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Breast

Cost Utility of Breast Tissue Expansion using Carbon Dioxide versus Saline: An Analysis of Infection Risk

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Background: The AeroForm System, a needle-free, patient-controlled carbon dioxide-filled tissue expander, represents a novel option for tissue expansion in 2-stage breast reconstruction. This technology has previously been found to decrease time to expansion, health-care utilization, and infection rates. The purpose of this study was to determine the economic impact of the reduced infection rate observed with the AeroForm tissue expander as compared with saline tissue expansion.

Methods: A decision model incorporating costs, quality-adjusted life years, and clinical outcomes of infection was designed to evaluate the cost-efficacy of AeroForm tissue expanders versus conventional saline expanders. All statistical calculations were performed in the R statistical computing environment.

Results: Pooled infection rates from the published literature following saline and AeroForm tissue expander placement were 5.83% and 2.62%, respectively. Cost-utility analysis resulted in a baseline expected savings of $253.29 and an expected gain of 0.00122 quality-adjusted life years with AeroForm tissue expanders. One-way sensitivity analysis revealed that AeroForm tissue expanders were dominant when the surgical site infection rate was greater than 4.56% with traditional saline expanders.

Conclusions: Clinical benefits of an innovation are no longer sufficient to justify its acquisition costs. Novel technologies must also demonstrate favorable economic outcomes. This cost-utility analysis demonstrates that the use of AeroForm expanders is likely a cost-saving technology for 2-stage breast reconstruction. *(Plast Reconstr Surg Glob Open 2019;7:e2501; doi: 10.1097/GOX.0000000000002501; Published online 29 October 2019.)*

INTRODUCTION

Breast reconstruction rates continue to increase in the United States of America with implant-based reconstruction rising at a faster pace than autologous modalities.[1] Among implant-based techniques, a 2-stage tissue expander-to-implant procedure remains, by far, the most common and has evolved considerably since the 1980s.[2–4] Multiple sequential refinements in both technique and technology have occurred that allow surgeons to achieve improved aesthetic outcomes whereas simultaneously minimizing patient complications. Some of these technical and technological improvements include the rise of nipple-sparing mastectomy, improved implant technology, acellular dermal matrices, perfusion imaging, prepectoral implant placement, and the adoption of autologous fat grafting.[5,6]

Despite the multiple refinements above to minimize patient morbidity, the overall technology behind saline tissue expanders remains quite similar to the concept introduced by Radovan almost 40 years ago.[7] These traditional saline expanders are resource intensive and typically involve the use of serial bolus injections in the office at weekly or biweekly interval during the postoperative period. Saline tissue expansion has certain disadvantages such as patient discomfort and anxiety associated with repeated percutaneous needlesticks, disruption of work or daily activity, the possibility for introducing bacterial inoculum percutaneously during fills, consumption of office and physician resources, and the risk of rupture.[8]

It is incumbent upon the surgeon to minimize postoperative complications. Taking steps to prevent surgical site infection is a critical factor from both a clinical and

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economic or cost-saving perspective. Surgical site infections are responsible for the greatest total annual cost of any health-care-associated infection, accounting for nearly 34% of the $9.8 billion per year spent on complications.[6] Moreover, studies demonstrate significant increases in mean length of stay and 30-day readmission rates for women with surgical site infections.[7,8]

The AeroForm (AirXpanders, Inc., San Jose, Calif.) device is a carbon dioxide-filled breast tissue expander that allows gradual, needle-free expansion via the patient's use of a handheld remote controller (Fig. 1). The controller communicates wirelessly with the tissue expander to initiate the release of 10 mL of carbon dioxide gas per dose. Multiple redundant safety mechanisms allow for a maximum of 3 patient-initiated expansions per day. The expander is programmed to release gas from an internal reservoir up to the labeled volume of the expander.[9] Importantly, additional volume expansions can be administered by the surgeon through the use of a master key. Chopra et al previously reported on the comparison of the AeroForm tissue expander versus saline expanders and demonstrated a reduced infection rate, full-thickness skin necrosis rate, and decreased utilization of health care and patient resources.[10] The authors also showed a trend toward reduction in seroma formation and dehiscence, but this did not achieve statistical significance due to the small study sample.

To date, no cost-utility analysis has compared breast reconstruction with AeroForm expanders to traditional saline expanders. The purpose of this study was to determine whether tissue expansion with AeroForm carbon dioxide tissue expanders is an economically viable alternative to the use of saline tissue expanders following mastectomy in breast cancer patients.

