Original Article

Efficacy of intermittent pneumatic compression on breast cancer-related upper limb lymphedema: a systematic review and meta-analysis in clinical studies

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Background: Complete decongestive therapy (CDT) and intermittent pneumatic compression (IPC) are the most common combination of treatments in breast cancer-related upper limb lymphedema. The effects of IPC as an addition to CDT are inconsistent in different studies. This meta-analysis aimed to explore whether IPC could bring additional benefits to CDT.

Methods: Literatures were retrieved from databases with full-text publications ranging from January 1995 to March 2024. Fixed-effect models were applied to subsequent analysis if no heterogeneity was detected by using the Inverse formula. Publication bias was assessed using the Begg's test and Eagger's test.

Results: Twelve studies were finally included for further analysis. Results showed that additional application of IPC to CDT could further improve lymphedema within 4 weeks after the treatment period [standard mean difference (SMD) =–0.2 mL, 95% confidence interval (CI): –0.33 to –0.07 mL]. However, this additional benefit was weakened within about 9.4±2.6 weeks' follow-up duration after ceasing physical therapy (SMD =–0.15 mL, 95% CI: –0.33 to 0.04 mL).

Conclusions: Periodically continuous treatment should be suggested to maintain the effect of CDT + IPC to promote lymph drainage and lymphedema improvement. Nonetheless, the treatment involved in the studies ranged from 4 to 12 weeks, therefore potential bias might exist.

Keywords: Breast cancer; lymphedema; intermittent pneumatic compression (IPC); complete decongestive therapy (CDT); lymphatic drainage

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Introduction

Surgery combined comprehensive treatment tremendously improves prognosis of breast cancer patients. However, in spite of the increased survival rate, breast cancer treatment related side effects draw a lot of attention from both medical staff and patients. Axillary lymph node dissection (ALND) is one of the main breast cancer surgery types. However, ALND can block lymphatic drainage, leading to upper limb lymphedema (1,2). Subsequent lymphedema of upper limb would not only affect appearance and body image, but also influence the upper limb function (3,4).

Lymphedema of upper limb can also bring discomfort feeling and affect patients' quality of life (QoL) (5,6). It has been widely recognized that lymphedema was both an acute and chronic threaten of health (7). Physical therapy, as a non-invasive and conservative method, is currently the mainstream treatment of breast cancer-related lymphedema (8). Complete decongestive therapy (CDT) or decongestive lymphatic therapy (DLT), manual lymphatic drainage (MLD) and other non-invasive methods such as intermittent pneumatic compression (IPC), Kinesio Taping, compression garments, or laser therapy are reported to decrease the degree of lymphedema and shrink the circumference of the involved limb (9-13). These conservative therapeutic methods have some limitations of their own, such as undesired or temporary sustainability of decongestive effect. Therefore, effects of comprehensive physical therapies have been explored in some appropriate medical settings.

CDT and IPC are the most common combination of treatments. CDT includes MLD, multilayer compression bandaging, skin care, and exercises. IPC device is a kind of pneumatic cuff connected to an air pump to simulate the physiological pumping effect of muscle contraction and relaxation which is indispensable for lymphatic drainage (14-17). The effects of IPC as an addition to CDT are inconsistent in different studies. There are studies (18,19) acclaim that IPC in combination with CDT or DLT has better performance than CDT-only in terms of improving limb lymphedema. A randomized controlled study conducted in 2020 acquired opposite conclusion (20). In 2014, a meta-analysis testified the additional effects of IPC to CDT or DLT, which summarized related clinical trials carried out in early period, and finally showed the percentage of volume reduction failed to be higher in CDT + IPC group compared with CDT-only (15). However, data from these three included studies had some heterogeneity, and the percentage of volume reduction as the primary outcome indicator seemed to be not enough. Therefore, updating the comparison between CDT + IPC method and CDT-only method is highly needed. Accordingly, we aim to synthetically analyse whether a supplemental IPC method could bring additional benefits based on existed clinical trials with high quality. To validate the efficacy of supplemental application of IPC, changes of involved upper limb on excess volume, excess circumference, ranges of shoulder join mobility, and pain feeling scores were comprehensively evaluated, trying to offer optimal strategy for clinical decision. We present this article in accordance with the PRISMA reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-123/rc).

Highlight box

Key findings

- Additional application of intermittent pneumatic compression (IPC) to complete decongestive therapy (CDT) could further improve lymphedema within 4 weeks after the treatment period.

What is known and what is new?

- There are many conservative therapeutic methods for breast cancer-related lymphedema, and CDT and IPC are the most common combination of treatments. The effects of IPC as an addition to CDT are inconsistent in different studies. For example, there are studies acclaim that IPC in combination with CDT has better performance than CDT-only in terms of improving limb lymphedema. However, a meta-analysis showed the percentage of volume reduction failed to be higher in CDT + IPC group compared with CDT-only.
- Results of this paper showed that additional application of IPC to CDT could further improve lymphedema within 4 weeks after the treatment period. However, this additional benefit was weakened within about 9.4±2.6 weeks' follow-up duration after ceasing physical therapy.

