What Is the Optimal Strategy for Drain Removal After Mastectomy and Axillary Surgery in Breast Cancer Patients? A Multicentre, Three-arm Randomized Clinical Trial

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Abstract

Purpose

The best strategy for drain removal after mastectomy and axillary surgery in breast cancer patients has remained controversial. We conducted a multicentre, three-arm randomized clinical trial to determine the optimal strategy.

Methods

A total of 187 eligible breast cancer patients who underwent mastectomy and axillary surgery were randomized into 10 ml (n=62), 20 ml (n=63) and 30 ml (n=63) groups for drain removal on the first day when the output decreased to corresponding volume/24 h. The drain duration, total drain duration, incidence of seroma, quality of life (QoL), outpatient visit times, healthcare costs and postoperative complications were evaluated.

Results

The median axillary drain durations and total drain durations were all significantly different between three groups (both $p<0.001$). The incidences of seroma were 31.1%, 38.3% and 52.1%, and the difference between the 30 ml and 10 ml groups was significant (RR=2.41). 20 ml group reported significantly better QoL in terms of physical functioning (PF) at the 2-week (30 ml vs 20 ml, HR:-14.18) and 3-week (20 ml vs 10 ml, HR: 11.65) follow-up and role functioning (RF) at the 2-week follow-up (20 ml vs 10 ml, HR: 18.15). No between-group differences were found in QoL, outpatient visits, costs or complications.

Conclusion

The 20 ml group had a moderate drain duration, total drain duration and incidence of seroma but a significant advantage over the other two groups in terms of PF and RF, with relatively low outpatient costs and comparable postoperative complication rates. These findings could aid in clinical decision-making regarding drain removal timing.

Introduction

Although breast-conserving therapy (BCT) is a well-established local therapy for early invasive breast cancer, mastectomy is still widely used, especially in Asian countries, in which patients' breasts are mostly small to moderately sized; thus, significant contour deformities can occur after BCT in these patients (Olasehinde et al., 2018; Yang, Roh, Yun, Kim, & Lew, 2014). The placement of drains is routinely performed under surgical management following mastectomy and axillary surgery to reduce the incidence of postoperative seroma, which is the most frequent complication(Suarez-Kelly et al., 2019; Wu, Luo, Zeng, Peng, & Zhong, 2020). However, drain removal practices vary widely between surgical units and even among surgeons within the same department(Kelley, Thomson, & Furniss, 2012). Several randomized control trials and systematic reviews focusing on this issue over the past 20 years have concluded that early drain removal is safe and favourable for increasing patient activity and reduces the length of hospital stay, but these benefits should be balanced against an increased odds of developing seroma and more demanding outpatient care (Baas-Vrancken Peeters, Kluit, Merkus, & Breslau, 2005; Kelley et al., 2012; Thomson, Sadideen, & Furniss, 2013; Thomson, Trevatt, & Furniss, 2016). Similarly, late drain removal leads to a longer drain duration and higher related costs and can limit patient activity. Therefore, the optimal strategy for drain removal, which is important for both patient quality of life and medical resource savings, is still unclear.

To this end, we performed a multicentre, randomized, controlled clinical trial to determine the optimal strategy for drain removal by comprehensively assessing drainage conditions, patient-reported outcomes, postoperative complications, outpatient visits and healthcare costs among Chinese breast cancer patients underwent mastectomy and axillary surgery.

Patients And Methods

Study design

This multicentre, randomized trial compared three parallel groups of patients undergoing mastectomy with axillary surgery who underwent drain removal when drainage was less than 10 ml, 20 ml or 30 ml in 24 hours (http://www.chictr.org.cn/: ChiCTR2000028729) and were recruited from 5 hospital sites in Sichuan Province, China. The trial interventions were delivered by 8 surgeons and 14 wound care nurses.

Ethics approval was obtained from the Biomedical Ethics Committee of West China Hospital, Sichuan University, as well as from the local ethics committee from each participating site.

Participants

Participants were eligible if they 1) were 18 years or older; 2) presented with a clinical diagnosis of stage I-III malignant breast tumour; and 3) underwent mastectomy with either sentinel lymph node biopsy (SLNB) or axillary node dissection. The exclusion criteria were as follows: 1) were undergoing immediate reconstruction; 2) had hypothyroidism, severe liver and kidney dysfunction, or coagulation function abnormalities; 3) underwent thoracic radiotherapy within 3 months of admission; 4) were unable or unwilling to give informed consent; and 5) were unable to cooperate with the follow-up. Informed written consent was obtained from all trial participants at each participating site.