Fig. 1. Illustration demonstrating a paradigm shift of tissue expansion for women with breast cancer previously requiring weekly saline injections (left) to modern approaches allowing at-home patient-controlled tissue expansion with carbon dioxide and a handheld remote controller.

METHODS

Model Development

A decision model was designed to compare the risk of infection associated with a patient-controlled expansion with the AeroForm tissue expander versus conventional saline tissue expanders in women who had undergone implant-based reconstruction. Costs, quality-adjusted life years (QALYs), clinical outcomes of infection, and their probabilities were incorporated into this model. All data for the model were extracted from a review of the literature and an ad hoc survey of expert physicians in this field. Patients who underwent implant-based reconstruction via the use of conventional saline tissue expanders or with the AeroForm tissue expander at our facility were also included. Patients who did not undergo breast reconstruction with saline tissue expanders or AeroForm were excluded.

Perspectives

The perspective of a third-party payer (eg, Medicare) was adopted for the decision analysis. Only direct costs (eg, surgical fees, anesthesia, hospital charges) were factored into the utility estimates.

Health States

In a recent study, Chopra et al demonstrated that prepectoral breast reconstruction with AeroForm tissue expanders was associated with fewer surgical site infections as compared with patients receiving traditional saline-filled tissue expanders.[10] This potentially lower rate of infection risk in AeroForm is corroborated by other studies that examined this approach to reconstruction (Table 1).[9–14] Additional benefits of the AeroForm tissue expanders include elimination of virtually any risk associated with implant rupture from inadvertent needle injury, and many fewer required clinic visits for implant fills. As the only significantly different complication between AeroForm and traditional saline tissue expanders, the presence or lack of infection in these patient cohorts was defined as a distinct health state with associated probabilities, costs, and utilities for use in the decision model.

Costs

Costs of each health state and clinical outcome in the decision analysis were obtained by using Medicare's Current Procedure Terminology (CPT) codes and Diagnosis-related Group codes. The cost associated with placement of a carbon dioxide-filled tissue expander was based on the price of the commercially available AeroForm tissue expander system. The cost of the traditional saline expander was obtained by the calculation of national out-of-network billing charges for patients undergoing saline implant-based reconstruction. The expected costs were calculated by multiplying the total cost of a "health state"

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Table 1. Results from Literature Review of Infection Rates with Saline and AeroForm Tissue Expanders

Article	Study Design	Date Range	Pocket Location	Total Cases (N)	Infections (N)	Infection Rate (%)
Aeroform Expander						
Connell[11]	Prospective, single-arm cohort study	22 June 2009 to 30 June 2009	Subpectoral	10	0	0
Connell[11]	Prospective, single-arm cohort study	July 2011 to June 2012	Subpectoral	61	1	1.60
Zeidler et al[13]	Randomized controlled trial	2017	Subpectoral	97	1	1.00
Connell[12]	Prospective cohort study	6 months in 2014	Subpectoral	34	1	2.90
Hsieh and Lam[14]	Prospective cohort study	May 2013 to November 2013	Subpectoral	14	0	0
Ascherman et al[8]	Randomized controlled trial	October 2011 to December 2014	Subpectoral	168	9	5.30
Chopra et al[10]	Retrospective cohort study	2017	Prepectoral	74	0	0

Weighted average: 2.62%; 95% confidence interval: 1.50%–4.52%.

by the probability of that "health state" occurring. The total expected cost was the sum of the expected cost of the successful surgery plus the sum of the expected cost of all complications. This information as related to the health state of major infection is shown in Table 1 with costs of surgical site infection being based on a recent meta-analysis analyzing the financial impact of the most common health-care-associated infections.[6] All costs were corrected for inflation to represent 2018 US dollars.

Probabilities

Probabilities of health states for traditional implant-based breast reconstruction were derived from an extensive review published by Phillips et al, in which the authors report that among 64 studies on implant-based breast reconstruction, the infection rate was 5.78%.[15] This number was utilized to represent the rate of infection associated with saline-filled tissue expanders. The probabilities of health states for AeroForm breast reconstruction were determined by reviewing Cochrane, MEDLINE, and EMBASE electronic databases for studies reporting outcomes on AeroForm tissue expansion. This search yielded 6 published studies, which included 384 AeroForm and 127 saline-filled tissue expander placements (Table 1). In addition, our institution has performed 74 AeroForm and 111 saline-filled tissue expander placements, yielding totals of 458 AeroForm and 238 saline-filled placements that were included in this analysis. The pooled infection rate for the AeroForm group was 2.62%. Data were extracted and pooled from the relevant publications and summarized showing the number of patients involved and specific complications.