What is the implication, and what should change now?

- This study showed that a complementary treatment of IPC to CDT could strengthen the effect of lymphatic drainage and slightly but significantly increase the range of abduction. But IPC as a complementary therapy to CDT failed to bring additional benefit of alleviating limb pain.
- In the future, more rigorous randomized controlled study should be conducted to compare the effects of CDT and CDT + IPC on breast cancer-related lymphedema. If IPC could bring more benefits, it is suggested to be added in the intensive phase of CDT.

Methods

Database searching strategy

Online electronic database including PubMed, EBSCO, Science Direct, Springer Link, CINAHL Complete, Ovid Technologies, Web of Science, Cochrane Central Register of Controlled Trials, ProQuest and Network Digital Library databases were searched, and the interval of time span was ranging from January 1995 to March 2024. Intermittent pneumatic compression pump, limb lymphedema, breast cancer, clinical study, randomized control trial and complete/complex/comprehensive/combined decongestive therapy were used as keywords for literatures retrieve.

Eligibility of study inclusion/exclusion and types of intervention

Two independent researchers were assigned to manually scrutinize the eligibility of literature and responsible for the quality control and data collection of candidate studies. Screening and filtration steps of retrieved literatures followed requirements of the instruction concerning on four factors, including population, interventions, comparisons and outcomes. The standards of inclusion criteria were depicted as: written in English; with clear parallel control group; full-text publication; female patients; clear description of study design; and clear description of implementation of IPC, such as values of pressure and action time. Exclusion criteria included: animal studies; case-reports; case-series; studies about surgical method; without CDT treated group as parallel control; and review articles. If different publications were searched from the same cohort, the largest sample size should be chosen as eligible for further analysis, and the rest literatures should be excluded. In general, IPC and CDT were two major conservative therapies. Accordingly, sub-group analysis was fulfilled to compare effects of these two methods, respectively.

Principles of data extraction

Interested data such as the number of total patients and the number of patients with clearly defined events were carefully collected. Besides, basic demographic data and follow-up duration were collected by two reviewers independently. If the information provided in the study was equivocal, it was required to obtain or confirm data from study investigators. A certain type of analysis method was chosen based on the heterogeneity among included studies. For studies with homogeneous characteristics, a fixed-effect model was applied to integrate extracted data. Oppositely, if significant heterogeneity was detected, a random-effect model was suggested to adopt for analysis. After data process, the suitable formula was chosen to calculate the pooled standard mean difference (SMD) or weighed mean difference (WMD). Data visualization of analysis was achieved by forest plot. Additionally, publication bias was assessed using the Begg's test and Eagger's test.

Quality assessment of eligible studies

Quality assessment tools from Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument were used. The 10-item quality assessment tool was used for randomized controlled trial (RCT) or quasi-experimental trials. The 9-item quality assessment tool was used for cohort/case-control studies. Two researches assessed the literatures, and any disagreements between the researches were resolved through discussion, or invited the third researcher to decide. The results of assessment were classified into "Yes, No, Unclear and Not applicable". Results of quality assessment involving some dimensions were presented in a table.

Statistics

Statistical heterogeneity of the extracted data was evaluated by using the Inverse Variance (I-V) formula. Fixed-effect models were applied to subsequent analysis if no heterogeneity was detected by using the Inverse formula. If the most significant heterogeneity was found, sensitivity analyses was conducted to assess robustness of the synthesized results. Statistics of meta-analysis was performed by the operation of Stata software 12.0 (Stata Corp, College Station, TX, USA). For continuous variables extracted from each study, SMD was calculated. All P values were 2-tailed, and the statistical significance was set at 0.05 [95% confidence interval (CI)]. Original data presented as quartile value (median value, first quartile and third quartile) were transferred to mean ± standard deviation (SD) format by previously published method (21,22).

Results

Demographic information of patients from each included studies at baseline

Demographic and clinical characteristics at baseline between CDT + IPC group and CDT group among different studies are showed in *Table 1*. There was no significant difference in these factors: age, body mass index (BMI), duration of lymphedema, concomitant disease condition, breast cancer surgery related characteristics and adjuvant radiotherapy. However, the course of CDT or IPC treatment showed some heterogeneity among different studies. Characteristics of included studies are shown in *Table 2*. Duration of treatment ranged from 4 to 12 weeks (*Table 2*), therefore potential bias might exist.