Randomization

Randomization took place on the day of surgery. The participants were randomly allocated to 10 ml, 20 ml, or 30 ml groups at a 1:1:1 ratio by computer-generated randomization code in blocks of 4. Random assignment was placed in sequentially numbered sealed, opaque envelopes. Research staff members were unaware of the assignment until the envelope was opened. Because of the nature of the intervention, study staff were not blinded to group allocation.

Study interventions

All procedures were performed by experienced breast surgeons using an electrosurgical knife. At the end of the surgical procedure, drains were placed in the wound (one was placed in the axilla and one was placed in the chest wall; for thin patients who underwent SLNB, just one was placed from the axilla to the chest for thin patients). The drain was connected to a low suction drain bottle. Patients were given a form to record the daily drainage volume starting on the first day after operation, and the data were simultaneously recorded by the investigators, who communicated with the patients daily and informed them to of when they would undergo drain removal or any other treatment (like treat seroma) at a ward or outpatient setting after discharge. The drain was removed on the first day

when the output decreased to the corresponding volume per day based on the group assignment. Patients whose drain removal was delayed for more than 2 days were excluded from the analysis.

The patients who developed seroma following surgery treated by aspirations, and indwelling cannula (IC) were used if more than 3 aspirations were required or volume of aspiration exceeded 30 ml. The IC was removed when the output was less than 10 ml/24 h for 3 consecutive days. All patients were discharged from the hospital based on the clinical course and in accordance with national guidelines unless serious complications were detected prior to discharge.

Outcome assessments

The primary outcome measures were drain duration, incidence of seroma formation and total drain duration. Drain duration was defined as the time from surgery until drain removal. Seroma was defined according to the Common Terminology Criteria for Adverse Events (CTCAE) 4.0. Only grade 2 and 3 seroma, which is symptomatic and requires medical intervention or even operative intervention, was considered as the primary outcome(Ouldamer et al., 2016). Total drain duration was defined as to the time from surgery until the last drain was removed (patients without seroma) or until final seroma resolution (patients with seroma). The secondary outcome measures were health-related quality of life, common postoperative complications (wound infection and lymphedema), number of outpatient visits and resulting healthcare costs. Quality of life was assessed by the EORTC (European Organization for Research and Treatment of Cancer) QLQ-C30, which is an internationally validated and widely used cancer-targeted quality of life questionnaire, at baseline and every week within one month post-operation.

Statistical analysis

The sample size was calculated based on our preliminary pilot study, and the incidences of seroma were 29%, 39% and 56% in the 10 ml, 20 ml, and 30 ml groups, respectively. Using NCSS-PASS software version 11.0, we calculated that a sample size of 250 would achieve 80% power to detect an effect size (W) of 0.1756 using a 2-degree-of-freedom chi-square test with a significance level (alpha) of 0.05. To account for an approximate 20% loss to follow-up, a total sample size of 312 was needed.

P values for baseline characteristics and results were calculated using the chi-square test of association for categorical variables and nonparametric test for continuous variables. Univariate Cox regression was performed to analyse curves of drain duration and total drain duration. Univariate logistic regression was used to calculate relative risks (RRs) and associated 95% confidence intervals (CIs) for categorical outcomes. Analysis of covariance (ANCOVA) was used to assess the difference in EORTC QLQ-C30 scores among the three groups. we included baseline scores as covariates. Data were analysed using IBM® SPSS® version 22 statistical package for Windows.

Results

Patient characteristics

The consort diagram is shown in Fig. 1. Consecutive enrollment began in February 2020 and closed in August 2020 from 5 medical groups in 5 institutions, with 270 patients assessed eligible. After excluding 83 patients due to not meeting inclusion criteria or declining to participant, 187 patients were randomised into three groups. A total of 62 patients were assigned to the 10 ml group, 63 were assigned to the 20 ml group, and 62 were assigned to the 30 ml

group. Due to COVID-19, patient recruitment was slow, and the number of recruited patients did not meet expectations. Thirty-one patients were excluded due to delayed drain removal for more than 2 days, and 16 patients were lost to follow-up. The demographic and disease characteristics were well balanced among the three groups (Table 1).

