Air Travel and Postoperative Lymphedema—A Systematic Review

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Abstract

Lymphedema is not uncommon after axillary dissection for breast cancer. Improved survival of patients with breast cancer from advances in adjuvant therapy has resulted in increased awareness of the quality of life for long-term survivors. Air travel has been postulated as 1 of the risk factors of lymphedema exacerbation. In the present systematic review, we sought to critically evaluate the current data on this topic. The present study was registered in the Research Registry. A systematic review of lymphedema and air travel was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. The Medline, EMBASE, CINAHL, and Cochrane databases were searched for English-language studies up to June 2017 with a predefined strategy. The retrieved studies were independently screened and rated for relevance. Data were extracted by 2 of us. A total of 55 studies were identified using predefined keywords; 12 studies were included using the criteria stated in the study protocol. A pooled analysis of 2051 patients with a history of air travel revealed that $\leq$ 14.5% developed lymphedema after air flight. However, a subsequent analysis of 4 studies with a control arm showed that 107 of 1189 patients (9%) with a documented history of air travel developed lymphedema compared with 204 of 2356 patients (8.7%) who had not flown (χ^2 test; $P = .80$). Two studies (1030 patients) evaluated the effect of lymphedema on patients' air travel patterns. Of the 1030 patients, 141 (13.7%) had totally avoided air travel after the development of lymphedema. However, air travel was not adversely associated with the development of lymphedema.

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Introduction

Lymphedema is a condition due to the disruption of the lymphatic system. Protein-rich fluid accumulates in the soft tissues of the affected body parts, commonly involving the limbs and, occasionally, the trunk or even the head and neck region.[1,2] The etiology of lymphedema can be classified into primary and secondary causes.[3] In the modern era, in which chronic parasitic infestation within the lymphatic system is no longer common in developed areas, postaxillary dissection lymphedema in breast cancer patients has become the major cause of lymphedema worldwide.[4]

Lymphedema is considered 1 of the most debilitating and distressing complications of breast cancer treatment, including axillary dissection and, to a lesser extent, sentinel lymph node biopsy. Depending on the method of measurement and threshold of reporting, it occurs in 10% to 20% of patients who have undergone axillary dissection for breast cancer,[5] which is currently the reference standard treatment of lymph node-positive breast cancer.[6,7] Several precipitating factors have been identified to be closely associated with lymphedema. These include obesity, skin infection, prolonged use of the affected limbs, and trauma to the affected limbs. In addition, air travel has been postulated to be associated with worsening of lymphedema.

Improved breast cancer survival has been observed in recent years with the introduction of different adjuvant chemotherapy regimens and targeted therapy, including trastuzumab.[8,9] Thus, the quality of life of long-term breast cancer survivors has become an important aspect in the management of breast cancer. In fact, the ability to live a normal life after recovering from breast cancer is as important as being disease free.

Air travel has become popular worldwide. The International Air Transport Association reported 3.8 billion air travelers in 2016, and this is expected to increase steadily at a rate of 3.7% annually.[10] This is partly because air travel is becoming more affordable with the introduction of newer commercial jets designed with more cost-effective fuel consumption. Implementation of the "open skies" policy has also promoted fair competition between commercial airlines.[11] For

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example, in the busiest international commercial airline route, > 5 million passengers had traveled from Hong Kong to Taipei in 2015.[12]

However, air travel has been suggested to exacerbate lymphedema. The low cabin pressure at high altitude and the changes in cabin pressure during the ascent and descent of aircraft have been postulated to be the culprits of the problem. Although controversial, for many women with lymphedema, air travel still poses a significant dilemma and hinders their social and work life.

