Effectiveness of Clinical Pathway in Breast Cancer Patients: A Meta-Analysis

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Abstract: *Purpose*: To evaluate the use of clinical pathways (CPs) for breast cancer when compared with usual medical care. *Methods*: The Cochrane Library, PubMed, EMBASE, Web of science and four Chinese databases were searched from inception to November 2012 to identify randomized controlled trials (RCTs) that reported the effect of CPs for breast cancer. Two reviewers independently selected studies, extracted data and assessed included studies. The assessment of methodological quality of the included studies was based on the Jadad score. Meta-analyses were performed using RevMan software (version 5.2). *Results*: Six randomized controlled trials (597 patients) were included. There were 297 patients in the CPs group and 300 patients in the usual medical care group. The results showed that compared with usual medical care, CPs could significantly shorten the length of hospital stay (MD = -3.83d, 95% confidence interval [CI] [-5.20, -2.46]), decreased hospitalization costs (SMD = -3.44, 95%CI, [-4.79, -2.09]) and preoperative hospitalization (MD = -0.56d, 95%CI, [-0.77, -0.34]). There was no statistically difference in patients' satisfaction (OR =2.39, 95%CI, [1.00, 5.70]) and postoperative complications (OR = 0.34, 95%CI, [0.11, 1.08]). *Conclusions*: The current evidence showed that CPs could effectively improve the quality of the care provided to the breast cancer patient. It may be able to shorten the length of hospital stay, decreased hospitalization costs and preoperative hospitalization.

Keywords: Breast neoplasms, Critical Pathways, Meta-analysis.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in female worldwide, accounting for 23% (1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths in 2008. About half the breast cancer cases and 60% of the deaths are estimated to occur in economically developing countries [1]. As a developing country, China has documented a 20–30% increase in urban areas over the past decade [2]. With the development of breast cancer awareness and screening activity, the incidence rates increased and mortality decreased. China became the one of countries which breast cancer incidence raised dramatically, what's more, the age of patients became younger and younger [3].

Clinical pathways are evidence-based multidisciplinary care plans which describe the essential steps needed in the care of patients with a specific clinical problem. They are used to translate clinical guidelines into local protocols and clinical practice [4]. CPs aim to link evidence to practice for specific health conditions, therefore, optimize patient outcomes and maximize clinical efficiency [5].

Although many hospitals have carried out CPs, the real impact of it is unclear. Decision maker and policy executors still need more powerful evidence to support their decisions. We conducted this meta-analysis was aimed to evaluate the use of clinical pathways for breast cancer patients when compared with usual medical care. The effect of clinical pathways was evaluated by analyzing length of hospital stay, hospitalization costs, preoperative hospitalization, postoperative complications and patients' satisfaction as five primary outcomes.

MATERIALS AND METHODS

Study Selection

PubMed (1966–2012.11), the Cochrane Library (Issue11, 2012), EMBASE (1974–2012.11), Science citation index (1974–2012.11), The China Journal Fulltext Database (1994–2012.11), Chinese Scientific Journals Fulltext Database (1989–2012.11), Chinese Biomedical Literature Database (1978–2012.11), WANFANG database (1980-2012.11) were searched. The following key terms were used to access the records: breast neoplasm, breast tumor, breast cancer, breast tumour, breast carcinoma, mammary neoplasm, clinical pathway, clinical path, critical pathways, critical path, care pathway, care path, care map and care protocol. After identifying the key relevant articles, both

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references and citation of them were looked into for widening the search results.

Inclusion Criteria

Types of Studies

Randomized controlled trials were included in the meta-analysis, although the method of randomization was not always adequately described.

Types of Participants

We included breast cancer patients; Patients underwent radical or modified radical mastectomy and postoperative chemotherapy were all contained. Sex, age, ethnicity and nationality were not limited.

Types of Interventions

All the included studies compared the CPs care with usual medical care.

Types of Outcome Measures

The primary effectiveness outcome was as follows: 1. Length of hospital stay, defined as hospital stays from patient admission to discharge. 2. Hospitalization costs reported as any expense on medical treatment, medicine and hospitalization at the time of hospitalization. 3. Preoperative hospitalization, reported as hospital stays from patient admission to undergo operation. 4. Postoperative complications, complication defined as factors affecting recovery that required re-admission or prolonged hospital stay such as wound infection [6]. 5. Patients' satisfaction, Measurement of how satisfied they were with the care they received.

Exclusion Criteria

Trials that did not assess at least one of the five primary outcomes (length of hospital stay, hospitalization costs, preoperative hospitalization, postoperative complications and patients' satisfaction) were excluded.