Table 1
Demographic and disease characteristics

	10ml(n = 45)	20ml(n = 47)	30ml(n = 48)	P
Age (years), Mean ± SD	51.40 ± 8.40	51.13 ± 8.77	50.05 ± 9.75	0.76
Height (m), Mean ± SD	1.57 ± 0.05	1.57 ± 0.05	1.56 ± 0.06	0.64
Weight (kg), Mean ± SD	58.46 ± 7.28	59.50 ± 7.65	56.96 ± 8.16	0.27
BMI (kg/m^2), Mean ± SD	23.73 ± 3.03	24.27 ± 3.33	23.36 ± 3.10	0.37
Diabetes, n (%)	3(6.7)	5(10.6)	1(2.1)	0.24
Hypertension, n (%)	5(11.1)	8(17.0)	10(20.8)	0.45
Tumor site				0.24
Left breast (%)	25(55.6)	27(57.4)	20(41.7)	
Right breast (%)	20(44.4)	20(42.6)	28(58.3)	
Neoadjuvant chemotherapy (%)	14(31.1)	12(25.5)	11(22.9)	0.66
Histological type				0.47
IDC (%)	42(93.3)	42(89.4)	41(85.4)	
DCIS (%)	3(6.7)	5(10.6)	7(14.6)	
Molecular subtypes				0.71
Luminal A (%)	9(20)	10(21.3)	9(18.8)	
Luminal B (%)	15(33.3)	9(19.9)	17(35.4)	
Luminal B(ERBB2+)(%)	5(11.1)	4(8.5)	2(4.2)	
ERBB2+ (%)	10(22.2)	15(31.9)	13(27.1)	
Basal-like (%)	6(13.3)	9(19.9)	7(14.6)	
Stage BC				0.30
0 (%)	3(7.1)	1(2.1)	4(8.3)	
I (%)	10(23.8)	13(27.7)	5(10.4)	
II (%)	24(571)	27(57.4)	35(72.9)	
III (%)	5(11.9)	6(12.8)	4(8.3)	
Axillary surgery				0.89
ALND (%)	18 (40.0)	17 (36.2)	17 (35.4)	
SLNB (%)	27 (60.0)	30(63.8)	31 (64.6)	
Operation time				0.81

IDC: Invasive ductal carcinoma; DCIS: ductal carcinoma in situ; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection.

	10ml(n = 45)	20ml(n = 47)	30ml(n = 48)	P
≤2h	25(55.6)	29(61.7)	32(66.7)	
2-3h	15(33.1)	13(27.7)	13(27.1)	
≥3h	5(11.1)	5(10.6)	3(6.2)	

IDC: Invasive ductal carcinoma; DCIS: ductal carcinoma in situ; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection.

Primary outcome

The drains were removed at 24 h for patients with a relatively higher drainage volume; these patients obtained a shorter drain duration, which was significant in terms of axillary drainage ($p < 0.001$) but not chest drainage ($p = 0.21$) (Table 2). The median axillary drain durations for the 10 ml, 20 ml, and 30 ml groups were 12, 8, and 6 days, respectively. There was no significant difference in the delayed axillary or chest drain duration (Table 2). Patients in the 30 ml group were more likely to have their drains removed than those in the 10 ml (HR = 3.19, 95% CI: 2.05, 4.98) and 20 ml groups (HR = 2.30, 95% CI: 1.48, 3.60) (Fig. 2A). Patients in the 20 ml group received greater benefit than those in the 10 ml group (HR = 1.37), although the difference was not statistically significant (95% CI: 0.91, 2.09). Similar results were observed in regard to total drain duration: patients in the 30 ml group were more likely to achieve drainage resolution than those in the 10 ml (HR = 2.18, 95% CI: 1.49, 3.49) and 20 ml groups (HR = 1.58, 95% CI: 1.05, 2.37) (Fig. 2B), and patients in the 20 ml group were more likely to achieve drainage resolution than those in the 10 ml group (HR = 1.37), with no significant difference observed (95% CI: 0.91, 2.09).

Table 2
Postoperative drainage duration in patients according to drain removal at different times.