Study characteristics and quality assessment

Quality assessment and data extraction were fulfilled by

Table 1 Demographic information of patients in included studies

Author	Year	Age, years		Number		BMI, kg/m^2		Duration of lymphedema, months		Number of axillary lymph nodes removed [%]		Left arm with LE [%]		Radical/modified mastectomy [%]		RT [%]		Pressure, mmHg
		CDT	CDT + IPC	CDT	CDT + IPC	CDT	CDT + IPC	CDT	CDT + IPC	CDT	CDT + IPC	CDT	CDT + IPC	CDT	CDT + IPC	CDT	CDT + IPC	
Haghighat *et al.* (18)	2010	53.4±11.4	52.7±10.8	496	248	29.9±4.1	30.9±4.3	34±36.9	35±41.6	10.6 [5.5]	10.7 [6.2]	NG	NG	NG	NG	NG	NG	NG
Szuba *et al.* (19)	2002	68.8±9.11	65±10.8	12	11	NG	NG	41.1±62.3	35.6±21.6	NG	NG	NG	NG	NG	NG	NG	NG	40–50
Szuba *et al.* (19)	2002	65.9 [43–81]		25		NG	NG	60 [3–480]		NG	NG	NG	NG	NG	NG	NG	NG	40–50
Tastaban *et al.* (20)	2020	53.6±7.7	51.2±11.6	38	38	28.7±1.3	28.7±1.3	12.4±2.3	12.7±3.1	13.0 [4.6]	13.2 [5.4]	20.1 [9.4]	20.6 [9.9]	NG	NG	NG	NG	30–40
Fife *et al.* (23)	2012	63.9±12.2	59.7±12.6	18	18	28.2±4.6	30.6±7.4	NG	NG	11.9 [8.7]	12.6 [11.2]	13 [72]	11 [61]	12 [67]	15 [83]	12 [67]	13 [72]	30
Dini *et al.* (24)	1998	62±10	62±12	40	40	26.7±4.1	26.4±4.1	7.9±2	5.2±1.3	NG	NG	NG	NG	9 [22.5]	4 [10]	14 [35]	21 [52.5]	NG
Moattari *et al.* (25)	2012	50.38±9.92		21		NG	NG	NG	NG	3.28±3.60		10 [47.6]		4 [19]		20 [95.2]		NG
Uzkeser *et al.* (26)	2014	54 [37–65]	56 [43–75]	13	12	32.7 [26–41]	31.7 [23.8–40.8]	NG	NG	10 [8–23]	11 [3–22]	NG	NG	NG	NG	NG	NG	20–60
Uzkeser *et al.* (27)	2015	56 [37–75]	55 [42–75]	15	16	32.79 [26.62–41.07]	32.44 [23.80–43.01]	8 [2–108]	14 [1–72]	10 [7–23]	10 [3–22]	NG	NG	NG	NG	25 [20–30]	25 [20–32]	40
Tsai *et al.* (28)	2010	57.9±9.8		12	11	24.5±3.9		26.3±28.8		18.4±4.6		12 [52.2]		15 [83.3]		15 [83.3]		NG
Gurdal *et al.* (29)	2012	58.13±10.54	50.13±10.83	15	15	30.71±5.63	31.39±4.91	NG	NG	NG	NG	7 [46.7]	6 [40.0]	10 [66.7]	7 [46.7]	15 [100.0]	15 [100.0]	25–30
Johansson *et al.* (30)	1998	64 [52.5–69.5]	57.5 [47.5–69.5]	12	12	NG	NG	14 [3–76.5]	6.5 [2.3–68.3]	NG	NG	6 [50]	5 [41.7]	1 [0.8]	2 [1.7]	10 [83.3]	8 [66.7]	40-60
Ridner *et al.* (31)	2012	56.9±8.1	50.8±8.1	21	21	30.1 [26.1–32.6]	30.8 [26.1–35.5]	44.0 [13.0–109.5]	42.0 [16.5–69.0]	NG	NG	10 [47.6]	10 [47.6]	9 [42.9]	6 [28.6]	3 [14.3]	3 [14.3]	30

Continuous variables are shown as mean ± standard deviation or median [first quartile – third quartile] based on the information given by included studies. BMI, body mass index; LE, lymphedema; RT, radiotherapy; CDT, complete decongestive therapy; IPC, intermittent pneumatic compression; NG, not given.