Data Extraction and Quality Assessment

Detail information such as author, affiliations of authors, publication journal and country, publication year, duration of the studies, sample size of each group, baseline information of the population studied, study design, study outcomes and information of the development of CPs were extracted. Assess of studies was carried out independently by two reviewers (CQ and SX). The eligibility of the studies was identified by screening all the titles, abstracts or the full text. All disagreements were resolved by discussions or appeal for the third researcher's opinion.

Jadad score (7-point) was using to assess the quality of included RCTs [7]. The quality items included were randomization, blinding, withdrawals and dropouts. The concealment of allocation was also assessed [8]. Each study was subjected to a quality assessment by two authors. In case of disagreement between two reviews, resolved by discussion.

Data Analysis

Meta-analyses were performed using Cochrane Collaboration software RevMan 5.2. We summarized available data from all studies reported results. For dichotomous variables, the relative treatment effect was expressed as odds ratio (OR) with 95% confidence levels (95%CI). For continuous variables, the mean difference (MD) with 95%CI was used. When trials report their outcome in different scales, the standardized mean difference (SMD) is more appropriate. Heterogeneity and extent of inconsistency were indicated by the chi^2 statistic and I^2 statistic respectively. We used fixed effects model when statistical heterogeneity was show (heterogeneity test, $p>0.1$ and $I^2<50\%$) and random effects model when heterogeneity was present (heterogeneity test, $p < 0.1$ and $I^2>50\%$).

RESULTS

Studies Selection

According to search strategy above, 606 studies were identified. Only 6 records could be seen to meet the study inclusion criteria, the flow of study selection was shown in Figure **1**.

Characteristics of Included Studies

Characteristics of all six included studies are presented in Table **1**. 597 patients were included, 297 under CPs care and 300 under usual medical care. Six studies were all performed in China. The patients of four studies were all woman but the other two studies were unreported. Except one study, all patients of other five studies included patients' age ≥ 27.

Methodological Quality of Studies

All six trials described as randomized. Three of them reported the method to generate the sequence of randomization, but only one trial [9] involved random

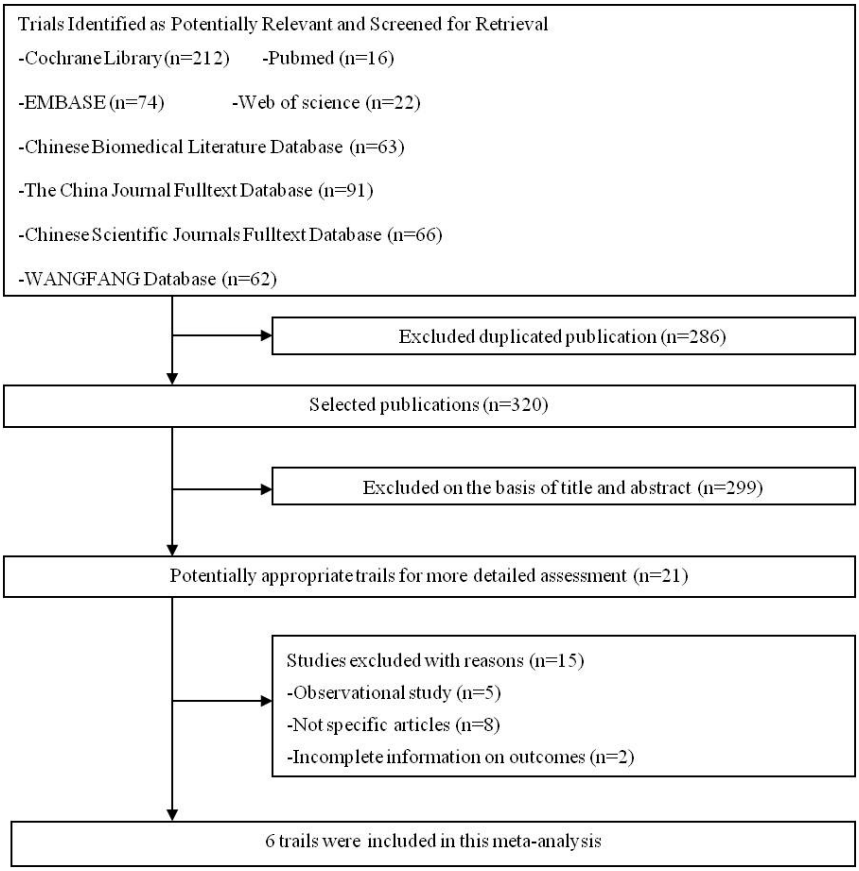

Figure 1: Flow diagram of trial selection.

