)	**Physiotherapy group** PT sessions in a private office of their own choice. Enrolled physiotherapists received information about treatment guidelines: advice and exercises for arm/shoulder, posture correction, coordination exercises, exercises for muscular strength, improvement of general physical condition, exercises to prevent LE and instruction for soft tissue massage of the scar if required *Initiation*: 2w following Sx *Duration*: 3 months *Frequency*: 1-2/w for the first 3w and then once a fortnight or less + 10 min of home exercises daily **Control group** Leaflet flyer with advice and exercises for the arm/shoulder and had no further contact with the physiotherapist *Initiation*: 1st w following Sx	Arm/shoulder pain (VAS) Shoulder mobility (digital inclinometer) Disabilities in daily life (DASH) Arm edema (water displacement) Grip strength (hand-held dynamometer) Quality of life (SIP questionnaire short version)	*Disclosed for general population* DASH SIP questionnaire *Undisclosed* VAS Digital inclinometer Water displacement Hand-held dynamometer	Thirty women completed the study protocol. In the follow-up period one patient from the control group died before the last assessment
Box (2002) Australia	RCT	N= 65 **Treatment group; n= 33** *Age, mean ± SD*: 53.03 ± 9.49 Stage: N/A *Sx type (%):* BCS + ALND: 46.9/ MRM: 53.1 **Control group; n = 32** *Age, mean ± SD*: 59.00 ± 10.95	**Treatment group** *Physiotherapy Management Care Plan (PMCP)* Included a thorough preop assessment and explanation with postop reviews to monitor shoulder ROM, progress exercise program, LE	Shoulder ROM (goniometer) Function (12-items functional questionnaire)	*Undisclosed*	Dropouts (9%): relocation interstate or overseas (2), unavailability for final assessment (1) and death (3).

		Stage: N/A *Sx type (%):* BCS + ALND: 51.5/MRM: 48.5	awareness ED and individualized intervention as required. **Control group** Exercise instruction booklet *Follow up* Day 5, 1 month, 3, 6, 12 and 24 months postoperatively			Both groups: reduction in their compliance with the prescribed exercise protocol from the 1 m. review onwards It is possible that the greater compliance of the TG women over the first 12 months may have been due to the PTs reinforcement of the benefits of the continued exercise programme.
Box (2002) Australia	RCT	N= 65 **Treatment group; n= 33** *Age, mean ± SD*: 53.03 ± 9.49 *Stage*: N/A *Sx type (%):* BCS + ALND: 46.9/ MRM: 53.1 **Control group; n = 32** *Age, mean ± SD*: 59.00 ± 10.95 *Stage*: N/A *Sx type* (%): BCS + ALND: 51.5/MRM: 48.5	**Treatment group; n = 33** *Physiotherapy Management Care Plan (PMCP)* Included a thorough preop assessment and explanation with postop reviews to monitor shoulder ROM, progress exercise program, LE awareness ED and individualized intervention as required. **Control group; n = 32** Exercise instruction booklet *Follow up* Day 5, 1 month, 3, 6, 12 and 24 months postoperatively	Arm size- *CIRC* Arm VOL (water displacement) Multi-frequency bioimpedance-*MFBIA* (spectroscopy) Incidence of secondary LE (based on preop CIRC, preop VOL and MFBIA ratio)	Disclosed but unable to retrieve the study	In this current study, 28% of women (n=16/57) reported that they felt that their arm was swollen at 24 mo. More than 50% of these women reported subjectively that the swelling was in the upper arm but that it occurred intermittently and could not always be associated with a precipitating event
Cho (2016) South Korea	RCT	N= 48 BC patients with AWS **PTMLD group; n= 24** *Age, mean ± SD*: 50.7 ± 9.6 *Stage, n (%):* I: 5 (24)/III: 16 (76) *Sx type, n (%):* MX: 12 (57)/ LUMP: 7 (33)	**PTMLD group** Underwent a PT program combined with MLD Initiation: At least 4w after BSx *Supervised PT program* UE strengthening and stretching exercises combined with MT session	Arm VOL (CIRC tape measurements) Muscular strength (dynamometer) Active ROM (inclinometer)	*BC-specific outcomes:* CIRC tape measurements EORTC QLQ-BR23	Six of the 20 patients in the PT group developed LE after 4 weeks. Seven patients were unable to complete the final

		Breast recons: 2 (10) *Systemic treatment, n (%):* *Ch:* 9 (43)/*RT:* 21(100)/*HT:* 14 (67) **PT group; n = 24** *Age, mean ± SD*: 46.6 ± 6.8 *Stage, n (%):* I: 12 (60)/III: 8 (40) *Sx type, n (%):* MX: 16 (80) / LUMP: 3 (15) Breast recons: 1 (5) *Systemic treatment, n (%):* *Ch:* 11 (55)/*RT:* 19(95)/*HT:* 12 (60)	(ST mobs and stretching, shoulder stretching exercises, shoulder girdle mobs and PROM exercises Duration: 4w Frequency: 3 times/w Repetitions/Sets/Int :10/3/60-80% 1 RM *MLD* Frequency: 5 days/w for 4w MLD sessions duration: 30 min *w1*: performed by 2 certified PT *w2-4*: self-A **PT group; n = 24** PT program solely	Pain (NRS-11) Arm disability (DASH) QoL (EORTC QLQ-C30 v3, EORTC QLQ-BR23) Visible cording (Subjective assessment by a rehab doctor)	*Cancer-specific outcomes:* EORTC QLQ-C30 v3 *Disclosed for general population:* Dynamometer DASH NRS-11 *Undisclosed:* Inclinometer	evaluation: therefore, only 41 patients completed the study
Cinar (2008) Turkey	RCT	N = 57 **Treatment group; n = 27** *Age, mean ± SD*: 51.1 ± 13.0 *Stage, n (%):* N/A *Sx type*: *MRM* *Systemic treatment, n (%):* Ch: 29 (97)/RT: 14 (47) **HB exercise program; n= 30** *Age, mean ± SD*: 52.6 ± 12.2 *Stage, n (%):* N/A *Sx type*: *MRM* *Systemic treatment, n (%):* Ch:23(85)/RT:10(4)	**Treatment group** Early shoulder ROM exercises (to be started on the 1st post-op day) and PT program *Day1:* AROM exercises supervised by a PT *Day2*: Isometric hand and forearm exercises *Day3-4*: Active assistive and AROM exercises of the shoulder joint *PT program* Included ROM, stretching and strengthening exercises Initiation: Following drains removal Duration: 15 supervised sessions and 8w self-A **Home-based exercise program group** Postoperative exercise forms to perform at home *Follow up* Day 5, 1 month, 3 and 6 months postoperatively	ROM (Myrin goniometer) Arm VOL (CIRC tape measurements) Function (10-item functional questionnaire)	*Undisclosed:* CIRC tape measurements Functional questionnaire Myrin Goniometer	No statistically significant difference in postoperative complication like seroma and wound infections. None of the patients had postoperative hematome Early rehabilitation started on the first postoperative day did not have an adverse effect on local infection, hematoma, and seroma formation and did not cause an increase in duration and amount of LD
De Groef (2017) Belgium	RCT	N= 147 **Intervention group; n= 72** *Age, mean ± SD* :53.9 ± 11.5	**Both groups** Individual standard physical therapy program consisting of different PT	Point prevalence of pain (Yes/No question)	*BC-specific outcome*	*Dropouts*

		Stage, n (%): 0: 7 (10)/ I: 16 (22) /II: 36 (50)/ III: 13 (18) IV: 0 (0) *Sx type, n (%):* MX: 46 (64)/ BCS: 26 (36) *Systemic treatment, n (%):* RT, IMC and medial supraclavicular: 72(100) RT, axilla: 8(11)/Ch: 60(83)/Neoadj Ch: 29(40) Target therapy: 22(31)/HT: 57(79) **Control group; n = 75** *Age, mean ± SD*: 54.7 ± 11.9 *Stage, n (%):*0: 2 (3)/ I: 20 (27)/ II: 37(48)/ III:14(19)/ IV:2 (3) *Sx type, n (%):* MX: 50 (67)/ BCS: 25 (33) *Systemic treatment, n (%):* RT, IMC and medial supraclavicular: 75 (100) RT, axilla: 9(12)/Ch:55(73)/Neoadj Ch:21(28) Target therapy: 9 (12)/HT: 62 (83)	modalities: passive mobs to improve PROM and AROM, stretching and transverse strain of pectoral muscles, scar tissue massage, exercises schemes to restore and improve muscle flexibility, endurance and strength, posture and movement control and active shoulder ROM Initiation: immediately after Sx Duration: 4 months Exercise sessions duration: 30 min Frequency: 2 session/w, reducing to once/w after the first 2 months **Intervention group** Individual standard physical therapy program + myofascial therapy Initiation: 2 months post-Sx Duration (MT): 2 months Frequency of MT sessions: once/w **Control group** Individual standard physical therapy program + placebo treatment consisting of static bilateral hand treatment at the upper body and arm Initiation: 2 months post-Sx Duration (placebo): 2 months Frequency: once/w Placebo treatments duration: 30 min *Follow-up* 1w, 2, 4, 9 and 12 months post-Sx	Pain intensity (VAS) Pressure hypersensitivity (digital Wagner FPX algometer) Pain quality (McGill Pain Questionnaire) Point prevalence of impaired shoulder function (DASH score of more than 15%) Shoulder function (DASH) Quality of life (SF-36)	SF-36 *Disclosed for general population* Pressure algometer McGill Pain Questionnaire DASH *Undisclosed* VAS	Intervention group: not able to come to the hospital (n=3) Control group: No dropouts
De Rezende (2006) Brazil	RCT	N= 60 **Directed exercises group; n = 30** *Age, mean ±SD*: 54.00 ± 10.11 *Stage, n (%):* I: 5 (17)/ IIA: 4 (13)/ IIB: 5 (16) IIIA: 4 (13)/ IIIB: 8 (27)/ IIIC:2 (7)/ IV: 2 (7) *Sx type, n (%):* Halsted RMX: 5(17)/MRM:16 (53)/ QT: 9 (30)	**Directed exercises group** 19 ROM-exercises program performed in groups of 5 to 20 women and supervised by a team of PT and students Initiation: 1st post-op day Duration: 3 days/w for 42 days Exercise sessions duration: 40 min Repetitions: 10 rep each exercise, with a 60-s interval between exercises	Shoulder ROM (Manual goniometer) Lymphatic disturbance (Drainage VOL) Arm CIRC (Tape measure)	*Undisclosed:* Manual goniometer Drainage VOL Tape measure of arm CIRC	The groups were homogeneous with respect to the number of physiotherapy sessions performed, with 13.83 ± 3.05 sessions in the

		Systemic treatment, n (%): Previous Ch: 8 (27) **Free exercises group; n = 30** *Age, mean ±SD*: 55.40 ± 11.24 *Stage, n (%):* I: 6 (20)/ IIA: 10 (33)/ IIB: 6 (20) IIIA: 3 (10)/ IIIB: 3 (10)/ IIIC: 0 (0)/IV: 2 (7) *Sx type, n (%):* Halsted RMX: 1 (3)/ MRM: 21 (70)/QT:8 (27) *Systemic treatment, n (%):* Previous Ch: 9 (30)	**Free exercises group** Same ROM exercises program without a previously defined sequence or number of repetitions			directed group and 13.19 ± 1.9 sessions in the free group.
Devoogdt (2018) Belgium	RCT	N= 160 **Experimental group; n = 79** *Age, mean ± SD*: 56 ± 13 *Stage, n (%):* 0: 1(1)/ I:21(27)/II: 38(48)/III: 13(17)/ IV: 6 (8) *Sx type, n (%):* MX + ALDN: 52 (66)/BCS + ALDN: 27 (34) *Systemic treatment, n (%):* Ch: 50 (63)/Target therapy:14(18)/ HT: 55(70) **Control group; n = 81** *Age, mean ± SD:* 55 ± 11 *Stage, n (%):* 0: 0 (0)/ I: 26 (32)/ II: 39 (48)/III: 12 (15)/IV: 4 (5) *Sx type, n (%):* MX + ALDN: 56 (69)/BCS + ALDN: 25 (31) *Systemic treatment, n (%):* Ch: 58 (72)/ Target therapy: 7 (9)/HT: 66 (82)	**Both groups** *During hospitalization:* Received information about the prevention of LE + exercise therapy (mobilizing exercises) *After hospitalization:* 30-min individual exercise sessions were provided at the hospital, consisting of passive shoulder mobs, stretching of the breast muscles, scar tissue massage and active mobilizing and stabilizing exercises. Duration: 6 months Frequency: 2 times/ w, but gradually diminished to 1/ 2w **Experimental group** Protocol described above + MLD Initiation: one week after removal of axillary drains Duration of MLD: 20 weeks Frequency of exercise sessions during this period: one to 3 times/ w and then gradually decreased to once/w **Control group** Protocol described above without MLD *Follow-up:* 6, 12, 24 and 60 months post-Sx	Incidence of arm LE (water displacement, arm CIRC) Point prevalence of arm LE (water displacement, arm CIRC) Point prevalence of subjective arm and trunk LE (Questioned at interview) Arm VOL difference (Water displacement) Shoulder ROM-abd, flexion, ext and int rotation (Goniometer, tape measure) Health-related QoL (SF-36) Problems in functioning (Lymph-ICF)	*BC-specific outcome(s)* Lymph-ICF *Disclosed for general population* SF-36 Water displacement *Undisclosed* Goniometer Tape measurement Arm CIRC	*Lost to follow-up:* Exp: died (n=5), withdrew (n=6), unable to contact (n=3), cancer recurrence (n=1) Control: died (n=4), withdrew (n=6), unable to contact (n=2), cancer recurrence (n=2) The main reason for absence during the therapy sessions was illness related to Ch and/or RT. Other reasons were problems with transport, holiday, and illness from other causes.