Table 2 Characteristics of included studies

Author	Year	Study design	Follow-up duration
Haghighat *et al.* (18)	2010	Randomized controlled trial	12 weeks
Szuba *et al.* phase I (19)	2002	Randomized controlled trial	6 weeks
Szuba *et al.* phase II (19)	2002	Self-control prospective cohort	6 weeks
Tastaban *et al.* (20)	2020	Randomized controlled trial	4 weeks
Fife *et al.* (23)	2012	Randomized controlled trial	12 weeks
Dini *et al.* (24)	1998	Case-control study	9 weeks
Moattari *et al.* (25)	2012	Self-control prospective cohort	8 weeks
Uzkeser *et al.* (26)	2014	Randomized controlled trial	4 weeks
Uzkeser *et al.* (27)	2015	Randomized controlled trial	7 weeks
Tsai *et al.* (28)	2010	Self-control prospective cohort	4 weeks
Gurdal *et al.* (29)	2012	Randomized controlled trial	6 weeks
Johansson *et al.* (30)	1998	Randomized controlled trial	4 weeks
Ridner *et al.* (31)	2012	Randomized controlled trial	4 weeks

two researchers in this study who were independent of each other and not informed with the study design, mainly concentrating on four characteristics of studies: population, interventions, comparisons and outcomes. As was shown in the flow chart, the process of publication filtration was presented (*Figure 1*). Totally, 360 articles were searched, and after skimming & scanning 130 articles were excluded for duplications; 218 articles were then excluded for not being in accordance with the inclusion and exclusion criteria. Finally, 12 studies (18-20,23-31) were selected as candidates for further synthetic analysis. Results of quality assessment were presented in *Tables 3,4*. The majority RCTs had good randomization, baseline comparability, parallel and reliable measured outcomes, and appropriate statistical analysis. All the cohort/case-control studies had preeminent sampling, comparability in the course of condition, minimized bias, least confounding factors, objective and reliable measured outcomes, sufficient time of follow-up, clear description of withdrawn participants, and appropriate statistical analysis. All candidate studies achieved "Yes" to more than 50% of applicable questions, so they all passed literature quality assessment, and the results were shown in *Tables 3,4*.

CDT combined with IPC could further reduce limb volume in short term after treatment

Because of the treatment of CDT, regardless of in alliance with IPC or not, the excess volume of the lymphedema involved upper limb was significantly reduced compared to baseline in each included study. In addition, within 4 weeks' follow-up duration, CDT in combination with IPC could further reduce the excess volume of lymphedema in comparison with CDT-only (SMD =–0.2 mL, 95% CI: –0.33 to –0.07 mL) (3.4±0.5 weeks), which indicated that a complementary treatment of IPC could strengthen the effect of lymphatic drainage (18-20,23,25,27,30) (*Figure 2*). In the included studies, the volume of the limb was measured through calculation of the circumference in Tastaban's (20), Fife's (23) and Uzkeser's study (27). While water displacement was used to calculate limb volume in Moattari's (25), Haghighat's (18), Szuba's (19) and Johansson's (30) study. After lengthening the follow-up duration (9.4±2.6 weeks), the degree of lymphedema relapsed, and the excess volume of lymphedema between CDT + IPC group and CDT group showed a tendency of difference without statistical significance (SMD =–0.15 mL, 95% CI: –0.33 to 0.04 mL), indicating the impaired effect of