Table 1: Baseline Characteristics of the Included Studies

Trials	Year	Sample size (case/control)	Country	Duration of the studies	Object of study	Age(years)		Sex	Outcome Measurements
						CPs	Usual care		
Wang 2007[9]	2007	25/25	China	200503-200602	radical mastectomy	51.7±3.5*	50.6±4.5*	not stated	①; ②; ⑥; ⑦
Rong 2007[10]	2007	40/40	China	200206-200606	breast cancer	not stated		not stated	①; ②; ③; ⑤; ⑥
Jiang 2009[12]	2009	31/30	China	200806-200810	radical mastectomy; breast-preservation operation	47.55	49.63	female	①; ②; ③; ④; ⑧
Mo 2011[13]	2011	75/78	China	2006-2009	operable primary breast cancer	age(27-72), average age:47		female	①; ②; ③; ④; ⑤; ⑧; ⑨; ⑩
Zhang 2010[11]	2010	43/43	China	200607~	Breast cancer neoadjuvant and metastasis –free	age(35-7l), average age:55		female	①; ②; ⑪; ⑫
Liuet.al 2007[14]	2007	83/84	China	2004-2005	operable primary breast cancer	age(29-76)		female	①; ②; ③; ④; ⑤; ⑧; ⑨; ⑩

① length of hospital stay; ② hospitalization costs; ③ preoperative hospitalization; ④ postoperative complications; ⑤ patients' satisfaction; ⑥ Health knowledge; ⑦ self-help ability; ⑧ variation of CPs; ⑨ rate of accidental events; ⑩ admissions to ICU; ⑪ complications of chemotherapy; ⑫ adverse reaction; * Mean ± SD

Table 2: Methodological Quality of Included Studies

Trials	Randomization (Sequence Generation)	Concealment of allocation	Blinding	Withdrawals and dropouts	Total Jadad Score
Wang 2007 [9]	random digits table	unclear	unclear	unclear	2
Rong 2007 [10]	Hospital numbers	unclear	unclear	unclear	1
Jang 2008 [12]	unclear	unclear	unclear	No dropout	2
Mo 2011 [13]	unclear	unclear	unclear	No dropout	2
Zhang 2010 [11]	Odd /even of number	unclear	unclear	unclear	1
Liu *et al.* 2007 [14]	unclear	unclear	unclear	No dropout	2

digits table. The hospitals number were used in two trails to generate the sequence [10, 11]. All the trials did not report whether blinding and allocated concealment were adopted. Three trials [12-14] reported the dropouts. Included studies' methodological quality was assessed using the Jadad score (7-point) in Table **2**.

Outcomes

Length of hospital stay

Six studies [9-14] reported the length of hospital stay. Heterogeneity among the study results was substantial (p<0.00001, I^2=89%). CPs group was associated with significantly shorter hospital stays (MD =-3.83d, 95% CI, [-5.20, -2.46]) (Figure **2**).

Preoperative Hospitalization

Four studies [10, 12, 13] reported preoperative hospitalization. The analysis indicated no statistical heterogeneity (p<0.00001, I^2=0%). The result showed a significantly shorter preoperative hospitalization for the CPs group when compared with usual care (MD = -0.56d, 95%CI, [-0.77, -0.34]) (Figure **3**).

Hospitalization Costs

Three studies [9, 10, 12] reported hospitalization costs. Heterogeneity was high between studies

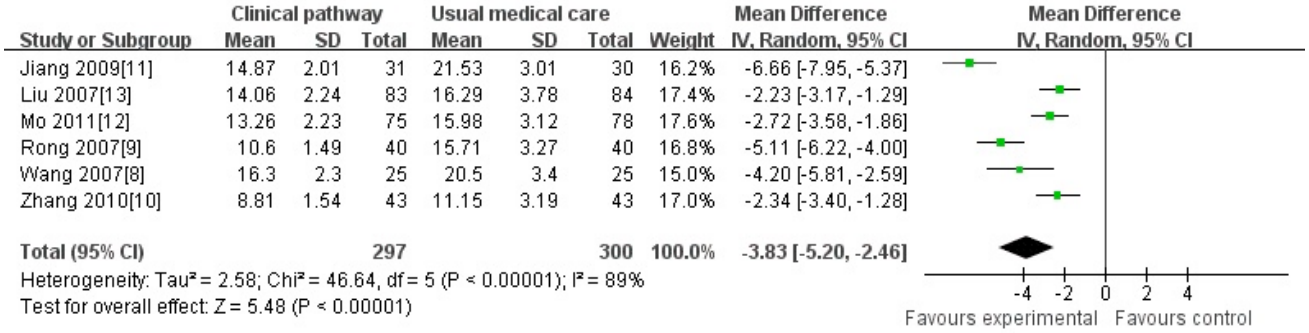

Figure 2: Effects on length of hospital stay.