Air Pressure at High Altitude and Cabin Pressure

Air pressure decreases with increases in altitude. As a rule of thumb, the air pressure decreases ~1 in. of mercury for each 1000-ft increase in altitude. At sea level, the atmosphere is ~14.7 psi. In contrast, the pressure of the atmosphere at an altitude of 8000 ft is ~10.9 psi.[13]

Modern commercial aircraft are capable of flying at altitudes that are incompatible with human life; yet, the passengers and crew are generally not negatively affected owing to the onboard environmental and pressurization systems.[14] The cabins of aircraft traveling at extreme altitudes are maintained pressurized within the mechanical limits of the fuselage. Although pressurized at cruising altitude, the cabin pressure will still be lower than that at ground level. The cabin pressure of an aircraft at cruising level (40,000 ft) is designed to decrease gradually from the altitude of the departing airport to the pressure at a level of ~8000 ft (ie, cabin altitude of 8000 ft instead of the 40,000 ft outside the cabin).

Pathophysiology

The cabin pressure experienced during air travel is lower than the atmospheric pressure at sea level. At altitudes > 12,500 ft (3800 m), cabin pressurization is necessary to protect the air crew and passengers from the risk of a number of physiologic events, such as hypoxia and altitude sickness at extreme altitudes. Cabin pressurization is achieved by pumping compressed air from the turbine engine such that the cabin pressure is maintained at that of lower altitude (cabin altitude), which is typically ~8000 ft even at cruising level of 40,000 ft.

Although a cabin altitude of 8000 ft will not pose major health hazards, the decreased cabin pressure can result in lymphedema secondary to the pressure difference. The possible mechanisms include increased fluid retention in the connective tissue, increased fluid production in the soft tissues, and reduced fluid return to the lymphatic system at the low cabin pressure at cruising level.

Theoretically, the low cabin pressure during air travel can aggravate lymphedema. However, the evidence from the published data has been conflicting. We performed a systematic review of the effect of air travel on breast cancer patients with postoperative lymphedema.