Feyzioğlu (2020) Turkey	RCT	N= 40 **Kinect-based rehabilitation group; n =20** *Age, mean ± SD*: 50.84 ± 8.53 Stage, n (%): N/A *Sx type*: Unilateral BSx + ALND *Systemic treatment, n (%):* Ch: 4 (21)/ RT: 13 (68)/ HT: 2 (11) **Standardized physiotherapy group; n = 20** *Age, mean ± SD*: 51.00 ± 7.06 *Stage, n (%):* N/A *Sx type*: Unilateral BSx + ALND *Systemic treatment, n (%):* Ch: 2 (12)/ RT: 13 (77)/ HT: 2 (12)	**Both groups** w0-2: Breathing, ROM and pumping exercises. Limitations for shoulder ROM amplitudes, weightlifting, jumping and running up to 6w post-op Initiation: 1st post-op day Duration: 2w **KBR group** Xbox 360 Kinect video game program (requiring AROM of the UL) combined with tissue massage and passive mobs Initiation: 2nd post-op w Duration: 2 days/w for 6 w **SPT group** Standard UE PT program (shoulder ROM, stretching and strengthening exercises) including scar tissue massage and mobilizations Initiation: 2nd post-op w Duration: 2 days/w for 6 w Program sessions duration (for both groups): 45 min	Pain intensity (VAS) Shoulder ROM (Digital goniometer) Shoulder muscle strength (Handheld dynamometer) Handgrip strength (Hydraulic hand dynamometer) Upper extremity function (DASH) Fear of movement (TKS)	*BC-specific outcome(s):* DASH *Disclosed for general population:* VAS Handheld dynamometer *Undisclosed:* Digital goniometer Hydraulic hand dynamometer TKS	Dropouts: KBR group (n=1) Declined to participate SPT group (n =3) New metastasis focus (n=1) Declined to participate (n =1) Ch side effect (n =1) No complications occurred during Xbox Kinect VR training performed early in the postop period after BSx. The patients in the KBR group participated more motivationally and had less fear of movement during the entire program
Kilbreath (2012) Australia	RCT	N= 160 **Exercise group; n = 81** *Age, mean ± SD*: 53.5 ± 12.1 Stage, %: I: 17 / II: 44 / III: 38 *Sx type, %:* MX + SNB: 48/ ALDN: 62 *Systemic treatment, %:* Ch: 68/ RT: 79 **Control group; n = 79** *Age, mean ± SD*: 51.6 ± 11.0 *Stage, n (%):* I: 19/ II: 37/ III: 44 *Sx type, %:* MX: 47/ ALDN: 58 *Systemic treatment, %:* Ch: 71/ RT: 76	**Both groups** Postoperative care which included written information outlining postop arm exercises they were to perform, literature on prevention of LE Initiation: 4-6w post-Sx Duration: 8 w **Exercise group** Supervised exercise sessions of resistance training and passive stretching for shoulder muscles + home program of resistance training and stretching (positions maintained 5-15 min) Initiation: 4-6 w post-Sx Duration: 8w	Self-reported arm symptoms (EORTC- BR23) Breast symptoms (EORTC-BR23) Shoulder ROM (Digital inclinometer) Upper shoulder muscle strength (Hand-held dynamometer) Presence of LE	*BC-specific outcome* EORTC-BR23 Bioimpedance spectrometry *Undisclosed* Digital inclinometer Hand-held dynamometer	Both groups reported little impairment including swelling immediately following the intervention and at 6 months post-intervention. The median number of sessions attended was 7 out of 8 sessions, with adherence to the supervised training 78%.

			Frequency: once/w Sets/Reps (resistance training): 2/8-15 **Control group** Were seen fortnightly to assess their arm for the presence of LE. No exercises or advice was provided. If LE was detected, patient was seen by an OT form at minimum, fitting of a compression garment *Follow-up:* 6 months after the intervention	(Bioimpedance spectroscopy)		Home program mean compliance: 90%. Seven women completed less than 75% of their stretching sessions and 4 women completed less than 75% of their resistance training sessions
Kilbreah (2006) Australia	RCT	N= 22 **Exercise group; n = 14** *Age, mean ± SD*: 52.7 ± 14.0 *Stage*: N/A *Sx type, n (%):* MX + ALDN: 8 (57)/ WLE + ALDN: 6 (43) *Systemic treatment, n (%):* RT: 9(64)/Ch: 7(50) **Control group; n = 8** *Age, mean ± SD*: 51.5 ± 10.2 *Stage*: N/A *Sx type, n (%):* MX + ALDN: 4 (50)/ WLE + ALDN: 4 (50) *Systemic treatment, n (%):* RT:7(88)/ Ch:6 (75)	**Exercise group** Usual care + shoulder ROM, strengthening and stretching exercises Initiation: 4 to 5w post-Sx Frequency: performed daily and supervised once/w by a PT *Stretching exercises:* Was held passively for 5 min on day 1 and progressed up to 15 min over the next 2w *Strengthening exercises:* Focused on shoulder flexors, abductors, and external rotators, a Theraband was used Sets/Reps: 2/8-12 (Exercises were progressed by either increasing resistance or repetitions at subsequent weekly sessions) **Control group** Usual care (monitoring by a breast care nurse, may be seen by a PT to review UL exercises and by an OT who discussed prevention of LE) provided at the hospital, were discharged 2 to 7 days post-Sx *Follow-up:* Following the 8-week intervention period	Quality of life (EORTC-QLC-C30, EORTC-QLC-BR23) Presence of lymphedema (arm CIRC measurements) Shoulder ROM (inclinometer) Maximal isometric shoulder strength (dynamometer)	*BC-specific outcome* EORTC-QLC-BR23 Arm CIRC measurements *Cancer-specific outcome* EORTC-QLC-C30 *Undisclosed* Inclinometer Dynamometer	‘’No adverse events were reported during the conduct of this study’’

Lauridsen (2005) Denmark	RCT	N= 139 **Group A; n = 72** *Age (age range):* MRM + RT: 49 (40-70)/MRM: 60 (37-74) BCS: 54 (31-79) *Stage*: N/A *Sx type, n (%):* MRM + RT: 20(28)/ MRM: 21(29)/BCS: 31 (43) *Systemic treatment, n (%):* Ch: 26 (36)/ RT: 23(32)/ HT:25(35) **Group B; n = 67** *Age (age range):* MRM + RT: 51 (29-70)/MRM: 63 (32-77)/BCS: 54 (32-69) *Stage*: N/A *Sx type, n (%):* MRM + RT: 23 (34)/MRM: 13(19)/ BCS: 31(46) *Systemic treatment, n (%):* *Ch:* 21 (31)/ RT: 17(25)/HT: 17(25)	**Group A** Team instructed PT program consisting of relaxation and strengthening exercises, combined to vein pump therapy and instruction in stretching of scar tissue Initiation: 6th to 8th post-op w Duration: 2 days/w for 6w Exercise sessions duration: 60 min **Group B** ''Standard treatment of the ward'' and were offered the same PT program after the 26th post-op w *Follow up:* 6, 12, 26 and 56w post-Sx	Shoulder function (Constant Shoulder Score) Presence of ''strings'' in the axilla (Physical assessment)	*Undisclosed*	14 patients dropped out of the trial including two patients who died and two patients who had terminal disease, disabling them in attending the final follow-up.
Pace do Amaral (2012) Brazil	RCT	N= 131 **MT+UL exercises group; n = 65** *Age, mean ± SD*: 55.0 ± 11.4 *Stage, n (%):* I/II: 46 (72)/ III/IV: 18 (28) *Sx type, n (%):* BCS: 15 (23)/ RM: 50 (77) *Systemic treatment, n (%):* Ch: 22(88)/ RT: 13(52)/ HT: 15(60) **UL exercises group; n = 66** *Age, mean ± SD:* 56.7 ± 11.7 *Stage, n (%):* I/II: 38 (58)/ III/IV: 28 (42) *Sx type, n (%):* BCS: 13 (20)/ RM: 53 (80) *Systemic treatment, n (%):* Ch: 27 (90)/ RT: 24(80)/HT: 18(60)	**Both groups** Initiated physical therapy on the 1st post op day according to the institutional routine **MT+UL exercises group** UL exercises sessions, followed by an MT protocol consisting of scapular and glenohumeral joint mobs and therapeutic massage applied by trained PT Duration: 1 month Frequency: twice a week MT sessions duration: 20 min **UL exercises group** Outpatient physical therapy program combining UL exercises (19 movements of flexion, extension, abduction, adduction, internal and	Shoulder ROM (goniometer) UL function (Modified-University of California at Los Angeles Shoulder Rating Scale) Postoperative complications (Observations made by the main investigator)	*Undisclosed* Goniometer Modified-University of California at Los Angeles Shoulder Rating Scale	One hundred thirty-six women were invited to enroll. Two of them were excluded because of a lesion of the long thoracic nerve and three of them requested referral to another service (i.e., declined to participate).

			external rotation alone or combined) to precautions to prevent LE Initiation: 3rd post-op day Duration: 1 month Frequency: 3 times a week Exercise sessions duration: 45 min Sets/Reps: 1/10 *Follow-up* 1, 6, 12 and 18 months after Sx			
Petito (2014) Brazil	RCT	N=77 **Early group; n=40** *Age, mean ± SD*: 55 ± 8 *Sx type, n (%):* MX: 24 (59)/QT: 17 (42) **Late group; n=40** *Age, mean ± SD*: 53 ± 12 *Sx type, n (%):* MX: 21 (57)/ QT: 16 (43)	**Exercise program (both groups)** 9 exercises outside hospital with illustrated manual Duration: 105 post-operative days Frequency: daily at home **Early group** Initiation: 1st post op day **Late group** Initiation: After drain removal (postoperative day 7-10, mean postoperative day: 9) *Follow up:* Postoperative day 14, 45, 75 and 105	Evaluation incision (presence of seroma formation and dehiscence) ROM (goniometer)	*Undisclosed*	n=14 did not attend 45th postop day (8 in early group; 7 in late group) n=2 return to Sx (in late group), n=1 died (in late group)
Sagen (2009) Norway	RCT	N= 207 **No activity restriction group (NAR); n=104** *Age, mean ± SD*: 54 ± 90.6 *Sx type, n (%):* BSx: 46 (44)/ BCS: 57 (55) *Systemic treatment, n (%):* RT, nodes:47(45)/RT, breast:78(75) Ch: 42 (40)/ HT: 48 (46) **Activity restriction group; n=100** *Age, mean ± SD*: 55 ± 90.6 *Sx type, n (%):* BSx: 51(51)/BCS: 49(49) *Systemic treatment, n (%):* RT, nodes:40(40)/RT, breast:73(73) Ch: 38 (38)/ HT: 50(50)	**No activity restriction group** Supervised physical therapy program which emphasized moderate progressive resistance exercise training Duration: 6 months Frequency: 2-3 times a week Exercise duration: 45 min Rep: 15 / exercise Load: 0.5kg the first 2 w increasing individually after **Activity restriction group** Physical therapy program with restricted activities of the OA avoiding heavy (>3kg) and strenuous activity.	Development of arm LE (VOL diff in mL) Pain and sensation of heaviness (VAS)	*Disclosed for general population* Water displacement *Undisclosed* VAS	Adverse events: n=2 developed adhesive capsulitis with progressive immobilization and n=1 developed supraspinatus tendinopathy 31/238 eligible participants who met the inclusion criteria refused to participate The reasons for the 52 missing

			Program: 6 different standardized passive manual techniques emphasizing flexibility and light massage of the affected shoulder, arm and scar. Duration: 6 months Frequency: 1/ week Program duration: 45 min *Follow up:* 3, 6 months and 2 yrs			individuals at follow-up were: 14 had died, three had moved elsewhere, 13 were not available, 7 refused to participate, four were too frail or ill, two had gone through ALDN on the control side, and nine were lost during follow-up.
Schultz & al. (1997) Sweden	RCT	N=163 with MRM **Early postoperative shoulder exercise group; n=89** Age, median (range): 59 (35-83) **Delayed postoperative shoulder exercise group; n=74** Age, median (range): 62 (41-84)	**Early postoperative shoulder exercise group** Active shoulder exercise (anteflexion, abduction, rotation) Initiation: 1st postop day Frequency: 3 times/day **Delayed postoperative shoulder exercise group** Active shoulder exercise (anteflexion, abduction, rotation) Initiation: 1st postop w Frequency: 3 times/day *Follow up:* 1w, 4 and 6 months	Shoulder mobility (abduction and anteflexion) Volume of seroma aspirations and number of aspirations	*Undisclosed*	Postoperatively 31% (50/163) of the patients suffered from seromas, 38% (34/89) in the early group and 22% (16/74) in the delayed group (Fig. 1). The difference was statistically significant.
Siedentopf (2013) Germany	RCT	N=93 **Intervention group; n=48** *Age, mean ± SD*: 55.82 ± 10.72 *Sx type, n (%):* BCS: 29 (62)/RM: 18 (38) SND: 37 (71)/ ALND: 15 (29) *Systemic treatment, n (%):* Ch: 17 (53)/ RT: 23 (70) **Control group; n=41** *Age, mean ± SD*: 58.41 ± 9.91 *Sx type, n (%):* BCS: 24 (60)/ RM: 16 (40)	**Intervention group** Yoga classes Initiation: Immediately after Sx Duration: 5 w Frequency: 2 times /w Class duration: 75 minutes 10 classes over 5 w **Control group** *Yoga classes* Initiation: 5 weeks after Sx Duration: 5 w	Quality of life (German version of the European Organization of Research and Treatment of Cancer Quality of Life questionnaire (EORTC QLQ-C30) and its breast-cancer-specific module EORTC QLQ-BR23)	*Cancer-specific outcome(s)* EORTC QLQ-C30 *BC-specific outcome(s)* EORTC QLQ-BR23	Due to the high number of participants who dropped out for various reasons (16 in the IG, 16 in the WG) only 31 women completed the intervention in the IG and 28 women in the WG.