Utilities

Utility was initially assessed by obtaining utility scores using a validated assessment tool, the visual "feeling thermometer" visual analog scale, and surveying surgical experts.[16–18] We selected a preference measurement and used the following values: 1.0 for the individual's "perfect" health and 0.0 for death. Each surgeon was asked to rank his/her preference such that the quality of life for each health state was marked on the 0.0–1.0 scale. The overall utility of each health state was obtained by averaging the expert opinions. Utilities were converted to QALYs using the following formula:

QALY = (utility of health state × duration of health state) + (utility of successful surgery × remaining life years)

Duration of health state following successful tissue expander breast reconstruction was assumed to be 1.7 days based on a published data.[19] For the duration of the surgical site infection health state, 9.7 days were added to the duration of successful surgery based on data assessing extended hospital stay associated with surgical site infections, and an additional 5 weeks were added for home and outpatient therapy, which may include a course of antibiotics, expander removal/replacement, and skin re-expansion.[7] Remaining life years were calculated using a mean age at tissue expander breast reconstruction of 51.46 years and an average life expectancy for a female in the United States of 81.09 years.[20,21]

Data Analysis

A decision model was created with 2 main branches including AeroForm and saline tissue expanders (Fig. 2). Surgical site infection probability, cost, and QALY were included in the model. Expected costs and QALY were calculated for each tissue expander type and health state and used to calculate the incremental cost-utility ratio (ICUR), using the following formula:

ICUR = (expected cost of AeroForm tissue expander – expect cost of saline tissue expander)/(expected QALY of AeroForm tissue expander – expected QALY of saline tissue expander).

An intervention is considered cost-saving if the ICUR is less than $0, because the expected cost is less than the reference intervention and it has a greater utility as measured by QALY. An intervention is considered cost-effective if the ICUR is greater than $0 and less than a predefined willingness to pay per 1 added QALY ratio. A threshold of $50,000 per QALY is widely accepted as the willingness to pay in the US health-care system and was utilized in this study.[16]

One- and 2-way sensitivity analyses varying the probabilities for infection were used to judge the robustness of the model and address potential uncertainty surrounding the underlying assumptions. All statistical calculations were performed in the R statistical computing environment (The R Foundation, Vienna, Austria). The study was conducted in accordance with the principles promulgated by the Declaration of Helsinki.

RESULTS

Pooled infection rates from the published literature following saline and AeroForm tissue expander placement

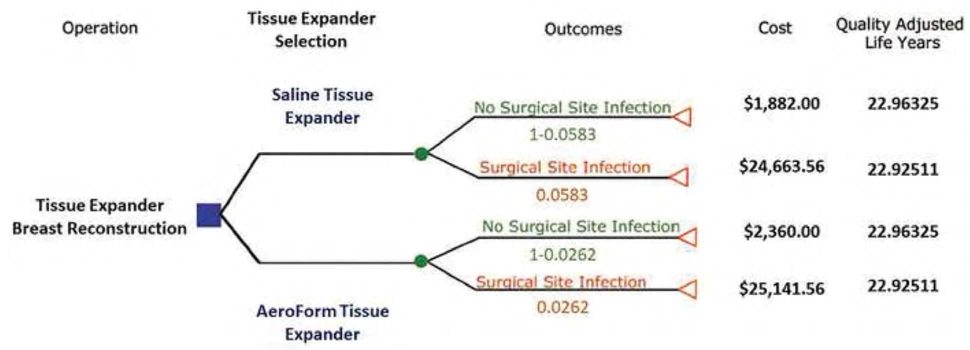

Fig. 2. Decision tree. Decision node represents the selection of a traditional saline vs AeroForm tissue expander for use in breast reconstruction. Probabilities are presented below each terminal branch. Cost and QALYs are displayed to the right of the terminal branches.

were 5.83% and 2.62%, respectively (Table 1). The overall costs associated with an AeroForm expander were $2,360 as compared with $1,882 with a saline tissue expander; surgical site infection carries a cost of $22,782.56 in 2018 US dollars (Table 2).