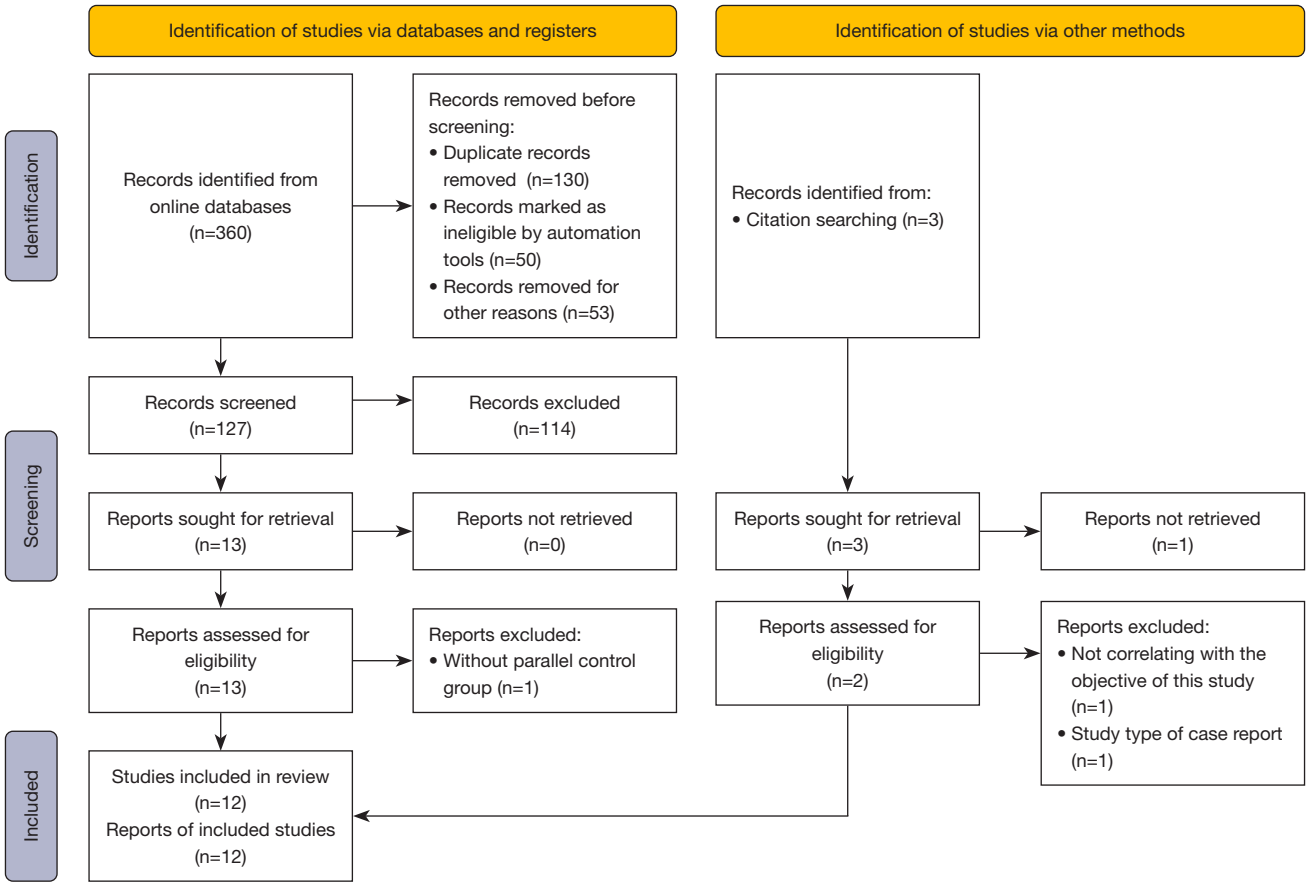

Figure 1 Literature retrieval flowchart.

Table 3 Quality assessment of eligible studies (JBI Critical Appraisal Checklist for RCT study)

Author	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]
Haghighat *et al.* 2010 (18)	Y	N/A	Y	Y	Y	Y	N	Y	Y	Y
Szuba *et al.* 2002 (19)	Y	N/A	U	Y	Y	Y	Y	Y	Y	Y
Tastaban *et al.* 2020 (20)	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y
Fife *et al.* 2012 (23)	Y	N/A	N	N	N	Y	Y	Y	Y	Y
Uzkeser *et al.* 2014 (26)	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y
Uzkeser *et al.* 2015 (27)	U	N/A	Y	Y	Y	Y	Y	Y	Y	Y
Gurdal *et al.* 2012 (29)	Y	N/A	Y	Y	N	Y	N	Y	Y	Y
Johansson *et al.* 1998 (30)	Y	N/A	N	Y	U	Y	N	Y	Y	Y
Ridner *et al.* 2012 (31)	Y	N/A	N	Y	Y	Y	Y	Y	Y	Y
Y (%)	89	N/A	56	89	67	100	67	100	100	100

[1] Was the assignment to treatment groups truly random? [2] Were participants blinded to treatment allocation? [3] Was allocation to treatment groups concealed from the allocator? [4] Were the outcomes of people who withdrew described and included in the analysis? [5] Were those assessing outcomes blind to the treatment allocation? [6] Were the control group and treatment groups comparable at entry? [7] Were groups treated identically other than for the named interventions? [8] Were outcomes measured in the same way for all groups? [9] Were outcomes measured in a reliable way? [10] Was appropriate statistical analysis used? Cited from Ha Dinh TT *et al.* (32) JBI Database System Rev Implement Rep 2016;14:210-47. JBI, Joanna Briggs Institute; RCT, randomized controlled trial; N, no; N/A, not applicable; U, unclear; Y, yes.

Table 4 Quality assessment of eligible studies (JBI Critical Appraisal Checklist for Comparable Cohort/Case Control study)

Author	A	B	C	D	E	F	G	H	I
Szuba *et al.* phase II 2002 (19)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Dini *et al.* 1998 (24)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Moattari *et al.* 2012 (25)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Tsai *et al.* 2010 (28)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Y (%)	100	100	100	100	100	100	100	100	100

A. Is sample representative of patients in the population as a whole? B. Are the patients at a similar point in the course of their condition/illness? C. Has bias been minimized in relation to selection of cases and of controls? D. Are confounding factors identified and strategies to deal with them stated? E. Are outcomes assessed using objective criteria? F. Was follow up carried out over a sufficient time period? G. Were the outcomes of people who withdrew described and included in the analysis? H. Were outcomes measured in a reliable way? I. Was appropriate statistical analysis used? Cited from Ha Dinh TT *et al.* (32) JBI Database System Rev Implement Rep 2016;14:210-47. JBI, Joanna Briggs Institute; RCT, randomized controlled study; N, no; N/A, not applicable; U, unclear; Y, yes.