	10 ml (n = 45)	20 ml (n = 47)	30 ml (n = 48)	p
Axillary drain				
Drain duration* (days) (median, IQR)	12.00[7.00, 16.00]	8.00 [7.00, 13.50]	6.00 [5.00, 8.00]	**< 0.001**
Delayed drain duration, n (%)				0.09
0	31 (68.9)	27 (57.4)	35 (72.9)	
1	7 (15.6)	4 (8.5)	7 (14.6)	
2	7 (15.6)	16 (34.0)	6 (12.5)	
Chest drain				
Drain duration* (days) (median, IQR)	6.00 [4.00, 7.00]	5.00 [4.00, 6.50]	4.00 [3.00, 6.00]	0.21
Delayed drain duration, n (%)				0.73
0	20 (44.4)	20 (42.6)	18 (37.5)	
1	3 (6.7)	3 (6.4)	4 (8.3)	
2	4 (8.9)	7 (14.9)	9 (18.8)	
Total drain duration# (median, IQR)	14.00[9.00, 17.00]	11.00 [7.00, 14.00]	8.00[6.00, 12.00]	**< 0.001**

*Drain duration was defined as the time from surgery to drain removal.

#Total drain duration was defined as the time from surgery until the last drain removal (patients without seroma) or until final seroma resolution (patients with seroma).

The incidences of seroma (all were grade 2) in the 10 ml, 20 ml, and 30 ml groups were 31.1%, 38.3% and 52.1%, respectively, and the difference between the 30 ml and 10 ml groups was significant (RR = 2.41, 95% CI: 1.03, 5.62) (Table 3). The resolution of seroma among the patients in the three groups is shown in Table 3, and no difference was observed. The seroma drain duration was longer in the 30 ml group (median = 6.00 days, IQR: 2.25-7.00) than in the 20 ml (median = 4.00 days, IQR: 3.00-6.50) and 10 ml groups (median = 3.00 days, IQR: 3.00–7.00), but the difference was not significant ($p > 0.99$) (Table 3).

Table 3
Seroma and its treatment in patients get their drain removal at different timing.

					RR (95% CI)		
	10ml(n = 45)	**20ml(n = 47)**	**30ml(n = 48)**	**p**	**20ml vs 10ml**	**30ml vs 10ml**	**30ml vs 20ml**
Seroma, n (%)	14 (31.1)	18 (38.3)	25 (52.1)	0.11	1.37(0.58,3.26)	**2.41(1.03,5.62)**	1.75(0.77,3.96)
Seroma resolutions				0.57	-	-	-
Aspirations	6 (13.3)	5 (10.6)	6 (12.5)	-	-	-	-
Once	2 (4.4)	2 (4.3)	3 (6.2)	-	-	-	-
Twice	3 (6.7)	2 (4.3)	2 (4.2)	-	-	-	-
Three times	1 (2.2)	1 (2.1)	1 (2.1)	-	-	-	-
Indwelling cannulas, n (%)	4 (8.9)	9 (19.1)	14 (29.2)	-	-	-	-
Aspiration + indwelling cannulas, n (%)	4 (8.9)	4 (8.5)	5 (10.4)	-	-	-	-
Seroma drained duration(median, IQR)	6.00 [2.25, 7.00]	4.00 [3.00, 6.50]	3.00 [2.00, 7.00]	> 0.99	-	-	-

Secondary outcome

Physical functioning (PF), role functioning (RF) and global quality of life (QoL) measured by EORTC QLQ-C30 are shown in Fig. 3 and Table S1. Preoperative baseline scores for the three factors were similar among the three groups. All groups showed some level of within-group reduction in the outcome measures after operation and showed improvements at the 2- to 4-week follow-up. Better PF and RF were observed in the 20 ml group than in the other two groups, but between-group differences were only found for PF at the 2-week (30 ml vs 20 ml [95% CI], -14.18 [-27.08, -1.28]) and 3-week (20 ml vs 10 ml [95% CI], 11.65 [0.83, 22.47]) follow-up and for RF at the 2-week (20 ml vs 10 ml [95% CI], 18.15 [1.11, 35.92]) follow-up. There were no between-group differences found in QoL at any follow-up time point.