Survey results yielded a utility of 0.775 for uncomplicated 2-stage implant-based breast reconstruction and a utility of 0.475 for 2-stage implant-based breast reconstruction complicated by surgical site infection (Table 3). Cost-utility analysis resulted in a baseline savings of $253.29 and a gain of 0.00122 QALY with AeroForm tissue expander use (Table 4). One-way sensitivity analysis revealed that AeroForm tissue expanders were dominant when the surgical site infection rate was greater than 4.56% with traditional saline expanders. Two-way sensitivity analysis (Fig. 3) determined a range of AeroForm and saline tissue expander infection rates at which the cost-effectiveness analysis crosses the $50,000/QALY threshold.

DISCUSSION

Clinical benefits of an innovation are no longer sufficient to justify its acquisition costs. The current state of health-care requires novel technologies to demonstrate favorable economic outcomes that appeal to value analysis committees. Moreover, this modern health-care economic climate demands the identification of cost-saving or cost-effectiveness measures. Although the days when surgeons could simply demand 1 product over another may be in the past, the clinical experience of the surgeon remains a key component in deciding which products are deemed clinically necessary in the operating room. Therefore, it behooves surgeons to understand how to navigate value analysis and economically justify products and technology they require to provide optimal care for their patients. The reduction in surgical site infection rate previously demonstrated with AeroForm tissue expanders prompted the present cost-utility analysis.[16] The present work aimed to establish the economic impact of AeroForm compared with standard traditional saline expanders following mastectomy.

Table 2. Costs Associated with AeroForm and Saline Tissue Expanders and Surgical Site Infection

AeroForm		Saline Tissue Expander		Surgical Site Infection*	
Tissue expander	**$2,800**	Tissue expander†	**$1,700**	Average total cost per incident, including resource utilization, diagnostic workup, medical and surgical management	$20,785 in 2012 USD
		Saline expansion supplies	$26		
		×7 expansions	**$182**		
New consult fee‡	$0				
×2.5 occurrences	**$0**			Inflation adjustment§	+9.4%
Total	$2,360	Total	$1,882	Total	$22,782.56

*Based on meta-analysis performed by Zimlichman et al.[22]
†Actual costs may vary based on hospital negotiations and the specific saline tissue expander manufacturer.
‡Based on average reimbursement for CPT codes 99201-99205. At-home expansion eliminates all but first (initial postoperative follow-up) and last (second-stage preoperative) clinic visits, for a total reduction of 5 follow-up appointments, allowing for on average 2.5 new patient consults during that time.
§Cumulative rate of inflation based on the latest US government CPI data through December 2018.

Table 3. Utilities, Costs, and QALYs

		Saline Tissue Expander				Aeroform Tissue Expander			
Health States	**Utility**	**Cost ($)**	**Expected Cost ($)**	**QALY**	**Expected QALY**	**Cost ($)**	**Expected Cost ($)**	**QALY**	**Expected QALY**
Successful surgery	0.775	1,882	1,772.28	22.96325	21.6244925	2360	2,800.00	22.96325	22.3616129
Infection	0.475	24,663.56	1,437.89	0	0	25,141.56	658.71	22.925113	0.60063796
Total	–	–	3,210.16	–	21.6244925	–	3,458.71	–	22.9622508

Table 4. Cost-utility Analysis

	Cost Difference ($)	QALY Gained	ICUR ($/QALY)
Baseline analysis	−253.29	0.00122	−206,901.36*
One-way sensitivity analyses			
Saline infection rate threshold†	4.56%	0.00122	50,000
Aeroform infection rate threshold‡	3.90%	0.00122	50,000

*An intervention is considered cost-saving there is an expected net cost-saving and greater utility (as measured by QALY) compared with the competing intervention.

†Given the existing costs and utilities, AeroForm tissue expander remains cost-effective using a willingness-to-pay threshold of $50,000 per QALY whereas the saline infection rate is ≥ 4.56%.

‡Given the existing costs and utilities, AeroForm tissue expander remains cost-effective using a willingness-to-pay threshold of $50,000 per QALY whereas the AeroForm infection rate is ≤ 3.90%.

The results of this study suggest that AeroForm tissue expanders are clinically superior and confer a beneficial cost-saving measure among women seeking implant-based breast reconstruction. When the probability of surgical site infection with saline expanders was varied from 0 to 1 with 1-way sensitivity analysis, AeroForm was cost-effective above a saline infection rate of 4.56% and below an AeroForm infection rate of 3.90%. Two-way sensitivity analysis further demonstrated the cost-efficacy of AeroForm expanders over a wide range of clinically relevant infection rates (Fig. 3). In other words, AeroForm tissue expanders are cost-effective not only in the setting of this study but also in all cases where the infection rate with traditional expanders is greater than 4.5%. A novel intervention is considered cost-saving when it results in improved QALY at less net cost than an alternative treatment strategy. When this situation occurs in cost-effect analysis, the novel option is referred to as "dominant" over a competing intervention and adoption of the new technology is warranted. Based on the results of the present analysis, AeroForm should be strongly considered to supplant the use of saline tissue expanders following mastectomy.