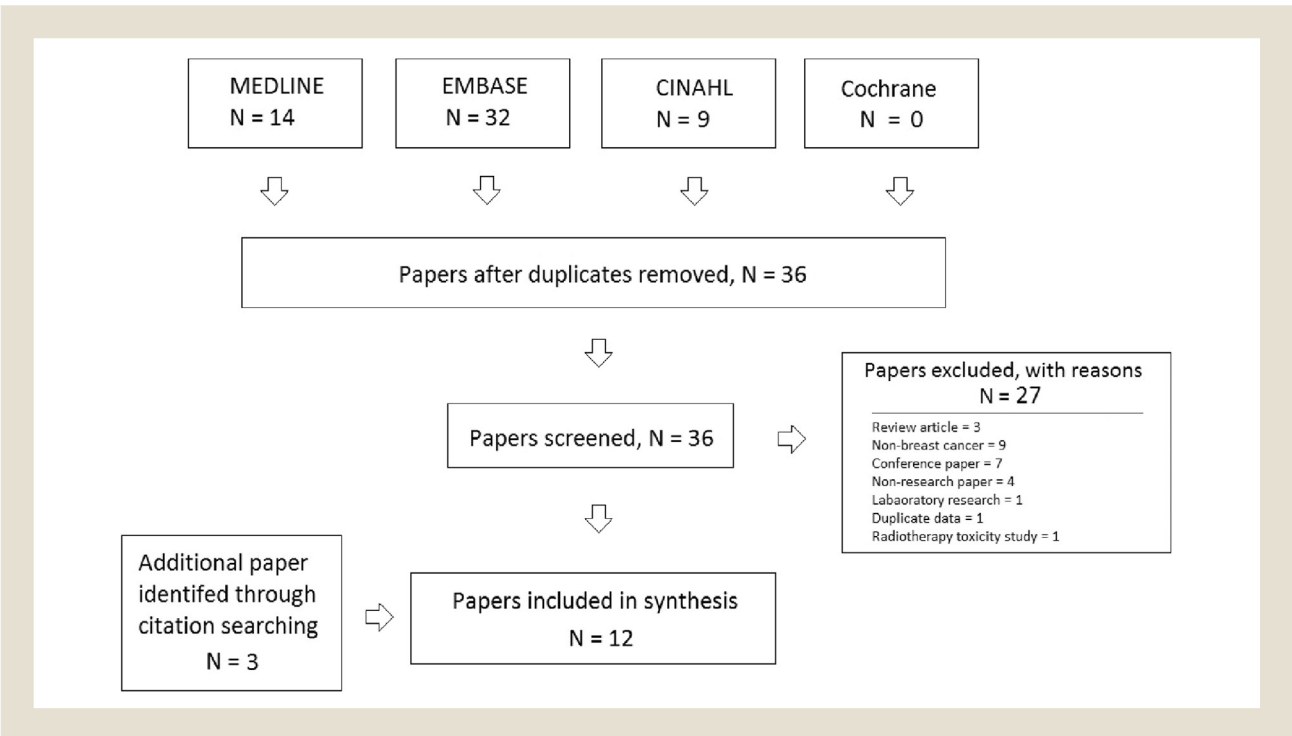
Materials and Methods

The present study was registered at Research Registry (available at: http://www.researchregistry.com). The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Figure 1) and current methodologic data.[15,16] Owing to the heterogeneity of studies, a meta-analysis was not performed. Because ours was a systematic review, institutional review board approval was not required.

Data Sources and Eligibility

The Medline, Cochrane, EMBASE, and CINAHL databases were searched for relevant English-language studies to June 2017. In

Figure 1 Flowchart of the Study Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines



addition, abstracts from the reference lists of the selected studies and titles identified using an electronic search of leading journals in breast surgery and nursing care were also retrieved and screened for relevance. A search of relevant gray data using the same combinations of keywords was also performed.

Search Terms

The search terms used were "lymphedema" AND "air travel," "lymphedema" AND "flight," "lymphedema" AND "cabin pressure," and "lymphedema" AND "airplane." A repeated search was performed using "lymphoedema" instead of "lymphedema" to avoid missing studies written in British English. The abstracts were screened by 2 of us independently for relevance and the level of evidence. The full text of the studies for the selected abstracts was retrieved.

Study Selection

Review studies, conference abstracts, and nonresearch articles (eg, editorials) were excluded. However, the references from the review studies were checked for cross-referencing. Identical studies and abstracts were identified to avoid duplications. Studies reported by the same institution were reviewed, with only the most recent study or the study with the most complete reporting of the outcomes of interest included to avoid data duplication. Data extraction was performed independently by 2 of us, and the results were combined for analysis.

Results

A total of 55 studies were identified using the preset keywords defined in the study protocol. After excluding review and other nonresearch studies such as letters to the editor, editorials, and guidelines, 12 studies were included for analysis[17-28] (Table 1). No randomized control trial on this subject was found. The best evidence was from the 4 prospective studies.[24,25,27,28]

Lymphedema and Air Travel—Current Evidence of Its Association

Air travel has been postulated as 1 of the major triggering factors of lymphedema by an early case report and a retrospective survey-based study,[17,21] which was subject to recall and selection bias. The findings from the remaining studies suggested no significant association between air travel and lymphedema (Table 1).

A pooled analysis of 2051 patients from 7 studies found that only $\leq$ 14.5% of patients with postoperative lymphedema had history of air travel (Table 2). In addition, according to the 4 studies with a control arm in the analysis (patients without air travel history), 107 of 1189 patients (9%) with a documented history of air travel developed lymphedema. In contrast, 204 of 2356 patients (8.7%) who had not flown developed lymphedema (χ^2 test, $P = .80$; Table 3).

Lymphedema and Air Travel—Effect on Patient Behavior

Two studies evaluated the effect of lymphedema on patients' travel behavior (Table 4). Of the 1030 studied subjects with lymphedema, 141 (13.7%) had totally avoided air travel. The study by McLaughlin et al[20] also demonstrated other avoidant behaviors in air travel. Of 936 patients, 100 had changed their travel patterns, and 6 were reported to travel by air using short-haul flights ($\leq$ 1 hour) only.