The results of outpatient visits, the resulting costs, and complications are shown in Table 4. There were more outpatient visits for patients in the 10 ml group (mean = 5.65 times, SD: 2.27) than in the 20 ml (mean = 5.02 times, SD: 1.45) and 30 ml groups (mean = 4.98 times, SD: 1.38), but with no significant difference (p = 0.42). The comparison of outpatient cost per person in the 10 ml group was 125.44 RMB (18.18 dollars, based on exchange rates in 2020, 1 USD = 6.8996 CNY) more than the 20 ml group and 139.46 RMB (20.21 dollars) more than the 30 ml group, although this difference was not significant. The incidence of postoperative lymphedema (p = 0.78) and wound infection (p = 0.91) were similar at different drain removal times.

Table 4
The results of outpatient visits, the resulting costs, and complications.

	10ml(n = 45)	20ml(n = 47)	30ml(n = 48)	P
Outpatient visits, Mean ± SD	5.65 ± 2.27	5.02 ± 1.45	4.98 ± 1.38	0.42
Outpatient costs(RMB), Mean ± SD	1106.84 ± 471.85	981.40 ± 317.42	967.38 ± 307.07	0.36
Complications				
Lymphedema, n (%)	5 (11.1)	6 (12.8)	4 (8.3)	0.78
Wound Infection, n (%)	2 (4.4)	3 (6.4)	3 (6.2)	0.91

Table 4 The results of outpatient visits, healthcare costs, and complications.

Discussion

Compared with drug therapy and surgical management for breast cancer patients, the issue of drain removal seems worthy of investigation and has been neglected by many surgeons. Determining whether the psychological, disease and economic burden on patients and the extra workload on medical staff are caused by seroma or the effects of active exercise after surgery on patients due to a long drain duration is highly important. Previous studies have had difficulty drawing firm conclusions on the timing of drain removal after mastectomy with axillary surgery because early and late drain removal strategies each have their own advantages and disadvantages; thus, more suitable indicators should be selected(Classe et al., 2006; Kelley et al., 2012; Taylor, Rai, Hoar, Brown, & Vishwanath, 2013; Thomson et al., 2013; Thomson et al., 2016). Our team tried to determine the optimal timing based on comprehensive evidence of drainage conditions, postoperative complications, quality of life and healthcare costs, among which the total drain duration and quality of life were first investigated. Through a 3-arm, multicentre randomized clinical trial, we explored whether drain removal on the first day decreased the output to 10 ml, 20 ml or 30 ml/24 h. It appears that 20 ml might be suitable due to its moderate drain duration, total drain duration, and incidence of seroma and improvements in quality of life and relatively low outpatient visit times and related costs.

Consistent with previous reports, when drain removal was performed according to a relatively higher daily drainage volume, drains could be removed early(Andeweg, Schriek, Heisterkamp, & Roukema, 2011; Clegg-Lamptey, Dakubo, & Hodasi, 2007; Gupta, Pate, Varshney, Goddard, & Royle, 2001; Thomson et al., 2013). It was also found that the total drain duration could be shorter as well, which may be because the retained drains encourage drainage by stimulating tissue reactions or by suction(Baas-Vrancken Peeters et al., 2005). It is generally thought that a shorter total drain duration could reduce the workload of medical staff and be favourable for patient activity. However, early drain removal has also been reported to lead to a higher incidence of seroma, which may cause counterproductive results and anxiety as well as patient discomfort(Barwell, Campbell, Watkins, & Teasdale, 1997; Tejler & Aspegren, 1985). Therefore, can the benefits of less drainage time be balanced against the incidence of seroma? We further explored the patient-reported outcomes measured by the EORTC QLQ-C30 and searched for answers from the patients, who have been neglected by most previous studies(Andeweg et al., 2011). We focused on RF, PF and QoL, which were the most likely factors to be affected by drainage. Patients in the 20 ml group exhibited superiority in terms of PF and RF at 2 and 3 weeks after the operation. This is most likely because early drain removal can aid in resuming physical activity and rapid rehabilitation. However, this benefit was not reflected in the 30 ml group. One possible explanation is that the incidence of seroma was too high, and patients needed to reduce their level of physical activity, offsetting

the benefits conferred to the patients. QoL was similar in three groups. This could be because the QoL was assessed by physical condition, which was mainly affected by the patient's breast cancer and their surgical condition.