		SND: 32 (78)/ ALND: 9 (22) *Systemic treatment, n (%):* Ch: 7 (30)/ RT: 16 (64)	Frequency: 2 times / w, 10 classes Class duration: 75 minutes Yoga class: started with lying postures and the gradual mobilization of arms and legs + breathing exercises + dynamic part of the exercises: standing and sitting positions + Eye exercises + series of concentration exercises.			
Temur (2019) Turkey	RCT	N= 72 **Intervention group; n = 36** *Age, mean ± SD*: 46.7 ± 9.96 *Stage, n (%):* I: 2 (7)/ II: 16 (53)/ III: 12 (40) *Sx type, n (%):* MRM: 22 (73)/ BCS: 8 (27) **Control group; n= 36** *Age, mean ± SD*: 45.6 ± 9.03 *Stage, n (%):* I: 2 (7)/ II: 16 (52)/ III: 13 (12) *Sx type, n (%):* MRM: 17 (55)/ BCS: 14 (45)	**Intervention group** Self-management of LE program (SMLP) + exercising program + simple LD+ closed monitoring to encourage the patient to do the exercises and to follow the instructions provided *SMLP program:* Training booklet containing information about mechanisms and risk factors of LE and about prevention interventions. *Exercising program:* 1st 24h: Hand squeezing exercises with a medium-level stress ball Frequency: 4 times/day Reps: 15 Active and passive arm exercises, the minimum amount of exercises required for the patient were determined by the doctor and nurse Initiation: within the first 24h post-Sx Duration: 6 months Frequency: 3-6 times/day at first and gradually increased to 10 Exercise sessions duration: 30-60 min *Simple lymphatic drainage* The researcher demonstrated and taught deep diaphragmatic breathing exercises, neck drainage, unaffected and affected side axillary drainage and UE drainage. Frequency of breathing exercises: 3 times a day	Upper extremity function (DASH) Presence of LE- upper extremity CIRC (Measuring tape) Quality of life (EORTC QLQ-30 and EORTC QLQ-BR23)	*BC-specific outcome* Upper extremity CIRC measurement EORTC QLQ-BR23 *Cancer-specific outcome* EORTC QLQ-30 *Disclosed for general population* DASH	*Lost to follow-up:* IG: did not follow the research program (n=2), wound site revision in the post-operative period during the research (n=3), developed skin reaction after RT (n=1) CG: did not follow the research program (n=1), wound site revision in the post-operative period during the research (n=2), developed skin reaction after RT (n=2) Feedback was received from the patients during the interviews, and it was found that telephone calls relieve and

			Breathing exercises duration: 3 min initially, gradually progress to 5 min Frequency of self-massage: 2 times a day Reps: 8-10 per session **Control group** No intervention during the study period, except usual post op care. Training booklets were distributed at the end of the study and patients who volunteered for ED were trained about SMLP *Follow-up:* 1, 3 and 6 months post-intervention			motivate the patients. The inclusion of the researcher's photograph in the booklet increased their motivation and adaptation to the program
Teodózio (2020) Brazil	RCT	N=572 **Free ROM group, n=254** *Age, mean ± SD*: 52.54 ± 12.03 *Sx type, n (%):* Segmentectomy: 107 (42) MX: 147 (58) **Restricted ROM group, n=211** *Age, mean ± SD*: 54.53 ± 10.95 *Sx type, n (%):* Segmentectomy: 94 (45) MX: 117 (56)	**Free ROM group** Active UL movements with ROM over 90° (flexion and abduction of shoulder) (leaflet + home guide) Initiation: 1st postop day Frequency: 3 times/day (at least once a day) **Restricted ROM group** Active UL movements with ROM restricted to 90° (flexion and abduction of shoulder) from postoperative day 1 until removal of all surgical stitches (leaflet + home guide) Frequency: 3 times / day (at least once a day) *Follow up:* Postoperative day 1 and 30 days	Presence of seroma Necrosis Dehiscence Hematoma Infection Bruise	*Undisclosed*	n=73 refused to participate n=34 Sx not performed on schedule date Drop out during follow up: non-return to the wound-dressing clinic (*n* = 1), hospitalization for reasons other than a surgical approach (*n* = 2) and changes to the treatment protocol (*n* = 1)
Testa (2014) Italy	RCT	N=70 **Treated group, n=35** *Age, mean ± SD*: 54.3 ± 8.02 *Stage*: N/A *Sx type, n (%):* Maddens' MRM: 19 (54) Segmental MX + ALDN: 16 (45) *Systemic treatment, n (%):*	**Treated group** Early physical rehabilitation program with instructions of a PT from latest guidelines for rehabilitation in BC published on 2005 by Italian society of senology Initiation: 2nd postop day Program duration: 40 min	Mobility of the glenohumeral joint (goniometer) Grade of pain perceived (VAS)	*Undisclosed*	-

		Ch: 24 (69)/ RT: 30 (86) **Control group, n=35** *Age, mean ± SD*: 55.3 ± 8.5 *Stage*: N/A *Sx type, n (%):* Maddens' MRM: 21 (60) Segmental MX + ALDN: 14 (40) *Systemic treatment, n (%):* Ch: 25 (71)/ RT: 27 (77)	Frequency: 5 times / w during all the duration of axillary drainage *Exercises:* active flexion, extension movement of the cervical spine, lateral flexion and rotation + passive and active assisted caution mobs of hand, wrist, elbow (flexion, extension, pronation, supination) 3rd postop day: Passives exercises of flexion, abduction, adduction and circumduction (25 min) + active internal, external rotation arms' movements (15 min) Once drainage removed (approximatively postoperative day 7): 20 PT sessions Frequency: 5 times / w Duration: 60 min / session Exercises: postural and stretching exercises (20 min) + active movements of abduction, flexion, internal and external rotation of glenohumeral joint (40 min) **Control group:** *N*o early physical rehabilitation program with no instructions of a PT Rehabilitation program from the old rehabilitation guidelines *Follow up:* Postoperative day 5 and 1, 6 and 12 months	Quality of life (EORTC QLQ30 and QLQ-BR23)		
Todd (2008) UK	RCT	N= 116 **Delayed shoulder mobs; n=58** *Age, mean ± SD*: 56.5 ± 12.4 *Stage, n (%):* I: 8 (14)/ II: 24 (41)/ III: 26 (45) *Sx type, n (%):* WLE: 36 (57)/ MX: 24 (43) *Systemic treatment, n (%):* RT: 39 (67)/Ch: 30(52)/HT: 34 (59)	**Delayed shoulder mobilization** Exercises program that limited arm movements < 90° in all planes, followed by a full shoulder ROM program Initiation: *Limited ROM program*: 2nd postop day *Full ROM program:* 2nd post op w	Incidence of LE-limb VOL difference (Water displacement) Shoulder ROM (Manual goniometer) Grip strength	*BC-specific outcome* FACT-B+4 *Disclosed for general population*	116 (36% of eligible patients) women agreed to take part in the study and seven (6%) withdrew during the 1st year Reasons for

		Early full shoulder mobs; n= 58 *Age, mean ± SD:* 57 ± 14 *Stage, n (%):* I: 8 (14)/ II: 27 (48)/III: 23 (38) *Sx type, n (%):* WLE: 29 (50)/ MX: 29 (50) *Systemic treatment, n (%):* RT: 41 (71)/Ch: 26(45)/ HT: 41(71)	**Early full shoulder mobilization** Full shoulder mobilization (i.e., movement > 90°) and shoulder ROM exercises Initiation: 2nd postop day **Both groups** Exercise sessions duration: 10 minutes Frequency: 4 times/day until full shoulder ROM was restored and then once/day for the 1st postop year Repetitions: 3-4 per exercise The exercise programme was supervised during inpatient stay (average 7 days). *Follow-up:* 1 week, 1 month and 6 months	(hand-held dynamometer) Health-related QoL (FACT-B+4 and SDQ)	Manual goniometer SDQ Hand-held dynamometer Water displacement	declining to participate: lack of interest or unwillingness because of anxiety about impending S_x The majority of women (73%, n = 85) claimed that they had adhered to their exercise programme
Torres (2010) Spain	RCT	N= 120 **Early physiotherapy group;n =60** *Age, mean ± SD*: 52.9 ± 10.7 *Stage*: N/A *Sx type, n (%):* QT: 24 (40)/Modified MX: 23 (38)/ LUMP:13 (22) *Systemic treatment, n (%):* RT: 44 (75)/Ch: 50(85)/HT: 39 (66) **ED strategy group; n = 60** Age, mean ± SD: 52.9 ± 12.5 *Stage*: N/A *Sx type, n (%):* QT: 26 (43)/ Modified MX: 20 (34)/LUMP:14(23) *Systemic treatment, n (%):* *RT*: 49 (86)/*Ch*: 45(79)/*HT:* 33 (58)	**Early physiotherapy group** MLD + progressive massage of the scar, stretching exercises and progressive active and action assisted shoulder exercises, combined with functional activities and proprioceptive neuromuscular exercises + educational strategy Initiation: 3 to 5 days after hospital discharge **Educational strategy only group** Instruction with printed materials about the lymphatic system, concepts of normal load vs overload, source of 2ndary LE, precipitating factors and 4 preventive interventions Initiation: 3 to 5 days after hospital discharge Duration of both programs: 3 w Frequency of both programs: 3 times/ w *Follow-up:* 1w, 3 months, 6 months and 12 months post-Sx	Incidence of secondary LE (Arm CIRC)	*BC-specific outcome(s)* Arm CIRC	Overall, 116 women completed the follow-up assessments; 59 in the intervention group and 57 in the control group.

Wingate (1989) USA	RCT	N= 115 **Treated group, n=61** *Age, mean*: 56.26 **Control group, n=54** *Age, mean:* 58.27	**Treated group** Physical therapy Initiation: 1st postop day 1 Duration: 8 w minimum Frequency: 2 session / day Exercise sessions duration: 30 min Exercises: motor and sensory status, active hand, wrist, elbow and postural exercises, active and active assisted shoulder exercises, functional activities and PNF After drain removal: home exercises program with progressive restrictive exercises and PNF **Control group** Untreated group with no physical therapy *Follow up:* Postoperative day 5 and 1-3 months	Psychopathologic self-report inventory (SCL-90-R) Shoulder ROM for flexion and abduction (goniometer) Functional evaluation of the ipsilateral shoulder (scale of difficulty) Upper extremity CIRC measurement	*Cancer-specific outcome:* SCL-90-R *Undisclosed:* Goniometer Scale of difficulty 5 levels of upper extremity CIRC measurement	-
Zhang (2016) China	RCT	N= 1000 **Physical exercise group; n=500** *Age group, n (%):* <50: 272 (54)/ ≥50: 228 (46) *Stage, n (%):* I/II: 211 (42)/ III: 289 (58) *Sx type, n (%):* MRM: 500 (100) **MLD group; n=500** *Age group, n (%):* <50: 266 (53)/ ≥50: 234 (47) *Stage, n (%):* I/II: 197 (39)/ III: 303 (61) *Sx type, n (%):* MRM: 500 (100)	**Physical exercise group** Physical exercise alone Initiation: 24h before Sx with ED (risk of postsurgical complications and importance of medical intervention and self-management) Frequency: post-operative day 1, 2, 3 and day of discharge Session duration: 20-30 min Postop day1-7 (before drain removal: Physical exercise program Passive exercises Frequency: 3 times / day Session duration: 15 min. Postop day7-30: (after drain removal to sutures removal): Exercises progressed to localized exercises on the affected UL After removal sutures to 6 months: Extensive active exercises involving affected shoulder Frequency: 3 times / day	Stage of UL LE (Observation and tape-measuring) Scar formation (Vancouver Scare Scale) Shoulder function (max. shoulder abduction)	*Undisclosed*	By the third month after Sx, only 4 patients in the MLD group had developed scar contracture, while 12 had developed scar contracture in the PE group.