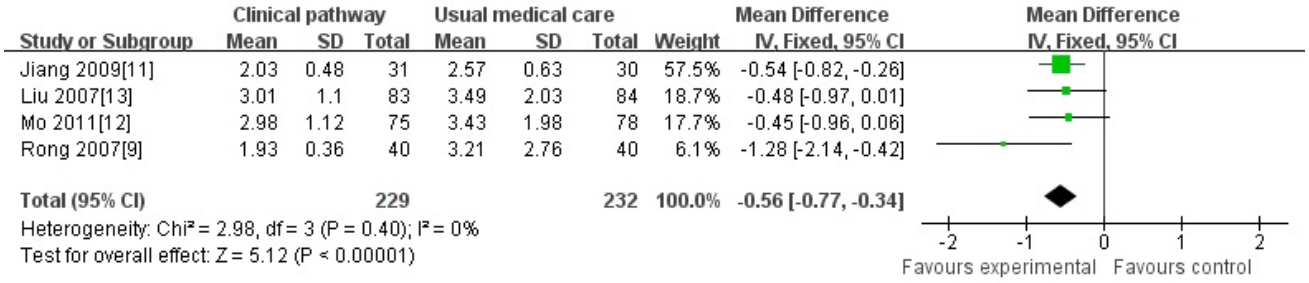

Figure 3: Effects on preoperative hospitalization.

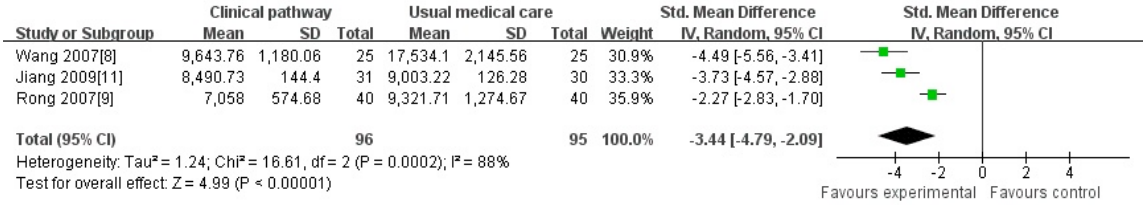

Figure 4: Effects on hospitalization costs.

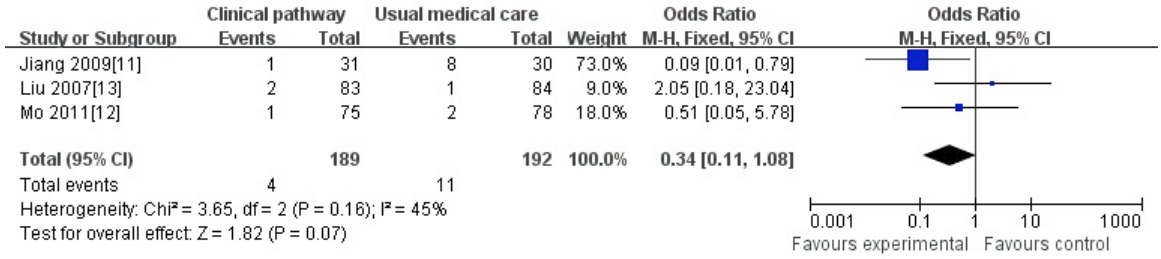

Figure 5: Effects on postoperative complications.

(I^2=88%). CPs group had better effect on lower hospitalization costs (SMD = -3.44, 95%CI, [-4.79, -2.09]) (Figure **4**).

Postoperative Complications

Three studies [12-14] reported the postoperative complications. Statistical heterogeneity was basically well among studies (p=0.16, I^2=45%). There was no significant difference in postoperative complications between CPs and usual medical care group (OR = 0.34, 95%CI, [0.11, 1.08]) (Figure **5**).

Patients' Satisfaction

Three studies [10, 13, 14] reported the patients' satisfaction. There was no statistically differences in patients' satisfaction (OR =2.39, 95%CI, [1.00, 5.70]) (Figure **6**).

DISCUSSION

Clinical pathway, provide an approach in the hospital setting by reducing variation in clinical processes, and improving the quality of care while keeping hospital length of stay to an acceptable minimum[15]. Four historical controlled studies cited a reduction in length of hospital stay, decrease duration before the operation and reduced hospital costs of breast cancer patient when using clinical pathway [16-19].