Advantages were also found in the 20 ml group in terms of outpatient visits and costs. Although the 30 ml group had a shorter total drain duration, the high incidence of seroma resulted in additional outpatient visits and extra associated costs, so their outcomes were equivalent to the 20 ml group. The same trend was identified in previous studies: a shorter drain duration but higher incidence of seroma caused even more outpatient visits(Andeweg et al., 2011; Okada et al., 2015). However, the 10 ml group had the most outpatient visits in the present study, probably because the visits for too-long drainage could not be balanced by seroma treatment. In addition, the outpatient costs were proportional to the number of visits. However, neither of them were significantly different among the three groups.

In terms of complications possibly associated with seroma and drain duration(Andeweg et al., 2011; Devoogdt et al., 2011; Torres Lacomba et al., 2010), there was no significant difference between the 20 ml group and the other two groups. We gave little concern to the length of hospital stay, although a significantly shorter stay was observed for patients with early drain removal in previous reports(Andeweg et al., 2011; Baas-Vrancken Peeters et al., 2005; Dalberg et al., 2004; Droeser et al., 2009; Jain, Sowdi, Anderson, & MacFie, 2004). Patients in China are discharged according to the clinical course and independent of the drain duration.

Altogether, the results of this study indicated that for patients who undergo mastectomy and axillary surgery (whether SLNB or ALND), drains should be removed when the output is less than 20 ml per day, which was found to be the best timing.

Limitations

The number of patients did not meet expectations, and 75 patients did not complete the follow-up evaluations or were excluded for delayed drain removal—mostly due to COVID-19. However, the contract period for temporary staff hired for patient follow-up ended. Fortunately, meaningful results were still obtained, and no obvious bias regarding between-group baseline similarities was observed. However, if a larger sample size could be obtained, subgroup analysis can be performed, such as comparing ALND and SLNB, to help make more nuanced clinical judgements.

In addition, approximately 1/3 of the patients in the analysis did not undergo drain removal in time, which was delayed for 1–2 days, but we think these data are more in line with true clinical conditions because, in reality, drain removal is likely to be delayed due to a variety of patient circumstances.

The average BMI of the general Chinese population is lower than that of European and American-African populations (Xiong, Wang, Zhao, & Zhang, 2017), and BMI could be an influencing factor on seroma(Granzier et al., 2019; van Bastelaar, van Roozendaal, Granzier, Beets, & Vissers, 2018), so the generalizability of the results to other populations is limited.

Conclusions

Despite numerous studies over the past few decades, the optimal strategy for drain removal after mastectomy and axillary surgery for breast cancer patients has remained unclear; it seems that the benefits of early drain removal could be balanced by more outpatient care and longer hospital stays. This study has answered this question. Among patients whose drains were removed according to a drainage volume of less than 10 ml, 20 ml or 30 ml in 24 h, the 20 ml group showed a moderate drain duration, total drain duration and incidence of seroma. In addition, this group

showed a significant advantage in terms of physical functioning and role functioning over the other two groups at 2 and 3 weeks after surgery, with relatively low outpatient costs and comparable postoperative complication rates. These findings should help clinicians make more reasonable decisions regarding drain removal timing.

Declarations

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The datasets analysed during the current study are available from the corresponding author on reasonable request.

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Ethics approval was obtained from the Biomedical Ethics Committee of West China Hospital, Sichuan University, as well as from the local ethics committee from each participating site. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