			Session duration: 15 min. **MLD group** Physical exercises + Self-MLD Initiation manual drainage: after sutures removal Frequency: 3 sessions / day Session duration: 30 min. 3 steps of 10 min. *Follow up:* Week 1, 1, 3, 6 and 12 months			
Zhou (2019) China	RCT	N=92 **Intervention group; n=46** *Age, mean ± SD*: 49.94 ± 8.88 *Stage, n (%):* I: 18 (35)/ II: 27 (53)/ III: 6 (12) *Sx type, n (%):* MX + SND: 24 (47)/MX + ALND: 15 (29) BCS + SND:10(20)/BCS +ALND:2(4) *Systemic treatment, n (%):* Ch: 41 (80) **Control group; n=46** *Age, mean ± SD*: 49.40 ± 9.88 *Stage, n (%):* I:14(28)/II: 29(57)/III: 8(16) *Sx type, n (%):* MX +SND: 25(49)/MX + ALND: 17 (33) BCS + SND: 6(12)/BCS +ALND: 3(6) *Systemic treatment, n (%):* Ch:43 (84)	**Intervention group** Progressive UL exercises and muscle relaxation training by nurses Initiation: before Sx Duration: 6 months Frequency: 1 session/ day at hospital and 1 session/ week at home after discharge **Control group** Routine nursing care (Sx district nursing, drainage tube nursing, routine health ED, physical exercises, vital sign monitoring and post-Sx complications) *Follow up:* 1, 3, 6 months	Quality of function (Constant-Murley Score) Health related quality of life (FACT-Bv4.0)	*Undisclosed*	All intervention group patients completed the exercises and training, with no adverse events and a compliance of 100%.
Zimmermann (2012) Germany	RCT	N=67 **MLD group; n=33** *Age, mean ± SD*: 60.3 ± 8.2 Stage, n (%): I: 12 (36)/ II: 15 (46)/ III: 6 (18) *Sx type, n (%):* BCS: 20 (61)/ MRM: 13 (39) SND:14 (42)/ ALND: 19 (58)	**Both groups** Exercises of limb and chest physiotherapy Initiation: 2nd postop day **MLD group** *Manual lymph drainage* Initiation: 14th postop day	VOL of both arms (water displacement With glass cylinder with water) VOL of LE	*Undisclosed*	In the present study, all women who had received MLD on day 2 after Sx and continued receiving it for the 6 ensuing months

		Systemic treatment, n (%): Ch: 13 (39)/RT: 22 (67) **Control group; n=34** *Age, mean ± SD*: 58.6 ± 12.2 *Stage, n (%):* I: 11 (32)/II: 16 (47)/III: 7 (21) *Sx type, n (%):* BCS: 20 (59)/ MRM: 14 (41) SND: 18 (53)/ ALND: 16 (47) *Systemic treatment, n (%):* Ch: 15 (44)/RT: 25 (74)	Duration: 6 months Frequency: 5 sessions/ week **Control group** Applied self-drainage from modification of the method described by Földi and Strönbenreuher *Follow up:* 6 months			did not develop secondary LE of the arm on the operated side. In the group of women without MLD, 6 months after Sx, 70.6% of the subjects suffered from LE.
Majed (2020) USA	RCT	N= 69 BC women undergoing MRM **Intervention group; n=35** *Age group, n (%):* 35-42: 14 (47)/43-48: 10 (33) 49-55: 6 (20) **Control group; n=34** Age group, n (%): 35-42: 14 (47)/43-48: 10 (33) 49-55: 6 (20)	**Intervention group** *Phase 1* Initiation: day prior to Sx Measurements: QoL-BC survey and shoulder ROM *Phase 2* Initiation: Prior to Sx Intervention: one-to-one ED (PowerPoint presentation regarding the therapeutic exercises, information about the surgery, and a booklet with pictures of the exercises to take home) in addition to routine hospital care. Demonstration of the exercises by the researcher with a return demonstration by the patient was done. Follow up every week by phone. *Phase 3* Exercise program Initiation: Immediately after Sx Exercises: deep breathing + shoulder exercises (extension of the triceps, bicep curl, paddling in sitting position, fluttering with both arms, hands behind neck, forward wall crawls, and side wall crawls). Shoulder flexion was limited to 90° of assisted AROM for the first few days post-Sx and until the drains were removed, gradually increased after the 3rd postoperative day.	Quality of life (Breast Cancer Patient Version (QoL-BC)) Shoulder ROM (Goniometer)	*BC specific outcomes* Breast Cancer Patient Version (QoL-BC) Goniometer	7 were excluded because they didn't fit criteria or declined to participate, 5 refused to do the exercises, 4 lost to follow up

			Rep: 10 of each exercise during hospitalization **Control group** *Phase 1* Initiation: day prior to Sx Measurements: QoL-BC survey and shoulder ROM *Phase 2* Initiation: Prior to Sx Intervention: routine hospital care (explanation by the surgeon on the surgical procedure). *Phase 3* Initiation: At home Frequency measurements of ROM and questionnaire: w2 and w4 after Sx			
de Almeida Rizzi (2020) Brazil	Randomized clinical trial	N= 62 **Free ROM group; n = 31** *Age, mean ± SD*: 49.90 ± 10.11 *Stage, n (%):*0: 10 (33)/ I: 4 (13)/ II: 3 (10) IIB:7(23)/III:5(17)/IIIB:1(3)/IV:0(0) *Sx type, n (%):* Breast sparing Sx: 14 (47) MX: 16 (53)/Breast recons: 30(97) *Type of node dissection, n (%):* SNB: 15 (50)/ALND: 14 (47) *Systemic treatment, n (%):* Neoadj Ch: 13 (43) **Limited ROM group; n = 31** *Age, mean ± SD*: 54.46 ± 10.68 *Stage, n (%):* 0: 11 (37)/ I: 4 (13)/ II: 7 (23)/ IIB: 5 (17)/ III: 2 (7)/ IIIB: 0 (0)/IV: 1 (3) *Sx type, n (%):* Breast sparing Sx: 10 (33) MX: 20 (67)/Breast recons: 30(97) *Type of node dissection, n (%):* SNB: 21 (70)/ ALND: 7 (23) *Systemic treatment, n (%):* Neoadj Ch: 10 (33)	**Both groups** Exercise protocol consisting of neck and UL stretching exercises and shoulder ROM exercises Initiation: First post-op day Day1-14: Exercises 1-6 From Day15: Exercises 1-8 **Free ROM group** Were allowed to perform the protocol exercises and ADL in free amplitude **Limited ROM group** Had ROM maintenance limited to 90° until the 30th post-op day, then started free ROM exercises *Follow up* Day 7, 15, 30, 60 and 90 postoperatively	Dehiscence (Inspection, palpation and tape measure) Seroma (Inspection and palpation, medical record) Infection (Inspection and palpation, medical record) Necrosis (Inspection and medical record) Shoulder ROM (Goniometer) Pain (VAS) UL function (DASH)	*Undisclosed*	Limited ROM group: Discontinued: reoperation before PO30: removal of extruded prosthesis The free ROM group presented one case of dehiscence that started after PO30 (late), and the limited ROM group presented two cases between PO15 and PO30 (intermediate) and one case after PO30 (late).

						Pain complaint was present in all the PT evaluations of both groups, from moderate to severe intensity
de Oliveira (2014) Brazil	Controlled non-randomized clinical trial	N= 96 **Exercise group; n = 48** *Age, mean ± SD*: 56.7 ± 15.1 *Stage, n (%):* I: 1 (2)/ II: 17 (37)/ III/IV: 28 (61) *Sx type, n (%): MRM:* 48 (100) *Systemic treatment, n (%):* *Neoadj Ch:* 22 (48) **MLD group; n = 48** *Age, mean ±SD*: 55.6 ± 11.9 *Stage, n (%):* I: 0 (0)/ II: 9 (20)/III/IV: 34 (79) *Sx type, n (%):* MRM: 42 (62)/Halsted RM: 1 (2) *Systemic treatment, n (%):* Neoadj Ch: 29 (67)	**Both groups** *Educational strategy:* Information leaflets about proper care for the OA and lectures Initiation: 1st post-op day **Exercise group** 19-exercise supervised program including neck and rotator cuff muscles stretching and active assisted and free AROM exercises Initiation: 3rd post-op day Duration: 2 days/w for 30 days Exercise sessions duration: 40 min **MLD group** Manual lymphatic drainage applied by 3 experienced PT Initiation: 3rd post-op day Duration: 2 days/w for 30 days MLD sessions duration: 40 min	UL CIRC (Measuring tape) Shoulder ROM (Goniometer) Scarring complications (Signs of wound dehiscence, infection, seroma and puncture)	*Disclosed for general population:* Goniometer *Undisclosed:* Measuring tape	-
Na (1999) South Korea	Non-randomized clinical trial	N= 33 **Rehabilitation group; n = 20** *Age, mean ±SD*: 43.8 ± 2.1 *Stage*: N/A *Sx type, n (%):* MRM: 15 (75)/Partial MX: 5 (25) **Control group; n = 13** Age, mean ± SD: 46.9 ± 9.8 Stage: N/A *Sx type*, n (%): MRM: 7 (54)/Partial MX: 6 (46)	**Rehabilitation group** Early postmastectomy rehabilitation program Initiation: 1st postop day Duration: Patients received instructions to pursue the program at home for 4w Program duration: 40 minutes of PT and 30 minutes of exercises Frequency: 4 times a day *1st postop day:* Postural exercises, AROM of the shoulder, elbow, wrist, and hands with active use of the involved arm	Symptoms Checklist (SCL-90-R) Shoulder ROM (Goniometer) Shoulder function (10 items provided by Wingate) UL CIRC (Tape measurement)	*Cancer-specific outcome(s):* SCL-90-R *Disclosed for general population*: Goniometer *Undisclosed:* Items provided by Wingate	Postoperative complications or problems Control group; wound breakdown (7.7%), adhesional bands (15.4%), sensory changes around surgical incisions (38.5%) Rehabilitation group; mild edema (5%), wound

			From the 3rd postop day: Physical modalities for pain relief (PENS, heat therapy, cold therapy) and therapeutic exercises including ROM exercises. Patients with LE received IPC and those with myofascial pain or muscle spasm received trigger points injection with lidocaine *After drains removal:* Progressive resistance exercises of the UE with an increase in functional activities **Control group** No rehabilitative treatment, instruction alone for ROM exercises pertaining to the affected shoulder and postural exercises *Follow up:* 3rd post op day, at discharge and 1 month after discharge		Circumference measurement	breakdown (5%), adhesional bands (15%), sensory changes (9%)
Oliveira (2018) Brazil	Non-randomized clinical trial	N=116 **Active exercise group; n=58** *Age group, n (%): <55:* 22 (42)/ *≥55:* 31 (59) *Stage, n (%):* I: 1 (20)/II: 17 (34)/III/IV: 32 (64) *Sx type, n (%):* MRM Patey: 29 (55)/MRM Madden: 24 (45) RM Halsted: 0 (0) *Systemic treatment, n (%):* Neoadj Ch: 24 (45)/Adj Ch: 8 (36) RT: 16 (73)/ HT: 14 (64)/ IT: 3(14) **MLD group; n=58** *Age group, n (%): <55:* 24 (45)/*≥55:* 29 (55) *Stage, n (%):* I: 0 (0)/II: 9 (18)/III/ IV: 43 (82) *Sx type, n (%):* MRM Patey: 19 (36)/MRM Madden: 33 (62) RM Halsted: 1 (2)	**Both groups** Educational strategy: Information leaflets about proper care for the OA and daily active exercises to do at home) + lectures delivered by the multidisciplinary team during the first month after Sx. Initiation: 1st postop day **Active exercise group** Initiation: 48h after Sx Duration: 30 days Frequency: 40 min group session, 2/w Exercises: 30% of the time – stretching of the scalene muscles, trapezius muscles, levator scapulae muscles, pectoralis major and minor muscles, rotator cuff muscles of the shoulder; 60% of the time – active assisted exercise and free active exercise for shoulder flexion, abd, add, internal and	Velocity visualization of axillary lymph nodes and degree uptake in axillary lymph nodes (Lymphoscintigraphy) ROM UL CIRC	*Undisclosed*	Active exercise group: 3 missed 2 consecutive sessions + 2 lost follow up at 2 months and 17 death and 13 lost to follow up at 30 months MLD group: 1 missed 2 consecutive sessions + 4 lost follow up at 2 months and 19 death and 4 lost to follow up at 30 months

		Systemic treatment, n (%): Neoadj Ch: 36 (68)/Adj Ch: 18 (62) RT: 26 (87)/HT:18 (60)/ IT: 5 (17)	external rotation of the UL alone or combined, followed by stretching of the deltoid, latissimus dorsi, rhomboids and pectoralis muscles; and 10% of the time-relaxation, according to treatment protocol of the service **MLD group** Manual lymphatic drainage Initiation: 48h after Sx Duration: 30 days Frequency: 40 min individual session, 2/w *Follow up:* one week before Sx, 2 and 30 months			
Kim (2019) South Korea	Retrospective case-control study	N= 115 **Early rehabilitation group; n = 49** *Age (age range):* 43 (34-61) *Stage*: N/A *Sx type*: Skin-sparing total MX and immediate Brecons with tissue expander *Type of node dissection, n (%):* SNB: 41 (84)/ ALND: 8 (16) *Systemic treatment, n (%):* Neoadj Ch: 3 (6) **Conventional protocol; n = 66** *Age (age range):* 42 (24-61) *Stage*: N/A *Sx type*: Skin-sparing total MX and immediate Brecons with tissue expander *Type of node dissection, n (%):* *SNB:* 46 (70)/ *ALND:* 20 (30) *Systemic treatment, n (%):* Neoadj Ch: 7 (11)	**Both groups** Self-exercise ED Initiation: 1st post-op w **Early rehabilitation group** Short term immobilization period (2w) followed by a self-exercise program including progressive shoulder stretch exercises and strengthening exercises Initiation: 3rd post-op w Frequency: 4 times a day/ 7 days per w Sets/Repetitions: 1 / 5-10 **Conventional protocol** Were asked to immobilize the OA for more than 4w and engaged themselves in the same self-exercise program after the immobilization period Initiation: From the 5th post-op w Frequency: 4 times a day/ 7 days per w Sets/Repetitions: 1 / 5-10 *Follow up:* 1 and 2 months postoperatively	Shoulder ROM (goniometer) Pain (NRS-11) QoL (SF-36) UL function (DASH) Postoperative complications (Plastic surgeon assessment)	*Disclosed for BC survivors:* SF-36 *Disclosed for patients with adhesive capsulitis:* Goniometer *Disclosed for general population:* NRS-11 DASH	No surgical sites complications that can be attributed to the intervention At the 1-month follow-up, 4 patients in the conventional group were diagnosed with secondary adhesive capsulitis
Lu (2015) Taiwan	Retrospective cohort study	N= 1217 **Group A; n= 415** *Age, mean ± SD*: 51.79 ± 11.97 *Stage, n (%):*0-2: 326 (79)/ 3: 89 (21)	**Group A** No ED or PT provided **Group B**	Occurrence of LE (Limb-to-limb CIRC difference) LE severity	*Disclosed for patients with LE*	-