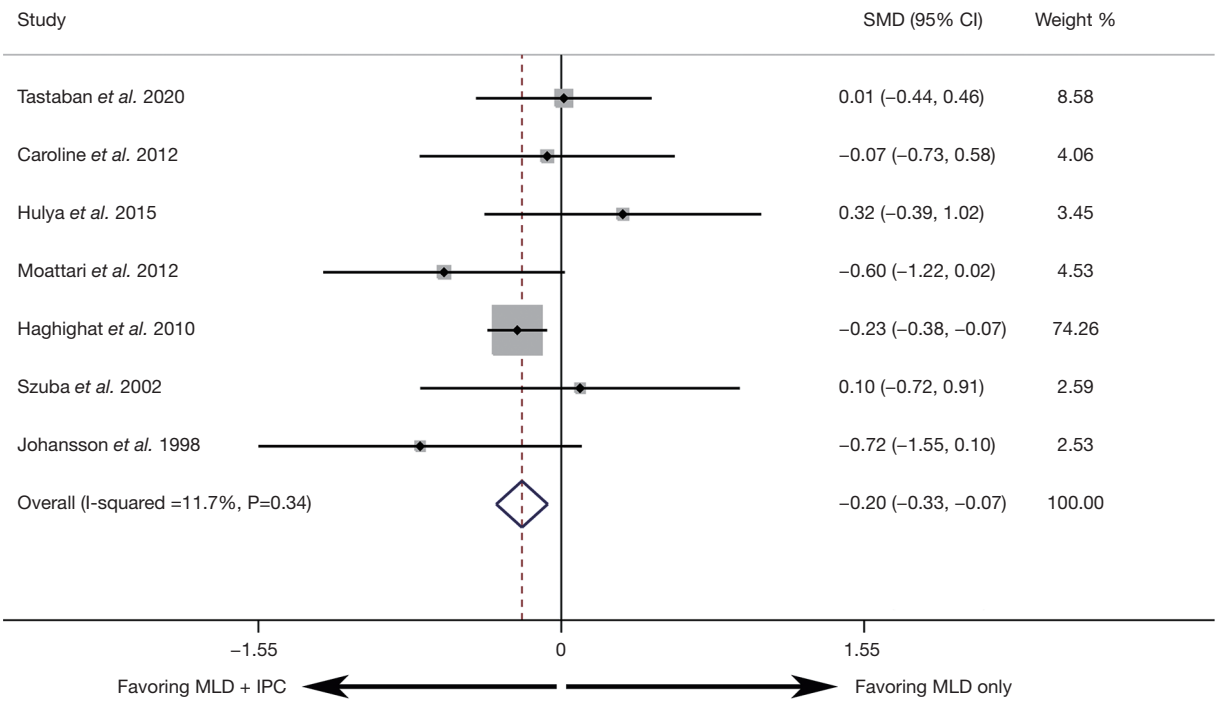

Figure 2 Forest plot of the fixed-effects model of excess volume of upper limb. SMD, standardized mean difference; CI, confidence interval; MLD, manual lymphatic drainage; IPC, intermittent pneumatic compression.

maintenance of CDT or CDT + IPC. Besides, three studies (24,27,31) showed that changes of excess circumference of the lymphedema involved upper limb were in consistency with the result of excess volume (*Figure 3*), and apparently reduced excess circumference was attained in CDT + IPC group, compared to CDT group (SMD =–0.33 cm, 95% CI: –0.65 to –0.01 cm), especially in the parts of arm and forearm.