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Figures

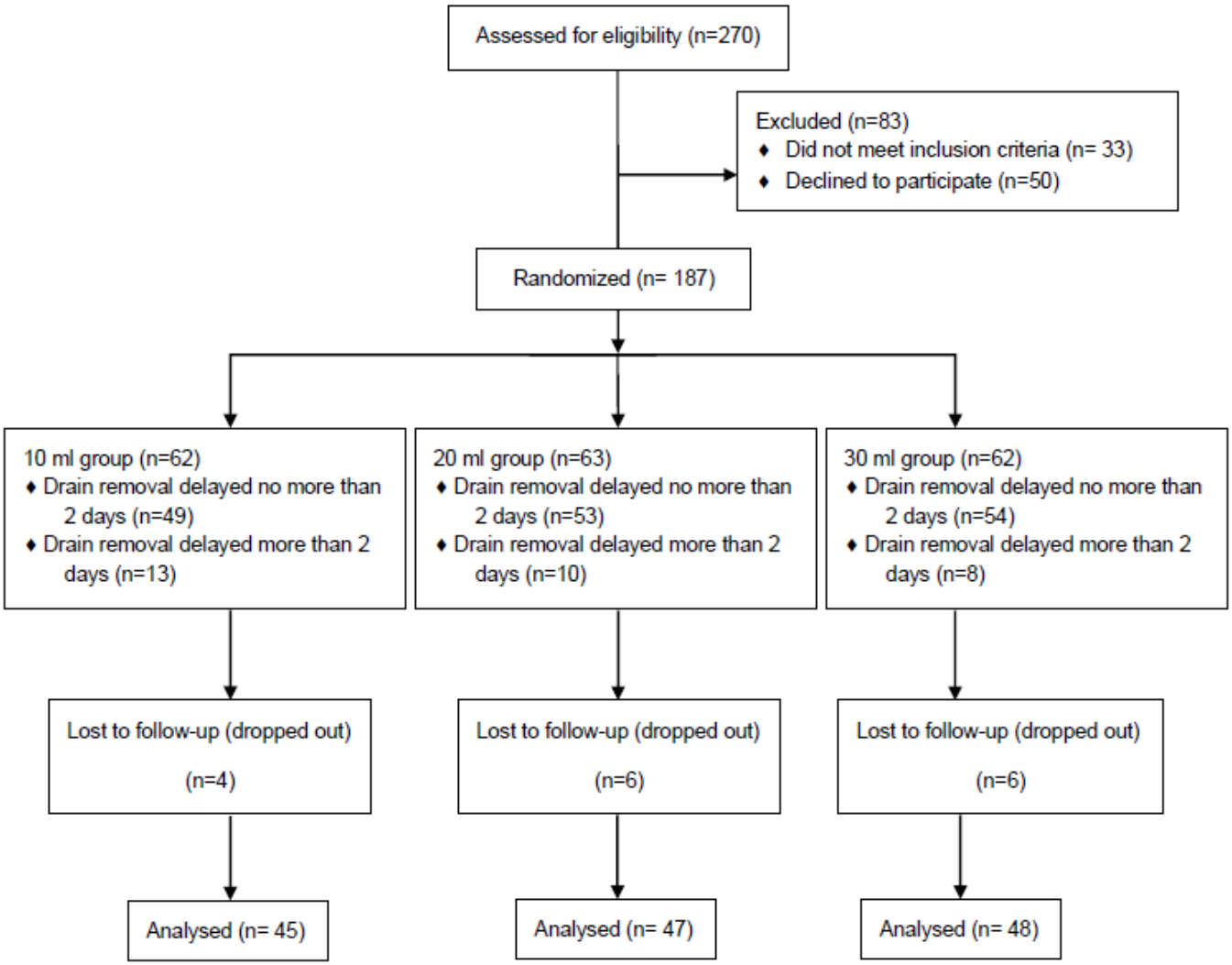

Figure 1

Consort diagram

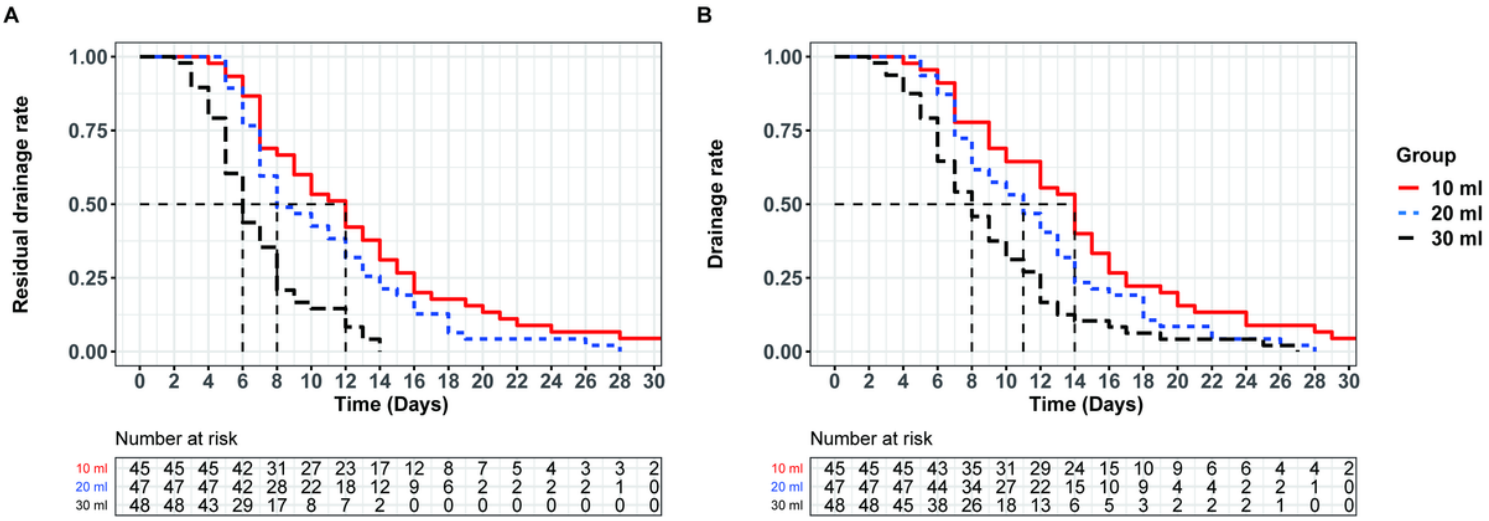

Figure 2

Kaplan–Meier curves of drain removal and drainage resolution in patients who underwent drain removal at different times after mastectomy and axillary surgery. The residual drainage rate in Fig. 2(A) refers to the proportion of patients who had not undergone all drain removal according to the drain removal strategy for each group. The drainage rate