		Sx type, n (%): BCS: 123 (30)/Simple MX: 25 (6) MRM: 267 (64) *Systemic treatment, n (%):* RT: 182 (44)/ Ch: 342 (82) **Group B; n = 672** *Age, mean ± SD*: 52.67 ± 11.01 *Stage, n (%):* 0-2: 503(75)/ 3:169 (25) *Sx type, n (%):* BCS: 152(23)/ Simple MX:11(2)/ MRM: 509(76) *Systemic treatment, n (%):* RT: 297 (44)/ Ch: 549 (82) **Group C; n = 130** *Age, mean ± SD*: 51.88 ± 10.08 *Stage, n (%):* 0-2: 92 (71)/ 3: 38 (29) *Sx type, n (%):* BCS: 303(25) Simple MX: 41(3)/MRM: 873(72) *Systemic treatment, n (%):* RT: 66 (51)/ Ch: 111 (85)	ED only which provided information on the lymphatic system, the symptoms and signs of LE, suggestions for preventing LE. **Group C** ED + PT sessions which included the following treatments: breathing exercise, postsurgical positioning, massaging of scar tissue, mobs of the shoulders and UE exercises, passive and active stretching of the major and minor pectoral muscles Initiation: 1st postop w in the hospital and was continued at outpatient clinics post discharge Frequency: 2 times/w PT sessions duration: 30 min	(Criteria defined by the International Society of Lymphology)	Criteria defined by the International Society of Lymphology *Undisclosed* Limb CIRC measurement	
Morimoto (2003) Japan	Prospective observational study	N=72 BC women stage I or II **PCM group; n=33** *Age, mean ± SD*: 50.0 ± 11.0 *Stage*: N/A *Sx type*: PCM **BCS group; n=38** *Age, mean ± SD*: 50.8 ± 8.8 *Stage*: N/A *Sx type*: BCS	**Both groups** Initiation: postoperative day 1 Duration: After hospital discharge (postop day 10-14) was entrusted to the patient's own initiative *Postoperative day 1:* Prevention of development of rigidity of shoulder joint on the OA: Lateral and forward arm raising on the affected side in the dorsal sitting positions *Postoperative day 2:* Training for force releasing through exercise of shoulder joint: Backward arm raising, finger crawling on a wall and force releasing/concentrating by keeping the arm on affected side at a position of backward raising at 90° *Postoperative day 3:* Exercise to approximate preoperative life: Exercises such as wing flapping	Shoulder joint ROM (goniometer) Grip strength (Instrument not provided) Pain after Sx (Instrument not provided) Movement associated chest pain (Instrument not provided) Operative wound pain (Instrument not provided) ADL	*Undisclosed*	At postoperative week 1 and 2, movement-associated pain was reported by 64% and 67% of the patients, respectively. At postoperative week 4 and 12, pain was reported by 49% and 44%, respectively, and its frequency remained high, especially in the BCS group. Either pain at night or operative wound pain were

			and touching the ears and back with the hands *Postoperative day 4:* Exercise to reduce functional differences between the normal and affected sides: Reduction of right and left side differences through the above-mentioned exercises on postoperative days 1–3 *Follow up:* Before Sx, postoperative w1, 2, 4, 12	(Ability to sleep on the affected side, ability to tie an apron, ability to air the futon in the sun)		reported by 6–12% and 3–15% of the patients at postoperative week 1 and 2 and postoperative week 4 and 12, respectively.
Scaffidi (2012) Italy	Prospective observational study	N=83 **Group A; n=25** *Age, mean ± SD*: 49.6 ± 8.8 *Sx type, n:* *LUMP:* 10 with 7 SND and 3 ALND *RM:* 15 with 2 SND and 13 ALND **Group B; n=58** *Age, mean ± SD*: 52.1 ± 11.9 *Sx type, n:* *LUMP:* 35 with 26 SND and 9 ALND *RM:* 23 with 6 SND and 17 ALND	**Group A** Preoperative information orally + home rehabilitation program (flexibility and elasticity of muscles surrounding shoulder joint) **Group B** Preoperative information orally + information materials + PT treatment at hospital: deep breathing, stretching neck muscles, elevation, abd, external and internal rotation of shoulder, flexion and extension of elbow in neutral position + home rehabilitation program PT at hospital: 1 per day, 30-40 min Home rehab program: 3 times/ day *Follow up:* 60 and 180 days	Shoulder arm mobility (goniometer) UL function (Constant and Murley Score) Presence of LE (Universal level meter)	*Undisclosed*	-
Springer (2010) USA	Prospective observational study	N=94 Age, mean ± SD: 53.39 ± 11.80 *Stage, n (%):* 0: 11 (12)/ I: 40 (43)/ II: 30 (32)/III: 13 (14) *Sx type, n (%):* BCT: 41(44)/MRM: 50(53)/Simple MX: 3 (3) Lymph nodes dissection, n (%): None: 8 (9)/SND: 20 (21)/ALND: 66 (70)	**UL ROM program** Flexion, abduction, internal and external rotation Pre-operative examination: subjects were instructed in a post-operative UL ROM exercise program, and were educated regarding UL LE precautions and physical exercise initiation and progression	Pain (NRS) Bilateral shoulder ROM (goniometer) Bilateral shoulder strength (Break testing of UL) Volume and girth measurements for both	*BC-specific outcome:* Perometer® *Undisclosed* NRS Goniometer	-

		Systemic treatment, n (%): Ch: 57 (61)/RT: 64 (66)/HT: 67 (7)	Initiation: post-Sx Reviewed at 1 month *Follow-up*: 3 post-surgical visits: 1, 3-6 and 12+ months	UL (Optoelectronic volumeter, Perometer®) UL function and disability (Upper Limb Disability Questionnaire)	Break testing of UL Upper Limb Disability Questionnaire	
Hsieh (2008) USA	Pretest and post-test quasi-experimental study	N= 96 Women referred by local oncologists for rehabilitative exercises *Sx type:* N/A *Stage*: N/A **Sx alone; n = 22** *Age, mean ± SD*: 55.6 ± 11.3 **Sx and Ch; n = 30** *Age, mean ± SD*: 55.6 ± 11.0 **Sx and RT; n= 17** *Age, mean ± SD*: 57.2 ± 9.4 **Sx, Ch and RT; n = 27** *Age, mean ± SD*: 63.1 ± 9.8	**All groups** Individualized exercise intervention based on the results of the medical and cancer history, physical examination, and the initial physiologic and psychological assessments Initiation: immediately following treatment for BC Exercise sessions in general: 10-min warm-up, 40-min of aerobic exercises, resistance training and stretching and concluded with a 10-min cooldown Intensity: 40-65% of HR reserve (based on the treadmill assessment results)	Cardiovascular endurance (Bruce Treadmill Protocol; HR, BP, predicted VO_{2max}, time on treadmill and oxygen saturation) Pulmonary function-FVC, FEV_1 (Flowmate™ spirometer) Cancer-related fatigue (Piper Fatigue Scale)	*BC-specific outcome(s):* Piper Fatigue Scale *Undisclosed:* Bruce Treadmill Protocol Flowmate™ spirometer	Participants' adherence to the exercise intervention was approximately 90%, which can be attributed to cancer exercise specialists who prescribed individualized cancer interventions that fit patients' circumstances.
Petito (2012) Brazil	Quasi-experimental, before and after study	N=64 **Mastectomy group; n=43** *Age, mean ± SD*: 52.2 ± 9.6 *Sx type, n (%):* MRM: 37(86)/ Simple MX:4 (9)/ RMX:2 (5) **QT group; n=21** *Age, mean ± SD*: 63.4 ± 9.0	**Exercise program (both groups)** 9 exercises Initiation: Postoperative day 1 Duration: 105 post-operative days Frequency: daily Rep: 10/exercise *Phase 1 (1st postop day until drain removal):* Two stretches for the cervical region, two exercises for movement of the scapular girdle, one for shoulder flexion and one for extension beyond the midline *Phase 2 (after drain removal until the 105th postop day:*	Shoulder ROM: flexion, extension, abduction (goniometer)	*Undisclosed*	N=22 did not attend the penultimate or last evaluation, n=5 required reoperation. Satisfactory adherence from the 7th PO until the 75th PO varied from 75.8 to 91.2%. Furthermore, it was observed that the adherence declined according

			Three additional exercises: one exercise for flexion and two for abduction of the shoulder. *Follow up:* Postoperative day 14, 45, 75 and 105			to the recuperation of the ROM.
Singh (2013) Canada	Quasi-experimental pretest post-test study	N= 73 **Experimental group; n = 42** *Age, mean ± SD*: 55.1 ± 14.8 *Stage, n (%):*0 or I: 2 (5)/ II: 14 (34) III: 19 (46)/ N/A: 6 (15) *Sx type, n (%):* MRM: 22 (54)/ Simple MX: 7 (17) BCS: 12 (29)/B recons: 22 (54) *Systemic treatment, n (%):* RT: 22 (54)/Ch: 16 (39) **Comparison group; n = 31** *Age, mean ± SD:* 62.8 ± 14.1 *Stage, n (%):* 0 or I: 2 (7)/ II: 10 (32) III: 13 (42)/ N/A: 6 (19) *Sx type, n (%):* MRM: 7 (23)/Simple MX: 9 (29) BCS: 15 (48)/ Brecons: 3 (10) *Systemic treatment, n (%):* RT: 14 (45)/Ch: 16 (32)	**Experimental group** Standardized preoperative ED delivered by 2 trained PT + 2 monitoring visits + PT treatment if needed focusing on teaching self-management strategies, scar tissue massage and AROM and assisted shoulder exercises *Standardized preoperative education program:* -General postop mobility exercises -AROM exercises: 10 reps every 4h -Education on LE -Scar management *Follow-up*: 1, 6 and 7 months post-Sx **Comparison group** Standardized preoperative ED alone *Follow-up:* 7 months post-Sx	Arm mobility-Shoulder ROM (goniometer) Presence of LE (Arm CIRC, tape measure) UE strength (Manual muscle testing) UE function (DASH) Quality of life (FACT-B+4) Postoperative pain (VAS)	*Cancer-specific outcome* FACT-G Arm CIRC *Disclosed for general population* DASH *Undisclosed* Goniometer VAS	One participant did not complete the 7-month follow-up visit and was therefore removed from the data analysis, leaving 41 participants in the experimental group and 31 in the comparison group.
Rekha (2020) India	Quasi-experimental study	N= 20 *Age range*: 40-60 *Sx type*: Unilateral BSx (MX or BCS) within a month	**Group A; n= 10** Swiss ball exercises + diaphragmatic breathing exercises (10 repetitions) Duration: 4w; 5 days/w **Group B; n= 10**: Stretching exercises + diaphragmatic breathing exercises (10 repetitions) Duration: 4 w; 5 days/w	Chest expansion (inch tape) -FEV_1 (computerized spirometer) - Shoulder ROM (goniometer)	*Undisclosed*	-
Kilgour (2008) Canada	Pilot study	N= 40 **Home-based exercise (HBE) group; n = 20** *Age, mean ±SD*: 50.6 ± 9.3 *Stage, n (%):* N/A *Sx type*: MRM + ALDN **Usual care (UC) group; n = 20** *Age, mean ±SD*: 49.1 ± 5.7	**HBE group** HB exercise video program that incorporated the exercises and guidelines described in a brochure from CCS Initiation: 3rd postop day Duration: 11 days	Shoulder ROM (goniometer) Shoulder strength (Manual muscle testing techniques) Grip strength	*Disclosed for general population:* Goniometer	HBE group: -3/16 women discontinued their home program after 4 days: pain around the shoulder joint and

		Stage, n (%): N/A *Sx type*: MRM + ALDN	*Phase 1* *Day3-9:* Self-A shoulder ROM and flexibility exercises Frequency: 3 set/day Sets duration: 5-7 minutes *Phase 2* *Day10-14:* Same exercises as Phase 1 Frequency: 2 sets/day Sets duration: 10-15 min **UC group** Received information on diet and skin scare and a 9-page brochure containing stretching and ROM shoulder exercises printed by the CCS, without further instructions	(Hand-grip dynamometer) Forearm CIRC (Tape measurement) Frequency of medication intake, VOL of fluid from the axillary drains and self-perceived pain level (CR-10 Pain Scale) and exertion (Borg Scale) (Diary)	Manual muscle testing techniques *Disclosed for patient with lower limb LE*: Tape measurement Undisclosed: Hand-grip dynamometer CR-10 Pain Scale Borg Scale	swelling of the axillary region. -2/16 unable to complete: lacked support from their spouse, family members or friends. -1/16 swelling around the axillary incision site: discontinued her program for 4 days. Explanations to describe adherence rates were: (1) they understood the importance of arm movement (2) the surgical oncologist appeared on the video recommending the program and (3) there was strong support from spouses or family members.
Baima (2017) USA	Feasibility study	N= 60 *Age, mean, stage and systemic treatment*: N/A *Sx type*: MX or lumpectomy **Gr 1- in person teaching; n= 36** **Gr 2- video-only teaching; n= 24**	**Both groups** Prehabilitation exercise program and post-Sx shoulder ROM exercises restrictions > 90° until drains were removed Initiation 1-4w prior to Sx Frequency: once daily, suspended post-Sx Sets/Rep: 3/10	Pain (NRS-11) Shoulder abduction ROM (Goniometer) Postoperative seroma formation	*Undisclosed* *NRS-11* *Goniometer* *Postoperative seroma formation*	*Reasons for attrition:* -Accessibility of study staff at follow-up oncology appointments to assess shoulder ROM -Delayed surgical treatment due to Neoadj Ch