CDT combined with IPC could improve shoulder mobility

Upper limb lymphedema could negatively influence

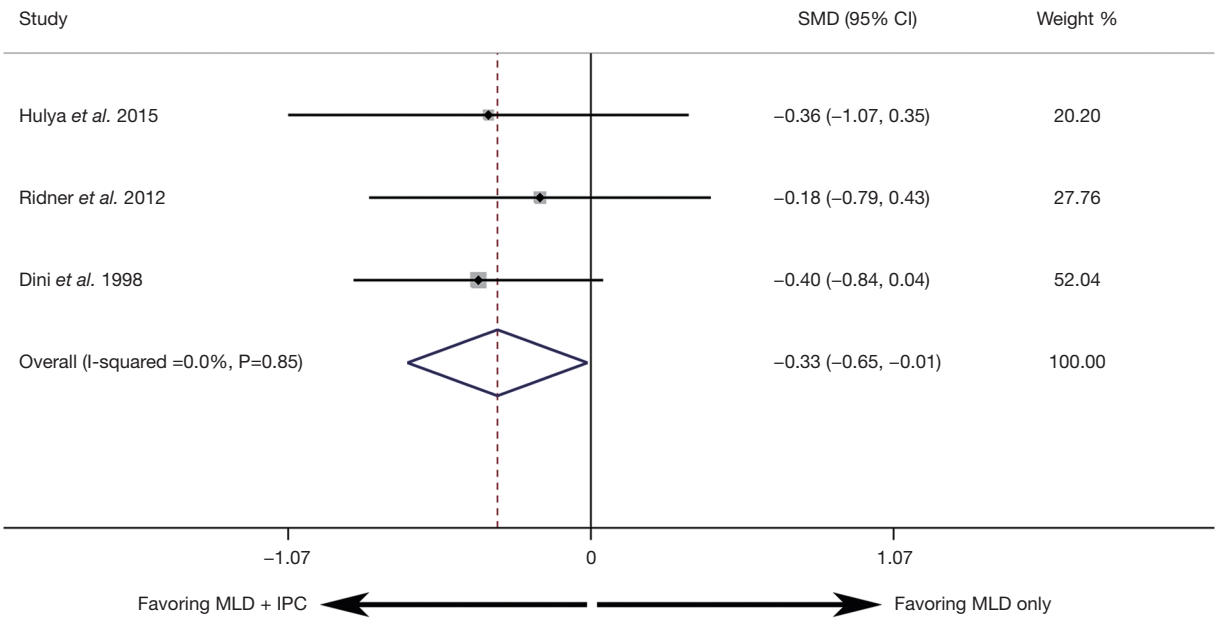

Figure 3 Forest plot of the fixed-effects model of excess circumference of upper limb. SMD, standardized mean difference; CI, confidence interval; MLD, manual lymph drainage; IPC, intermittent pneumatic compression.

shoulder mobility and restrain its range of motion. Alleviation of lymphedema could reasonably improve shoulder mobility. In some studies (25,26,30), angle scale was used as a measuring method to evaluate shoulder mobility. Accordingly, related data was collected to testify whether CDT + IPC could increase angle range of shoulder joint. Four functional positions (abduction, extension, flexion and external rotation) of shoulder were evaluated. Compared with CDT-only group, additional IPC to CDT could slightly but significantly increase the range of abduction (SMD =0.51, 95% CI: 0.02 to 1.00), extension (SMD =0.53, 95% CI: 0.04 to 1.02), flexion (SMD =0.50, 95% CI: 0.01 to 0.99) and external rotation (SMD =0.51, 95% CI: 0.02 to 1.00).

IPC as a complementary therapy to CDT failed to bring additional benefit of alleviating limb pain

Visual analogue scale (VAS) was applied to evaluate the degree of limb pain caused by lymphedema, which was secondary to breast cancer surgery and lymphadenectomy. However, there was no statistically significant difference of the VAS score between CDT + IPC group and CDT-only group (SMD =−0.06, 95% CI: −0.41 to 0.28), indicating that patients' subjective pain feeling hardly changed, no matter IPC was added or not. Results of three included studies reported related data (20,26,27).

Evaluation of publication bias

The publication bias was analysed by Begg's test and Egger's test. The symmetrical distribution of included studies was detected by Begg's test (P=0.81), and the result was visualized through a funnel plot. Moreover, Egger's test (P=0.92) consolidated that no publication bias existed in included studies via a bias plot.

Discussion

In the present study, the efficacy of IPC in addition to CDT on upper limb lymphedema secondary to breast cancer surgery was assessed using meta-analysis. At baseline, the demographic characteristics in included studies were comparable between different groups. After strict screening, filtration, and quality assessment, twelve studies were finally included for further analysis. CDT combined with IPC gained a significant decreased excess volume and excess circumference of upper limb lymphedema within a relative short follow-up duration. However, the additional decrease brought by CDT in alliance with IPC were weakened after

an elongated follow-up duration. Because of the minor significant difference, we would prudently conclude that CDT combined with IPC was more effective clinically than CDT. Additionally, there was no statistically significant difference in VAS scoring between CDT + IPC group and CDT-only group, indicating that patients' subjective pain feeling hardly changed, no matter IPC was added or not. No publication bias was detected in included studies. In conclusion, additional application of IPC to CDT could further improve lymphedema within about 4 weeks after the treatment period. Nonetheless, this additional benefit was weakened within about 8-week follow-up duration after ceasing physical treatment. Considering this discovery, periodically continuous treatment should be suggested to maintain the effect of CDT + IPC to promote lymph drainage and lymphedema reduction.