in Fig. 2(B) refers to the proportion of patients who had not undergone all drain removal (patients without seroma) or without final seroma resolution (patients with seroma).

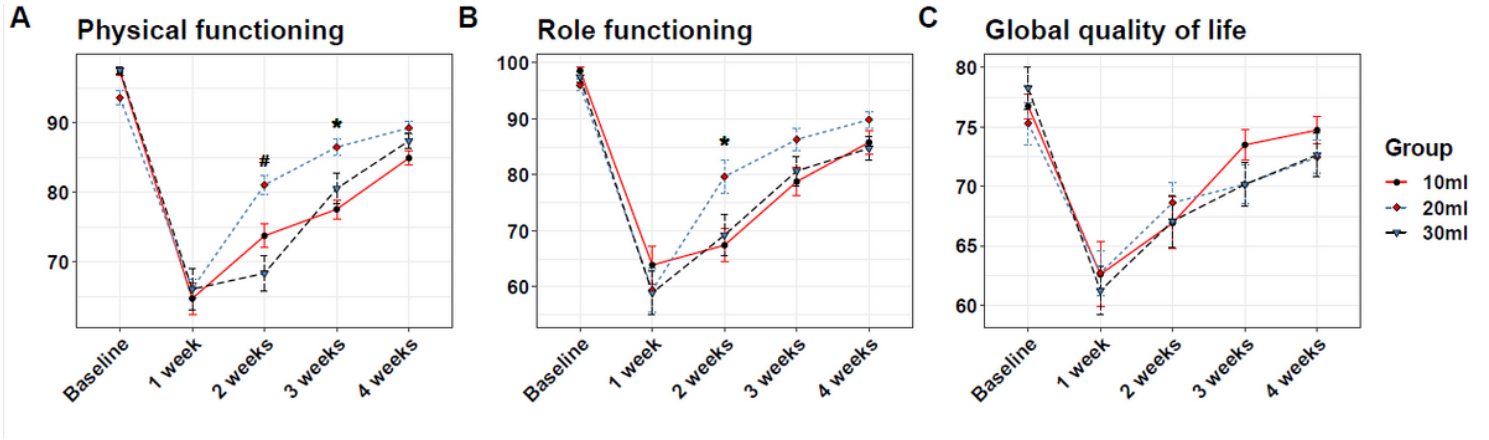

Figure 3

Quality of life was assessed by EORTC (European Organization for Research and Treatment of Cancer) QLQ-C30 at baseline and every week within one month post-operation. *The difference was significant between the 10 ml and 20 ml groups. # The difference was significant between the 20 ml and 30 ml groups.