			Participants could resume the same exercises as desired after Sx and after the drains were removed **Group 1- in person teaching** In-person physical demonstration and instructions of supervised shoulder ROM exercises (Codman, scapular squeezes, reach for the pillow) **Group 2- video-only teaching** Instruction's sheet of shoulder ROM exercises and optional exercises video without additional supervision *Follow-up:* Between 2w and 6 months post-Sx (variable across study participants)			-Disease worsening with changes in initial treatment plan -Computer or Internet access issues ''Several patients had drains in place for several weeks after their Sx, which prevent them from exercising''

***ADL**: Activities of daily living; **Adj Ch**: Adjuvant chemotherapy; **ALND:** Axillary lymph node dissection; **AROM**: Active range of motion; **AWS**: Axillary web syndrome; **BC**: Breast cancer; **BCS:** Breast conserving surgery; **BP**: Blood pressure; **BSx:** Breast surgery; **B recons**: Breast reconstructive surgery; **CCS**: Canadian Cancer Society; **CIRC**: Circumference; **Ch:** Chemotherapy; **CG**: Control group; **DASH**: Disabilities of the Arm, Shoulder and Hand; **DXA:** Dual-energy X-ray absorptiometry; **ED**: Education; **EORTC QLQ:** European Organization for Research and Treatment of Cancer quality of life questionnaire; **FACT-B**: Functional Assessment of Cancer Therapy-Breast; **FEV_1:** Forced expiratory volume in one second; **FVC:** Forced vital capacity; **HB**: Home-based; **HR**: Heart rate; **HRQOL:** Health-related quality of life; **HT:** Hormonotherapy; **IG**: Intervention group; **IPC**: Intermittent pneumatic compression; **IVLD**: Interlimb volume difference; **KBR:** Kinect based rehabilitation; **LE**: lymphedema; **LUMP**: Lumpectomy; **MFBIA**: Multi-frequency bioimpedance; **min**: minutes; **MLD**: Manual lymphatic drainage ; **Mobs:** mobilizations**; MRM**: Modified radical mastectomy; **MT:** Manual therapy; **MX**: Mastectomy; **N/A**: Not available; **Neoadj**: Neoadjuvant; **NRS:** Numeric Rating Scale; **OA**: Operated arm; **OT**: Occupational therapist; **PCM**: Pectoral muscle-conserving mastectomy; **PENS:** Percutaneous electrical nerve stimulation; **PROM**: Passive range of motion; **PT**: Physical therapy(ist); **QT:** Quadrantectomy; **RCT:** Randomized controlled trial**; RM:** Repetition maximum; **RMX:** Radical mastectomy; **ROM:** Range of motion; **RPE:** Rated Perceived Exertion; **RT:** Radiotherapy; **SD**: Standard deviation; **SDQ**: Shoulder Disability Questionnaire; **Self-A**: self-administered; **SIP**: Sickness Impact Profile; **SNB:** Sentinel lymph node biopsy; **SND**: Sentinel lymph node dissection; **ST**: Soft tissue; **TKS**: Tampa Kinesiophobia Scale; **UE:** Upper extremity; **UL:** Upper limb; **VAS**: Visual Analog Scale; **VOL**: Volume; **w**: week; **WLE**: Wide local excision; **6MWT**: 6-Minute Walk Test*

ANNEXE C

Description of the interventions of the included studies (modified based on TIDieR checklist)

First author (Year)	Intervention's name (Comparison arm)	Materials and procedures	Provider(s) and modes of delivery	Location, schedule, and intervention's characteristics	Tailoring and modifications	Adherence
Ammitzbøll (2019)	**PRT** (Usual care)	*Materials:* Dumbbells and resistance bands were provided for HB EX sessions *Procedures:* EX involved the major muscle groups in the UL, lower limb, and core	PTs with a short introduction to BC surgery, treatment, rehab needs, and complications *P1*: in group, SPV *P2:* Mixed (in group + self-A)	*Location:* *P1*: Study hospital *P2*: HB prompted by weekly mobile phone text messages for EX reporting. *P1 (w1-20)* Initiation: 3rd post-op w Freq: 3 days/w Int: started at <60% 1-RM *P2 (w21-50)* Initiation: after P1 Freq: 3 days/w Duration:50-55 min (10-15-min warm-up, 40 min of resistance training) REP/Load/Sets: w1-4 :15-20/25 RM/2-3 w5-8: 15-17/20 RM/3 w9-12: 10-12/15 RM/3 w13-50: 10-12/10-12 RM/3	*Individualized:* Monthly tests by supervisors guided individual progression in load and intensity *Modifications*: NR	*Adherence*: The rate of intervention adherence to 2 or more exercise sessions per week in phase 1 was 79%, and 85% reported exercising in more than 80% of the weeks in phase 2 (results not shown). *Dropouts:* IG: hospital anxiety (n=1), cancer recurrence (n=1), deaths (n=3) CG: pain due to scar tissue (n=1), recent breast recons (n=1), no time or resources (n=2), cancer recurrence (n=3)
Ammitzbøll (2019)	**PRT** (Usual care)	*Materials:* Dumbbells and resistance bands were provided for HB exercise sessions *Procedures:* EX involved the major muscle groups in the UL, lower limb, and core	*Providers*: NR Phase 1: in group Phase 2: Mixed (in group + self-A)	*Location:* Phase 1: study hospital Phase 2: HB, only prompted by weekly mobile phone text messages for EX reporting. *P1 (w1-20)* Initiation: 3rd post-op w Freq: 3 days/w Int: started at <60% 1-RM *P2 (w21-50)* Initiation: after P1 Freq: 3 days/w	NR	*Adherence:* NR *Lost to follow-up:* IG: death (n=3), logistics (n=3), unable to contact (n=1), hospital anxiety (n=1), personal reasons (n=1) and cancer recurrence (n=1) CG: unable to contact (n=3), other surgery (n=1), no time (n=2), personal reasons (n=3),

				Duration:50-55 min (10-15-min warm-up, 40 min of resistance training) REP/Load/Sets: w1-4 :15-20/25 RM/2-3 w5-8: 15-17/20 RM/ w9-12: 10-12/15 RM/3 w13-50: 10-12/10-12 RM/3		withdrew consent (n=1), pain from scar (n=1), cancer recurrence (n=3)
Anderson (2012)	**EX program + LPM** (UC)	*Materials:* LPM: Instructions and care for the affected arm and hand, video-taped tutorial of arm strengthening and lymph flow EX and instructions to wear a compression sleeve UC: ED (LE awareness, recommendations about PA nutrition and for improving function and strength EX program: If participants chose HB EX (*P3*), EX specialist contacted them during this time to discuss adherence/barrier issues, answer EX-related questions, and to modify EX prescriptions as needed. *Procedures:* Exercise program: aerobic warm-up, moderate to hard walking, upper and lower body strength training and stretching EX	Individual certified by the ACSM as an EX specialist and by the AHA's ACLS led the EX sessions *P1*: SPV *P2*: Mixed (self-A + SPV 1/w) *P3*: self-A	*Location:* *P1*: CRC/*P2*:CRC + HB/ *P3*:HB LPM Initiation: 4-12w post-op EX program Initiation: after LPM Freq: 2 days/w to once/w Int: weights were increased weekly by approximately 1–2.5 lbs on upper body exercises and 1-5 lbs on lower body exercises. Duration: 65 min (5-min warm-up, 30-min of walking, 20 min of strengthening EX and 10 min of stretching) REP/Load: Up to 12/50% 1 RM	The sessions were customized to meet baseline levels of strength and function. *Modifications*: NR	*Adherence:* Participants completing 71.2% of all prescribed exercise sessions with a range of 0–97%. 61% of participants attended more than 75% of sessions and only 13% attended less than 50% of sessions *Strategies used to ↑ compliance:* -Individual theory-based behavioral reinforcement sessions and a monthly group session to discuss barriers and obstacles in implementing an EX program -Monitoring of progress -Incentives for participation -Transportation provided
Bendz (2002)	**Shoulder EX program** (Early vs delayed)	*Materials:* (Preoperative instructions) were advised to use the arm as much as comfortable but to avoid lifting and carrying heavier items *Procedures:* Included intermittent hand contractions and comprehensive ROM program	Specialized PTs Mixed: 1st pod-14th: HB From 14th pod: SPV	*Location:* 1st pod-14th: HB From 14th pod: outpatient clinics Group A; Initiation: 1st pod Group B; Initiation: 2nd post op w Both groups Freq: 3 times/d Int: NR REP/Sets: 5/NR Duration: NR	*Tailoring:* NR *Modifications: NR*	*Adherence:* NR *Dropouts:* death (n=5), moving from the area (n=6), other diseases (n=3), surgery on the opposite side (n=3) and personal reasons (n=8)

Beurskens (2007)	**Exercise therapy** (Usual care)	*Materials:* Patients assigned to the CG received a leaflet flyer with advice and EX for the arm/shoulder for the first weeks following surgery and had no further contact with a PT. *Procedures:* NR	PTs Received information about t_x guidelines (EX for arm/shoulder, posture correction, coordination EX, EX for muscular strength, improvement of general physical condition, EX to prevent LE and instruction for soft tissue massage of the scar if required One-on-one sessions	*Location:* Private PT office of their own choice Initiation: 2nd post-op w Freq: 1-2/w for the first 3w and then once a fortnight or less + 10 min of home exercises daily REP/Sets: NR Duration: 3 months (9 t_x sessions, determined because of insurance coverage)	*Tailoring:* Unclear (PT had to comply with specific t_x regimes but judged the number of PT sessions that was sufficient to improve shoulder function) *Modifications:* NR	*Adherence*: NR Thirty women completed the study protocol. In the follow-up period one patient from the control group died before the last assessment
Box (2002)	**PCMP** (Usual care)	*Materials:* IG: progressive educational strategies (LE risk factors, discussion of the lymphatic system, signs of arm swelling, risk-minimization strategies) CG: received an EX instruction booklet *Procedures:* Preop assessment and explanation with postop reviews to monitor shoulder ROM, progress EX program, LE awareness ED and individualized intervention as required.	PTs One-on-one sessions	*Location*: Outpatient Breast Surgical Clinic at Royal Brisbane Hospital Initiation: unclear (post-BSx) Freq: NR REP/Sets: NR Duration: NR	*Tailoring:* Individualized intervention was provided as required *Modifications:* NR	*Adherence*: NR *Dropouts: 9%*; relocation interstate or overseas (2), unavailability for final assessment (1) and death (3) *Strategies used to ↑ compliance:* -Positive reinforcement by PT
Box (2002)	**PCMP** (Usual care)	*Materials:* IG: progressive educational strategies (LE risk factors, discussion of the lymphatic system, signs of arm swelling, risk-minimization strategies) CG: received an EX instruction booklet solely *Procedures:* NR	PTs One-on-one sessions	*Location*: Outpatient Breast Surgical Clinic at Royal Brisbane Hospital Initiation: unclear (post-BSx) Freq: NR REP/Sets: NR Duration: NR	*Tailoring*: NR *Modifications*: NR	*Adherence:* NR Reasons for the 9% loss over in the 2-year period were relocation interstate or overseas (2), unavailability for final assessment (1) and death (3)

Cho (2016)	**PT + MLD** (PT)	*Materials*: For strengthening EX, a Thera-Band was used *Procedures:* EX: UE strengthening and stretching combined ST and shoulder girdle mobs and PROM EX MT: Gentle circular mobs of tight and stiff tissues of the chest wall and antecubital fossa with full hand or 2-finger contact and longitudinal tissue stretch with the patient's arm in possible range of abd MLD: light form of circular massage and stationary circle, pumping and scooping, and rotary mvts performed with varying degrees of pressure.	EX: All exercises were performed under the supervision of PTs MLD: 2 LE therapists (1st post-op w) Self-A (2nd to 4th post-op w)	*Location*: Department of Rehabilitation Medicine of Asan Medical Center, Seoul, Korea Initiation: ≥ 4w after BSx PT program Freq: 3 times/w Int: 60-80% 1RM REP/Sets: 10/3 Duration: 4w MLD Freq: 5 days/w Duration: 30 min each session for 4w	Treatment intensity was progressively increased from comfortable to mild discomfort within the tolerable range	*Adherence*: NR *Dropouts*: Seven patients were unable to complete the final evaluation (reasons not stated): 41 patients completed the study protocol
Cinar (2008)	**ROM EX + PT program** (HB EX program)	*Materials:* Both groups were informed about skin care and issues that they should take care during ADL *CG:* Postoperative EX forms to perform at home *Procedures:* 1st pod: hand/elbow AROM EX; 2nd pod: Isometric hand/forearm EX; 3rd and 4th: AROM shoulder EX PT program: Passive stretching, strengthening and ROM EX (pendulum, wall climbing, overhead pulley, horizontal abduction, posture, wand, dorsal strengthening, and stretching EX for levator scapula)	Each EX was thought by PTs until it was performed properly 15 SPV and individual sessions and 8w self-A	*Location*: 15 sessions in the Department of Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital +8w HB Initiation: ROM EX: 1st pod PT program: > drains removal Freq: NR Int: NR REP/Sets: NR Duration: unclear (15 SPV PT sessions + 8w HB)	*Tailoring:* NR *Modifications:* NR	NR
De Groef (2017)	**PT + MT** (PT + placebo)	*Materials: NR* *Procedures:* PT program: passive mobs, stretching and transverse strain of pectoral muscles, scar tissue massage, EX schemes to restore and improve muscle flexibility, endurance and strength, posture and mvt control and shoulder AROM	MTs Both MTs had a master's degree in Rehabilitation Sciences, one with four years of clinical experience	*Location*: Department of Physical Medicine and Rehabilitation of the University Hospitals Leuven. Initiation: PT program: 1st pod MT: 2 m post-op Placebo: 2m post-op	*Tailoring:* PT program was standardized *Modifications*: NR	*Adherence:* NR *Dropouts:* *IG:* not able to come to the hospital (n=3) *CG:* No dropouts