The results of meta-analysis showed that CPs could effectively improve the quality of the care provided to the breast cancer patients. It was able to shorten length of hospital stay, lower hospitalization costs and decreased preoperative hospitalization. Meanwhile there are almost no difference in patients' satisfaction and postoperative complications between CPs and usual medical care.

Length of hospital stay and preoperative hospitalization from the studies included in this meta-analysis showed significantly reduced when CPs compared with usual medical care. The concept of CPs refers to specific guidelines for care that describe patient treatment goals and define a sequence and timing of intervention for meeting those goals efficiently

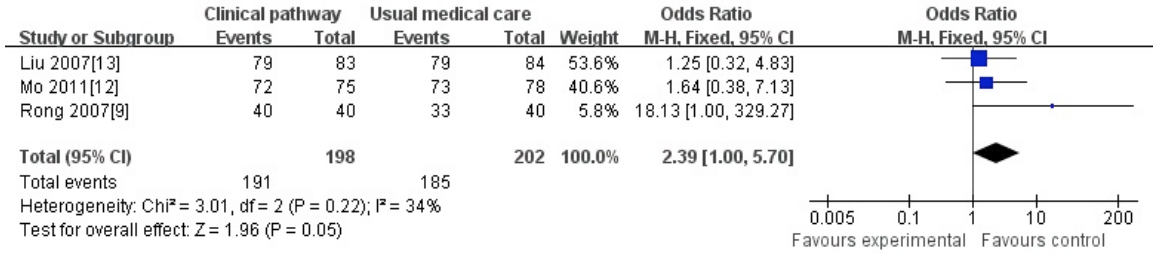

Figure 6: Effects on patients' satisfaction.

[20]. The limitation of time and patients in CPs made the reducing of length of hospital stay and duration before the operation.

The positive effect of CPs was also found in outcome of hospitalization costs. The findings of this study revealed that CPs has statistically significant effect on decreasing hospitalization costs. The results are due to the reducing of day in hospital also may be due to the fact that managing of resource consumption by using clinical pathway. Numerous studies have also proven that CPs reduce resource consumption [21, 22].

The results of postoperative complications showed that, no statistical significance between two groups despite the CPs reducing the variation in clinical process and better organization of the care [6].

Three studies reported patients' satisfaction, the results of meta-analysis show that there are no significant differences between the two groups. There were many causes like different evaluation criterion of patient' satisfaction and small simple size.

One study [9], of six included studies, provided adequate and appropriate descriptions of randomization process. Hospital numbers and treatment order was used to generate the random sequence in two studies [10, 11]. None of studies reported allocation concealment and blinding, which would yield selection bias and performance bias. The qualities of these included trials were relatively low.

While the strict inclusion criteria and comprehensive database retrieval were performed, our meta-analysis has its limitations. First, most of studies have small simple size resulting in limited statistical power to make meaningful conclusions and patient selection could have occurred. Second, five included studies were performed by single author in single sites in China. Same doctors and nurses who deal with the patients in CPs and usual medical care group in single-center at the same time. It may increase the risk of contamination. Last but not the least, six included studies use different type of clinical pathway, it could be increase the heterogeneity. As to the treatment measure, three studies [9, 10,12] choose surgical treatment, two studies [13,14] choose the method combination of traditional Chinese medicine with surgical and one study [11] choose neo-adjuvant chemotherapy; as to the development of CPs, there also exist many difference between four reported studies. Two studies [10,12] reported the clinical pathway developed by the clinical pathway management group, one study [13] reported it developed by four experts of breast surgery and one study [14] by five experts of traditional Chinese and western medicine. Four studies [10,12-14] all stated that the CPs developed according to the relevant literature, two of them mentioned the NCCN clinical practice guideline.

Definitive conclusions cannot be made although the date supports the effectiveness of clinical pathways in breast cancer. Measuring the effectiveness of CPs in reducing cost can not only consider the hospitalization cost. We should also think about the cost before and after the hospital. Clinical pathways that reduce hospital costs by merely shifting equal or more costs into the outpatient setting do not meet the true needs of patients or the health care system [23]. Development and implementation of clinical pathways is a multi-faceted and resource-intensive process involving all parties concerned [24]. Nevertheless, only a few studies reported the development and implementation of clinical pathway and the cost of it have not been reported.

CONCLUSIONS

Despite the possible limitation exists, the results of this meta-analysis showed that clinical pathways was able to shorten length of hospital stay, decreased hospitalization costs, reduced duration before the operation in breast cancer. Further high-quality RCTs should reported more about the cost of development and implementation of clinical pathway.

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