Previously published studies do not reach an agreement on the efficacy of IPC on alleviating limb lymphedema. To evaluate the role of IPC in the treatment of BCRL (breast cancer-related lymphedema) an RCT study was designed and accomplished by Tastaban *et al.* (20), and they concluded that IPC seemed to add no benefit when combined with CDT of lymphedema, however, may be functional in reducing the sensations of heaviness and tightness for the patients with pitting oedema. Likewise, Uzkeser *et al.* concluded that IPC did not contribute to the reduction of lymphedema (27). Whereas, this study provided an alternative method to gauge the dermal thickness by using ultrasonography, which might be proved to be a useful measurement method in the evaluation of lymphedema (27). Haghighat *et al.* demonstrated that either the use of CDT alone or in combination with IPC could significantly reduce limb volume in BCRL (18). In contrast, another RCT from Fife *et al.* suggested that during the home maintenance phase of treatment of lymphedema, the adjuvant treatment with an IPC would provide an additional benefit (23). IPC was reported to be implemented by professional therapists in clinic or by patients themselves at home (16). However, at-home maintained IPC treatment had some drawbacks, and patients might be incompetent to judge the outcomes of IPC treatment to adjust therapeutic parameters. Besides, timely distinguishing adverse events due to IPC treatment could be difficult to attain by patients themselves, and this could influence the efficacy of IPC treatment. Therefore, IPC treatment is recommended to be given in clinic or by patients themselves under the supervision of a professional physical therapist.

IPC was mostly reported to be effective on venous oedema in immobile even wheelchair-bound patients (33) and used for prophylaxis of venous thrombosis in different underlying aetiology (34-36). IPC could produce periodical pressure waves on the limb, simulating the working and resting pressures from muscle or compression bandages, through inflation and deflation of the air-filled cuffs. IPC not only reduces limb swelling but also augments the vein lymphatic pump, which is essential for the restoration of the damaged microcirculation of the skin (37). Szuba *et al.* argued that when IPC was adjunctively used with an established method of CDT, therapeutic response could be enhanced. Besides, they reckoned that IPC could be well tolerated and remarkably free of complications (19). However, application of IPC remained controversial due to its certain degree of adverse effects, including residual proteins remaining in the interstitial space and subsequent oedema recurrence. Furthermore, high pressure could cause potential lymphatic structure damage (17). Although the underlying mechanism is yet to be clarified, inappropriate mechanically compressive pressure is thought to be an important exogenous trigger (38). In the included studies in this meta-analysis, IPC was initiated after MLD, and the pressure ranged from 25–60 mmHg, most focused on 40 mmHg. The duration of IPC treatment was 30–60 minutes, most focused on 30–45 minutes. Different brands of IPC machines were used in those studies, and therapeutic modalities varied, such as starting with or without simulation of MLD, starting pressure on trunk or arm etc. Therefore, the optimized value of IPC parameters, such as pressure, working time, treatment period, etc., are worthy of being explored in future study.

In recent years, there are few synthetic data reporting the effect of CDT + IPC in comparison with CDT-only in the treatment of BCRL. A meta-analysis and systemic review conducted in 2014 summarized related clinical studies carried out in early period, and finally showed that volume reduction failed to be higher in CDT + IPC group compared with CDT-only group (15). In 2016, another meta-analysis reported different therapeutic methods to reduce lymphedema in breast cancer patients, and IPC was proved to be beneficial in helping to reduce limb volume in the intensive phase of treatment, nevertheless, IPC failed aiding in the volume reduction in the maintaining phase and preventing additional swelling (14), which is consistent with conclusions from this study. Therefore, the present meta-analysis updated data about upper limb lymphedema treatment modalities. In addition, the most valuable point of the present study is that, it prompts clinical staff to pay

more attention to the maintaining phase of lymphedema, such as implementing IPC treatment periodically in the clinic, encouraging patients' self-administered MLD, promoting patients' enhancing screening of lymphedema and providing more applied education to improve patients' compliance.

Limitations

Although included studies were characterized with prospective design and identified with high quality, the sample size was relatively small. This could weaken the representativeness of patients involved in this study, and limit the conclusion originated from the present study to be spread to more extensive population. Heterogeneity of follow-up duration existed among included studies, which could potentially result in bias. Lacking of enough data of treatment-related side effects being reported, the safety of CDT in combination with IPC could not be evaluated.

Conclusions

CDT combined with IPC was proved to be more effective in decreasing excess volume and excess circumference of upper limb with lymphedema within a relative short follow-up duration. However, the additional benefits brought from CDT in alliance with IPC were weakened after an elongated follow-up duration. Besides, VAS scoring showed no difference between CDT + IPC group between CDT-only group, indicating that patients' subjective pain feeling hardly changed no matter IPC was added or not. In conclusion, additional application of IPC to CDT could further improve lymphedema within about 4 weeks after the treatment period. Nonetheless, this additional benefit was weakened within about 8-week follow-up duration after ceasing physical treatment. Besides, CDT + IPC could improve shoulder mobility in four functional positions: abduction, extension, flexion and external rotation. Considering this discovery, periodically continuous treatment is suggested to maintain the effect of CDT + IPC to promote lymph drainage and lymphedema reduction.

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Footnote

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