Lymphedema and Air Travel—Does Flight Number and Duration Matter?

Patients with lymphedema had avoidant behavior and some even restricted air travel to trips of < 1 hour.[20] However, current

Table 1 Summary of Study Conclusions on Effect of Air Travel in Lymphedema Patients

Investigator	Study Design	Patients (n)	Conclusions	Evidence Level
Ferguson et al,[27] 2016	Prospective cohort	3041	Air travel was not a risk factor, regardless of the number and duration of flights	2
Kilbreath et al,[28] 2016	Prospective cohort	540	Number of domestic air travel flights was not associated with lymphedema	2
Showalter et al,[25] 2013	Prospective, subgroup analysis of PAL	295	Air travel and travel altitude were not significant risk factors for lymphedema	2
Kilbreath et al,[24] 2010	Prospective	72	No significant difference in pre- or postflight bioimpedance	2
Swenson et al,[22] 2009	Retrospective, case-control	94	47/94 patients totally avoided air travel; air travel was not associated with lymphedema	3
Mak et al,[23] 2009	Matched case-control	101	Lymphedema worsened (initiated) after flight in 48/101 patients	3
McLaughlin et al,[20] 2008	Prospective, case-control	936	100/936 changed their travel patterns, with 36 totally avoiding flying	3
Graham,[18] 2002	Retrospective, survey-based	287	Lymphedema worsened after flight for 16/145 patients; short-haul (<4.5 h) flight was low risk; inflight compression prophylaxis paradoxically associated with lymphedema	3
Casley-Smith,[17] 1996	Retrospective; survey-based	490	Lymphedema worsened after flight for 50/490 patients	4
Hayes et al,[19] 2005	Retrospective, observational	176	Air travel within 6 mo had no significant association with lymphedema	4
Ward et al,[21] 2009	Case report	1	Worsened symptoms and bioimpedance after flight	5
Ahn et al,[26] 2016	Case report	1	No documented lymphedema after air travel	5

Table 2 Studies Evaluating History of Air Travel for Patients With Worsened Lymphedema

Investigator	Study Type	Lymphedema Patients With History of Air Travel
Casley-Smith et al,[17] 1996	Retrospective survey-based study	94/490 (19.2)
Graham,[18] 2002	Retrospective survey-based study	16/145 (11)
Swenson et al,[22] 2009	Retrospective case control	46/115 (40)
Mak et al,[23] 2009	Matched case control	48/101 (47.5)
Showalter et al,[25] 2013	Prospective; subgroup analysis of trial	81/271 (30)
Ferguson et al,[27] 2016	Prospective cohort	36/878 (4.1)
Kilbreath et al,[28] 2016	Prospective cohort	9/51 (17.6)
Overall		297/2051 (14.5)

Data presented as n/N (%).

evidence to support avoiding long-haul flights is not strong. Only a few studies have considered the effect of the number and duration of flights on lymphedema. The conclusions were all negative. A study by Graham[18] concluded that short-haul flights (< 4.5 hours) have a low risk of lymphedema. Kilbreath et al[24] performed an experimental study to measure the bioimpedance in patients with lymphedema who had travelled by long-haul and short-haul flights, with no significant differences found. Another recent study by Ferguson et al[27] also reported similar findings showing air travel is not a risk factor for lymphedema, regardless of the number or duration of the flights.