		MT: manual myofascial release techniques on (1) active myofascial trigger points at the UL region and (2) myofascial adhesions in the pectoral, axillary and cervical regions, diaphragm, and scars. The pressure applied by the therapist hands proceed from the superficial to deep layers of the myofascial tissues. Where a resistance was felt, the barrier was softly maintained until a release was felt. Placebo: static bilateral hand treatment at the upper body and arm	and one just graduated. The latter underwent 2 m of training before the start of the study. 2 other MTs performed the MT/placebo interventions. Both MTs were educated in MT and had several years of clinical expertise. Individual sessions	Freq (PT): 2/w to 1/w after 2m Freq (MT and placebo): 1/w Int: NR REP/Sets: NR Duration: PT: 4m (30 min each session) MT: 2m Placebo: 2m (30 min each session)		
De Rezende (2006)	**ROM EX program** (Directed vs Free ROM)	*Materials:* NR *Procedures:* *Directed G:* The PT technique used was kinesiotherapy based on spontaneous EX including movements for flexion, extension, abd, add and internal and external rot of the shoulder, either isolated or combined (Regimen of 19 exercises; pictures and description provided) *FROM G*: Same ROM EX program without a previously defined sequence or number of repetitions	PTs and students trained in the specialization EX were practiced in groups of 5-20 women	*Location:* Physiotherapy Outpatient Center of CAISM-Unicamp Initiation: 1st pod Freq: 3 days/w Int: NR REP/Sets: 10/NR Duration: 42 days (40 min each session)	*Tailoring:* The course followed in these EX depended on PT ability and experience. *Modifications:* NR	*Adherence:* The groups were homogeneous with respect to the number of PT sessions performed (max 18): Directed G 13.83 ± 3.05 sessions FROM G :13.19 ± 1.9 sessions
Devoogdt (2018)	**ED + Exercise therapy +MLD** (ED+EX therapy)	*Materials:* *Both G*: Received information about the prevention of LE (elevate the arm in case of heaviness, avoid lifting heavy objects, use the arm in ADL, avoid limb constriction, avoid extremes of T°, apply skin care, and avoid an increase in body weight) + exercise therapy (mobilizing exercises) during hospitalization	All t_x (information, EX therapy and MLD) were performed by 4 therapists. Two of them had undergone MLD training with the Leduc method, and the two others	*Location:* Department of Physical Medicine and Rehabilitation of the University Hospitals Leuven. Initiation: EX: during hospitalization MLD: 1w > drains removal	*Tailoring: NR* *Modifications: NR*	*Adherence:* Reasonable compliance IG: 11 participants (15%) received 23-29 MLD sessions, 26 participants (36%) received 30-35 sessions, and 36 participants (49%) received > 35 sessions.

		Procedures: *EX:* passive mobs of the shoulder; stretching and transverse strain of the breast muscles, scar tissue massage; and active mobilising and stabilizing EX. MLD: neck and ALN were emptied, axilloaxillary anastomoses at the breast and back and lymphatics at the lateral side of the shoulder (Mascagni pathway) were stimulated, and the arm and hand were drained from proximal to distal. *CG*: Protocol described above without MLD	had undergone MLD training with the Vodder method Individual sessions	Freq (EX): 2/w to 1/2w Freq (MLD): 1-3/w to once/w REPS/Sets: NR Duration: 6m (30 min each session) MLD: 20w		Reasons for absence: illness related to Ch and/or RT, problems with transport, holiday, and illness from other causes
Feyzioglu (2020)	**Kinect-based rehab** (PT group)	*Materials:* Both groups: Received imitations for shoulder ROM amplitudes, weightlifting, jumping and running up to 6w post-op *Procedures:* *Both G:* HB EX program consisting of breathing, ROM and pumping EX (w0-2) *KBR G:* Xbox 360 Kinect video game program (requiring AROM of the UL) combined with tissue massage and passive mobs *PT G:* UE PT program (shoulder ROM, stretching and strengthening EX) including scar tissue massage and mobs	The treatment program (tissue massage and mobs) was performed by experienced PTs Mixed (SPV + HB)	*Location:* Unclear Initiation: General EX: 1st pod KBR and PT program: 2nd post-op w Freq (both groups): 2 days/w Int: NR REPS/Load/Sets: provided in Table 1, varied according to the EX Duration: 6w (45 min each session)	*Tailoring*: EX: standardized program *Modifications:* NR	*Adherence*: NR *Dropouts:* KBR G: refused the intervention (n=1) PT G: refused the intervention (n=1), Ch AEs (n=1), new metastasis focus (n=1)
Kilbreath (2012)	**EX group** (Usual care)	*Materials:* *Both G*: Postoperative care which included written information outlining postop arm EX they were to perform, literature on prevention of LE (avoiding lifting heavy objects, prolonged activities such as scrubbing, insect bites, injections, BP	PTs and/or OTs Mixed: SPV sessions + HB program	*Location:* HB + unclear (hospital?) Initiation: 4-6 w post-op Freq: once/w Int: instructed to work towards a target of about 15 (Hard) on the Borg Effort Scale	*Tailoring:* Adaptive strategies were used if women were unable to achieve > 90° elevation	*Adherence:* *EX group:* median number of sessions attended was 7 out of, with adherence to the SPV training 78%

		test on the at OA). For weekly SPV sessions, free weights were used; for the HB program, women were provided with a Thera-band *Procedures:* *EX group:* EX sessions of resistance training and passive stretching for shoulder muscles + home program of resistance training and stretching (positions maintained 5-15 mim)		REPS/Sets: 8-15/2 Duration: 8w	*Modifications:* NR	*HB program*: The minimum requirements were 40 sessions of stretching and 24 sessions of resistance training over the 8 weeks; mean compliance: 90%. Seven women completed less than 75% of their stretching sessions and 4 women completed less than 75% of their resistance training sessions
Kilbreath (2006)	**EX group** (Usual care)	*Materials:* Exercise booklet was given to patients before hospital discharge; a Theraband was used for strengthening EX *Procedures:* *Usual care G:* Monitoring by a breast care nurse, may be seen by a PT to review UL exercises and by an OT who discussed prevention of LE before discharge *EX group:* Usual care + shoulder ROM, strengthening (focused on shoulder flexors, abductors, and external rotators) and stretching exercises (was held passively for 5 min on day 1 and progressed up to 15 min over the next 2w)	PTs Mixed (HB once/w + SPV once/w)	*Location:* HB + unclear (hospital?) Initiation: 4-5w post-op Freq: 2/w Int: Low to ‘’somewhat hard’’ on the Borg Scale REPS/Sets: 8-12/2 Duration: 8w	*Tailoring*: EX intensity progressed according to participants perceived exertion (Borg scale) *Modifications:* NR	*Adherence*: NR
Lauridsen (2005)	**Standart t_x + PT** (Standard t_x + delayed PT)	*Materials:* NR *Procedures:* *Standard t_x:* daily demonstrations and instructions in shoulder and vein pump EX during the first postop w *PT program:* relaxation and strengthening EX, combined to vein	Standard t_x: Instructions were given by PTs and the patients were encouraged to continue exercising after hospital discharge	*Location:* NR Initiation: Group A: 6th to 8th post-op w Group B: 26th post-op w Freq: 2 days/w Int: NR REPS/Sets: NR	*Tailoring:* No individual therapy was applied *Modifications:* NR	Ad*herence:* NR *Dropouts:* 14/139 (10%); including two patients who died and two patients who had terminal disease, disabling them in attending the final follow-up

		pump therapy and instruction in stretching of scar tissue	PT program: To ensure that the patients received uniform t_x the same two PTs handled all sessions	Duration: 6w (60 min each session)		
Pace do Amaral (2012)	**MT + UL EX** (UL EX)	*Materials:* Women were advised to take precautions to prevent LE of the operated UL *Procedures:* *UL EX: (1st-3rd pod)* forward flexion, external rotation and shoulder abd; (> 3rd pod- 1m) 19 movements of flexion, extension, abd, add, internal, and external rotation of the UL, alone or combined *MT*: Scapular and GH mobs and therapeutic massage. Techniques used for mobs were gliding, oscillation, and traction for the GH joint; and add, abd, elevation, depression, and internal and external rotation for the scapula. Therapeutic massage (friction maneuvers and deep gliding) was used in the presence of wound adherence or lymphatic cording	PTs UL EX: Providers unspecified. All women underwent an exercise protocol in a group setting MT: Seven PTs were trained by the main investigator to perform the technique. Individual sessions	*Location:* Division of Physical Therapy of the Women's Integrated Health Care Center of the University of Campinas Initiation: 1st pod Freq (EX): 3/w Freq (MT): 2/w Int: NR REPS/Sets: 10/1 Duration: EX: 1m (45 min each session) MT: 1m (20 min each session)	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR *Dropouts:* *MT+UL*: 40/65 (62%) *UL:* 36/66 (55%); moved away or death
Petito (2014)	**EX protocol** (Early vs delayed)	*Materials:* Participants were supported by an illustrated manual prepared and validated for the study. All the patients received guidance regarding the management of the drain at home, and those in the EG received guidance and performed the initial EX under the supervision of the researcher *Procedures:* NR (Was composed of 9 EX)	HB (Guidance was provided by the principal investigator if needed)	*Location:* HB program Initiation: EG: 1st pod DG: > drain removal (postop day 7-10, mean postop day: 9) Freq: once/day Int: NR REPS/Sets: NR Duration: 15w (105 days)	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR *Dropouts*: *EG:* 8/48 (17%) *DG*: 9/46 (20%); lost to follow-up, death, returned to surgery

Sagen (2009)	**Physical therapy program** (AR vs no restrictions)	*Materials:* Each patient in the AR group was given standard detailed information on the restricted activities in a sealed envelope. *Procedures:* Moderate progressive resistance EX + 6 different standardized passive manual techniques emphasizing flexibility and light massage of the affected shoulder, arm and scar.	PTs SPV sessions	*Location:* Outpatient clinic Initiation: Freq (AR): once/w Freq (NAR): 2-3 days/w Int: NR REPS/Sets: 15/NR AR: restricted activities of the OA avoiding heavy weights (>3kg) NAR: 0.5kg the (0-2 w) ↑ individually after Duration: 6m (45 min each session)	*Tailoring:* PT program was standardized *Modifications:* NR	Ad*herence:* Adherence to the allocated rehabilitation programs was 83% in the NAR group and 89% in the AR group. *Dropouts* NAR: 36/104 (35%) AR: 16/104 (15%); death, moved away, not available, refused to participate, too frail or ill, other Sx, lost to follow-up
Schultz (1997)	**Shoulder EX** (Early vs delayed)	*Materials:* NR *Procedures: P*atients were instructed to do active shoulder EX to regain full range of motion, especially in the directions that may be difficult postoperatively, i.e., anteflexion, abd, and rotation	PTs EX were performed under individual guidance of PTs before discharge; HB > discharge	*Location:* Outpatient department; HB Initiation: EG: 1st pod DG: 1st post-op w Freq: 3 times/day Int: NR REPS/Sets: NR Duration: NR	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR
Siedentopf (2013)	**Yoga** (Early vs delayed)	*Materials:* NR *Procedures:* Each lesson started with lying postures and the gradual mobs of arms and legs to encourage flexibility and strength. Various breathing EX followed to allow participants to feel their chest wall expanding. During the dynamic part of the EX, a range of standing and sitting positions were shown. At the end of the class, participants were led through a series of concentration EX to help them relax and become aware of the effects of the yoga EX	Two certified yoga teachers, one demonstrating the asana, the other teacher assisting the participants with props	*Location:* Hospital's gym Initiation: EG: 1st pod DG: 5th post-op w Freq: 2/w Int: NR REPS/Sets: NA Duration: 5w (75 minutes each session)	*Tailoring:* Positions variations tailored to the needs of patients were included as needed. The teachers were careful to ensure that participants performed each EX according to their own optimal degree of Int.	Ad*herence:* Various reasons were cited for canceling classes, but most patients gave no reason (7 women in the EG, 8 women in the DG). The 2nd most frequently cited reason was ongoing adjuvant t_x The average number of attended yoga classes was 7.62 (SD ± 3.78) in the EG and 7.25 (SD