Prophylactic Compression Garment

The use of compression garments provides external pressure on the extremity to adequately support favorable resorption and decrease the potential for fluid accumulation in the tissue. Theoretically, the use of compression will prevent worsening of pre-existing lymphedema and has been recommended during air travel for those with lymphedema. Compression bandages will potentially increase the interstitial tissue pressure and enhance the muscle pump in the lymphedematous extremity. The beneficial outcomes are twofold. First, resorption of fluid at the capillary level is enhanced by the compression. Second, use of the garment or bandages can promote lymphatic circulation by way of the muscle pump. However, the use of compression garments has not been well studied. The only study was by Graham,[18] who found that $\leq$ 24% of their cohort of patients had taken lymphedema precautions (of which $\leq$ 90% were compression garments). On regression analysis, Graham[18] found that use of the compression garment is associated with the worsening of lymphedema (odd ratio, 5.6), although the underlying mechanism is still unknown. This finding is contradictory to our usual belief that external compression is beneficial in the context of lymphedema. However, in retrospective studies, the possibility of recall bias always exists. In addition, it is nearly impossible to ensure that all compression precautions were performed correctly and adequately by the patients.

Modern Aircraft Models and Lymphedema

The structural strength of the airplane determines how much pressure difference the airframe can withstand. It is usually 8 psi for airframes of aluminum alloy (the material used in most commercial jets in operation). The mechanical strength of the fuselage is the direct determinant of cabin pressure. The cabin pressure can be further elevated when stronger airframe materials are used. The Boeing 787 Dreamliners (Boeing Company, Chicago, IL) were among the first commercial aircrafts to use stronger composite material for airframe construction. Newer aircraft models such as the A350XWB series (Airbus Group, Toulouse, France) have used carbon fiber as the major structural material, resulting in better fuel consumption efficacy and stronger physical strength. Thus, a greater cabin pressure can be maintained in these 2 modern aircrafts. However, its beneficial effect on lymphedema has yet to be addressed scientifically.

Discussion

The early reports in the 1990s that suggested an association between air travel and lymphedema in breast cancer patients were confined to anecdotal evidence. However, these reports have already had a significant psychosocial effect on long-term breast cancer survivors.[20,22] Many of them had changed their usual air travel patterns, including restricting air travel to short-haul flights only, with some even totally avoiding air travel. In the current era in

Table 3 Studies Evaluating Lymphedema Events in Patients Stratified by History of Air Travel

Investigator	Study Type	Lymphedema/Patients Who Have Flown	Lymphedema/Patients Who Have Not Flown
Graham,[18] 2002	Retrospective survey-based	16/145	12/142
Swenson et al,[22] 2009	Retrospective case control	46/115	47/71
Ferguson et al,[27] 2016	Prospective cohort	36/878	133/2082
Kilbreath et al,[28] 2016	Prospective cohort	9/51	12/61
Overall	—	107/1189 (9.0)	204/2356 (8.7)

Data presented as n/N (%).
Overall difference: $P = .80$.

Table 4 Studies of Changes in Travel Behavior After Development of Lymphedema

Investigator	Study Design	Patients	Results
McLaughlin et al,[20] 2008	Prospective, case control	936	Behavior change after lymphedema development; avoids air travel: 36/936
Swenson et al,[22] 2009	Retrospective, case control	94	Behavior change in air travel; avoids air travel: 47/94
Overall	—	—	141/1030 (13.7) of lymphedema patients avoid air travel

Data presented as n (%).

which air travel has become an essential mode of transportation, the negative psychological effects from the early reports has significantly constrained the daily activities of long-term breast cancer survivors.

The present systematic review evaluated the best evidence of the effect of air travel on lymphedema from the published data. Although this topic has not been well studied by randomized controlled trials, our results suggest that only a very small proportion of lymphedema patients were adversely affected by air travel. Also, air travel was not associated with worsening lymphedema, regardless of the number or duration of the flights. With the introduction of new-generation aircrafts in the past decade, which are able to maintain an even greater cabin pressure than the older models, air travel should not be a concern for patients who have undergone axillary surgery and/or irradiation, regardless of whether they lymphedema. Breast cancer survivors should live a normal life that is as well-traveled as that of the normal population.

Conclusion

Our analysis has shown that air travel is not associated with lymphedema in postoperative breast cancer patients.

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