					Modifications: The yoga class encompassed a large variety of movements, all of which were easily doable in their modified versions. The modifications were created to meet post-op needs and to help during the period following therapy when the women were less flexible	± 4.21) in the DG with a range of 0–11 in both groups (p = 0.89, Mann-Whitney U-test). No statistical difference was found in the numbers attending classes.
Temur (2019)	**SMLP + EX + SLD** (Usual care)	*Materials:* (SMLP) Training booklet containing information about mechanisms and risk factors of LE and about prevention interventions were given to patients in the IG and distributed at the end of the study for patients in the CG *Procedures:* EX: Hand squeezing exercises with a medium-level stress ball + active and passive arm EX (pictures and description provided) SLD: deep diaphragmatic breathing EX, neck drainage, unaffected side axillary drainage, affected side axillary drainage, and UE drainage. Before the massaging started, the patients performed breathing EX	*Providers*: NR EX: Mixed (SPV then switched to HB) SLD: Self-A	*Location:* Adult Hospitals General Surgery Department + HB Initiation: 1st pod Freq (EX): 3-6 times/day; gradually increased to 10 Freq (SLD): twice/day Int: NR REPS/Sets: varied according to the EX and timing (see table 1) Duration: 6m (30-60 min per EX session)	*Tailoring:* The minimum amount of EX required for the patient were determined by the doctor and nurse taking into consideration the physical condition of the patient, and his general well-being during the postop period. *Modifications:* NR	Ad*herence:* NR *Dropouts:* IG: did not follow the research program (n=2), wound site revision in the post-op period (n=3), developed skin reaction after RT (n=1) CG: did not follow the research program (n=1), wound site revision in the post-operative period during the research (n=2), developed skin reaction after RT (n=2)
Teodózio (2020)	**ROM EX** (Free vs restricted)	*Materials:* Patients in both groups received an instructional leaflet and were information not to perform rough movements or	HB (Participants were instructed by the PTs regarding the UL	*Location:* HB Initiation: 1st pod Freq: 3 times/day (at least once/day)	*Tailoring:* NR *Modifications:* NR	Ad*herence:* Adherence was considered when the EX was performed three times a day or at least one

		lift high weights in these first 30 postop days *Procedures:* Free G*: A*ctive UL mvts with ROM over 90° for flexion and abduction of shoulder from the 1st pod Restricted G: Active UL movement with ROM restricted to 90° from the 1st POD until removal of all surgical stitches, when a ROM over 90° was allowed (pictures and description are not provided)	EX to be performed)	Int: NR REPS/Sets: NR Duration: 4w		time a day on some days during the intervention weeks (results not provided) *Dropouts:* 0,9%; non-return to the wound-dressing clinic (*n* = 1), hospitalization for reasons other than a surgical approach (*n* = 2) and changes to the treatment protocol (n=1)
Testa (2014)	**PT program based on the latest guidelines** (Based on old guidelines)	*Materials:* NR *Procedures:* IG: (From 2nd pod) active flexion, extension, lateral flexion and rotation of the C-spine + passive and active assisted caution mobs of hand, wrist, elbow (flexion, extension, pronation, supination). (From 3rd pod) Arms passive exercises of flexion, abd, add and circumduction + active internal, external rotation. (Once drains were removed) 20 PT sessions including Exercises: postural and stretching exercises + active movements of abduction, flexion, internal and external rotation of glenohumeral joint CG: No early physical rehabilitation treatment, neither has received instructions from PTs	PTs Individual and SPV sessions	*Location:* Breast Unit of ''San Giuseppe Moscati'' hospital Initiation: 2nd pod Freq: 5 times/w Int: NR REPS/Sets: NR Duration: (EX): 40 minutes (PT sessions): 60 minutes	*Tailoring:* Patients starting complaining pain was the limit beyond PTs did not go during EX *Modifications:* Patients of the CG from March 2010 to August 2010 were treated following the old rehabilitation guidelines. Patients of the IG from Sept 2010 to February 2011 were treated adopting exercises described in the guidelines for rehabilitation in BC patient published on 2005 by the Italian society of senology	Ad*herence:* NR

Todd (2008)	**Shoulder EX** (Early vs delayed)	*Materials:* NR *Procedures:* Delayed G: EX that limited movement of the arm below 90◦ in all planes of movement over the 1st week, followed by the introduction of a full range of shoulder movement in the 2nd week. Early G (control): Full shoulder mobs (i.e., movement above 90◦) was introduced immediately, with vigorous arm and shoulder exercises started within the first 2 pod.	Nursing staff was responsible for the delivery of exercise sessions in clinical setting The EX program was SPV during inpatient stay (average 7 days). Group sessions (number of participants per group not indicated) + HB	*Location:* Clinical setting (NR) + HB Initiation: DG: 2nd pod (limited ROM), 2nd w (full ROM) EG: 2nd pod (full ROM) Freq: 4 times/day until full shoulder ROM was restored and then once/day for the 1st post-op year Int: NR REPS/Sets: 3-4/1 Duration: 1 year (10 min each session)	*Tailoring:* Standardized EX program *Modifications:* NR	Ad*herence* There was regular telephone contact with all study participants, and the majority of women (73%, n = 85) claimed that they had adhered to their exercise program throughout the year *Dropouts:* 7 participants (6%) withdrew during the first year (death, moved away, refused the allocated intervention)
Torres (2010)	**PT + ED strategy** (ED strategy)	*Materials:* (ED strategy) Instruction with printed materials about the lymphatic system, concepts of normal load versus overload, the source of 2nd lymphoedema, the identification of possible precipitating factors, and the four categories of interventions to prevent 2nd lymphoedema (avoidance of trauma or injury, prevention of infection, avoidance of arm constriction, and use and EX of the arm) together with individual strategies for implementing these measures *Procedures:* PT: included MLD technique used for the t_x of post-op oedema (thorax, breast,axilla, and upper arm of affected side), using a modification of the strokes described by Leduc, progressive massage of the scar,	PTs Each group had one PT, who carried out all interventions. The PTs had more than five years' experience in the t_x of vascular diseases using LD	*Location:* unclear Initiation: 3-5 days after hospital discharge Freq: 3 times/w Int: NR REPS/Sets: NR Duration: 3w	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR *Dropouts:* Overall, 116 women completed the follow-up assessments; 59/60 in the IG and 57/60 in the CG (no reasons provided)

		stretching EX for levator scapulae, upper trapezius, pectoralis major, and medial and lateral rotators muscles of the shoulder; and progressive active and action assisted shoulder EX, started in conjunction with functional activities and proprioceptive neuromuscular facilitation EX without resistance				
Wingate (1989)	**Physical therapy** (No intervention)	*Materials:* Instructions with printed materials were provided for home exercise program. *Procedures:* IG: Motor and sensory status, active hand, wrist, elbow and postural exercises, active and active assisted shoulder exercises, functional activities and PNF (EX descriptions or pictures were not provided) CG: Untreated group with no physical therapy	*Providers:* NR SPV upon hospital discharge + HB	*Location:* Clinical setting (unclear) + HB Initiation: 1st pod Freq: 2 times/day Int: NR REPS/Sets: NR Duration: 8w minimum	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR
Zhang (2016)	**EX program** (EX + MLD)	*Materials:* Patients in both groups received ED regarding the risk of post-op complication sand the importance of medical intervention and self-management. *Procedures:* EX: Began with passive EX within the first 7 days after surgery, before removal of the drainage tube. Between removal of the drainage tube and the surgical sutures at 7–30 days, the EX progressed to localized active EX on the affected UL. After removal of the surgical sutures, extensive active EX involving the affected shoulder was undertaken MLD: Each session was divided into three sequential steps to activate	*Providers: unclear* Mixed (SPV + HB) MLD: Self-A	*Location:* San Yat-Sun University Cancer Center + HB Initiation: EX: < 24h surgery MLD: > sutures removal Freq: 3 times/day Int: NR REPS/Sets: NR Duration: 6m EX sessions: varied between 15 to 30 min MLD: 30 min	*Tailoring:* NR *Modifications:* NR	Ad*herence*: NR

		lymph vessels, to soften scar tissue, and to stimulate lymph drainage (details provided in the article)				
Zhou (2019)	**UL EX** (Usual care)	*Materials:* NR *Procedures:* IG: Progressive UL EX and PMRT (description provided in table 1) CG: Routine nursing care (surgery district nursing, drainage tube nursing, routine health ED, physical exercises, vital sign monitoring and post-surgery complications)	Nursing staff In individual or group format until the patients could perform the EX and training freely and easily without discomfort. Mixed: If the patients had difficulties in performing the EX and training following surgery, the nursing staff would help and encourage the patient via one-to-one supervision (in hospital) or home visiting (discharged from hospital) until the patients could do the EX and training independently	*Location:* A general hospital in Xi'an, China Initiation: before surgery Freq (EX): 3-7 sessions per day Freq (PMRT): twice/day Int: NR REPS/Sets: NR Duration: 6m (varied between 10 to 30 min per session)	*Tailoring:* For those patients without abnormal condition and complications after surgery, EX were performed in a step-by-step modality. If the patients had complications or abnormal conditions after surgery, the duration, freq, and shoulder ROM would be decreased accordingly *Modifications:* NR	Ad*herence:* All intervention group patients completed the EX and training, with AEs and a compliance of 100%.
Zimmermann (2012)	**EX + MLD** (EX + self-MLD)	*Materials:* NR *Procedures:* IG: (EX) PT program including exercises of limb and chest physical therapy (MLD) Massage strokes were applied to the side of the edematous limb, starting at the base of the neck and then progressing to the affected limb. The massage was always directed proximally from the upper arm to the axilla, and then from the hand to the elbow. Finally, the	PTs IG: SPV individual sessions CG: Mixed (EX SPV, MLD self-A)	*Location:* NR Initiation: EX: 2nd pod MLD: 14th pod Freq (EX): NR Freq (MLD): 5 sessions/ week Int: NR REPS/Sets: NR Duration: 6m	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR

		whole limb was massaged from the distal to the proximal extremity CG: Applied self-drainage from modification of the method described by Földi and Strönbenreuher				
Majed (2020)	**UL EX + ED** (Usual care)	*Materials:* The intervention group received pre-surgery ED and training on therapeutic EX. ED consisted of a PowerPoint presentation regarding the therapeutic EX, information about the surgery, and a booklet with pictures of the EX to take home. *Procedures:* IG: The EX included deep breathing as well as shoulder EX such as extension of the triceps, bicep curl, paddling in sitting position, fluttering with both arms, hands behind neck, forward wall crawls, and side wall crawls + ED CG: received routine hospital care that did not include any EX training or ED. Routine hospital care included explanation by the surgeon on the surgical procedure with follow-up at two and four weeks after discharge	ED: one-to-one sessions EX: Demonstration of the exercises by the PI was done to ensure proper techniques. The researcher called the patients at home every week to ensure that the women were continuing the EX + HB	*Location:* HB Initiation: prior to surgery Freq: NR Int:NR REPS/Sets: 10/NR Duration: 4w	*Tailoring:* NR *Modifications:* NR	Ad*herence:* NR *Dropouts:* IG: 5/35; refused to do the EX CG: 4/34; lost to follow-up
de Almeida Rizzi (2020)	**UL EX** (Free vs limited ROM)	*Materials:* *Procedures:* The patients started physical therapy at the hospital the day following surgery after they had learned and performed six EX (1–6 of protocol) At PO15, two EX were included (7 and 8 of the protocol) IG: was allowed to perform the protocol EX and ADL in free amplitude (i.e., at the limit of pain or the sensation of tightening of the scar)	All evaluations and physiotherapeutic interventions were performed by PTs with expertise in breast oncology.	*Location:* Mastology Outpatient Clinic Initiation: 1st pod Freq: Int: NR REPS/Sets: NR Duration: NR	*Tailoring:* NR *Modifications:* NR	Ad*herence*: NR *Dropouts:* IG: 4/31 (lost to follow-up) CG: 3/31 (reoperation, lost to follow-up)

		CG: limited-range group (control-standard center protocol), which had ROM maintenance limited to 90° for 15 more days (i.e., until the POD 30), when free-range EX also were allowed				

Abd: *abduction;* ***ACSM:*** *American Health Association for Advanced Cardiac Life Support;* ***Add:*** *adduction;* ***ADL****: Activities of daily living;* ***AR****: Activity restriction;* ***AROM****: Active range of motion;* ***BC****: Breast cancer;* ***BSx:*** *Breast surgery;* ***Ch:*** *Chemotherapy;* ***CG****: Control group;* ***CRC:*** *Clinical Research Center;* ***DG:*** *Delayed group* ***ED****: Education;* ***EG*** *: Early group;* ***EX****: Exercise(s);* ***Freq:*** *Frequency;* ***FROM****: Free range of motion;* ***GH:*** *Gleno-humeral;* ***HB****: Home-based;* ***IG****: Intervention group;* ***Int:*** *Intensity;* ***KBR:*** *Kinect based rehabilitation;* ***LD:*** *Lymphatic drainage;* ***LE****: Lymphedema;* ***min****: minutes;* ***LPM****: Lymphedema Prevention Module;* ***MLD****: Manual lymphatic drainage;* ***Mobs:*** *mobilizations;* ***MT:*** *Manual therapy;* ***NAR:*** *No activity restriction;* ***NR:*** *Non reported;* ***OT****: Occupational therapist;* ***pod****: postoperative day;* ***Preop****: Preoperative;* ***PROM****: Passive range of motion;* ***PT****: Physical therapy(ist);* ***REP:*** *Repetitions;* ***RM:*** *Repetition maximum;* ***ROM:*** *Range of motion;* ***RT:*** *Radiotherapy;* ***Self-A :*** *Self-administered;* ***SLD:*** *Simple lymphatic drainage;* ***SMLP:*** *Self-management of lymphedema program;* ***SPV****: Supervised;* ***ST****: Soft tissue;* ***Sx****: Surgery;* t_x*: Treatment(s);* ***UC:*** *Usual care;* ***UE:*** *Upper extremity;* ***UL:*** *Upper limb;* ***w****: week;*