The use of AeroForm technology may be beneficial to patients and institutions beyond the confines of this focused study. The technology virtually eliminates the possibility of accidental rupture through needlestick. This is a rare but dreaded complication because saline expanders require frequent percutaneous needlesticks through the skin and into a small port inside the implant. Rupture uniformly necessitates operative removal of the ruptured device and replacement with a new, intact implant. Patients also have reduced health-care-related travel expenses associated with expansion visits because visits for the sole purpose of saline fills are eliminated (eg, car wear, gasoline, tolls, and public transportation). This coincides with a reduction in expansion-visit-associated inconvenience (eg, time off from work and provisions for childcare).

Institution-related benefits include a similar reduction in opportunity cost of seeing patients within the global reimbursement period for saline expander fills which do not generate added hospital revenue because the CPT code 19357 includes the placement of the tissue expander and subsequent visits for expansion. Therefore, each subsequent visit allocated for expansion and the associated supplies could be relegated to income-generating activities including high margin, high cash flow procedures such as injectables, or scheduling future operations by evaluating new patients. Institution investment in technologies that can help prevent postoperative complications is particularly valuable when considering readmission fines and penalties that commonly affect large referral centers. This study justifies economic analysis of the use of carbon dioxide tissue expanders in a broader population

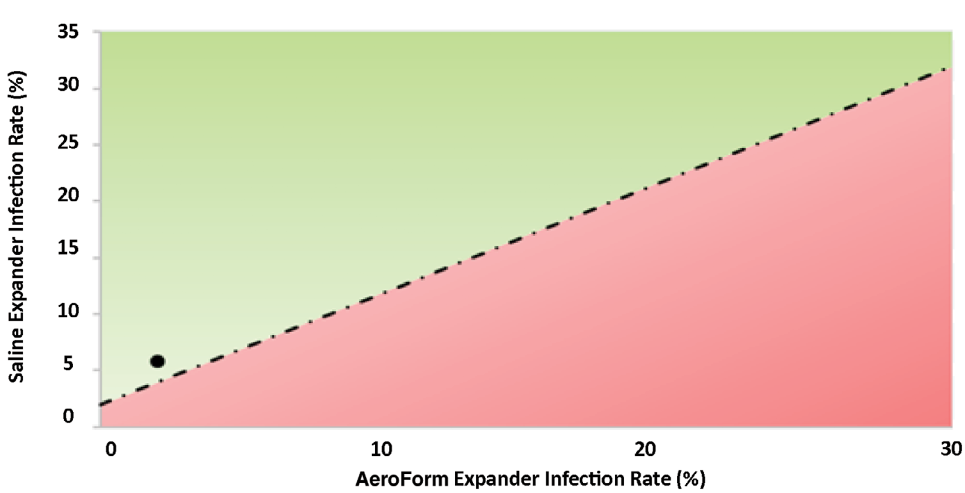

Fig. 3. Two-way sensitivity analysis. This analysis evaluates the robustness of our model by simultaneously varying 2 important variables: the risk of infection with an AeroForm tissue expander (*x*-axis) and the risk of infection with a traditional saline tissue expander (*y*-axis). Dashed line represents the threshold of infection rates at which our $50,000 per QALY willingness to pay is met. Any combination of infection rates resulting in a point above the dashed line (shaded green) supports the cost-efficacy of AeroForm tissue expanders. The black point represents the infection rates used in this study.

Table 5. One-way Sensitivity Analysis for Number of In-office Expansions Obviated with AeroForm

New Consults*	Total Expected Aeroform Cost* ($)	Cost Difference ($)	ICUR ($/QALY)
0	3,385.35	175.18	143,101.06
0.5	3,299.65	89.49	73,100.58
1	3,213.96	3.8	3,100.39
1.5	3,128.27	−81.9	−66,900.39
2	3,042.57	−167.59	−136,900.87
2.5	2,956.88	−253.29	−206,901.36
3	2,871.18	−338.98	−276,901.84

*Based on average reimbursement for CPT codes 99201-99205. At-home expansion eliminates all but first (initial postoperative follow-up) and last (second-stage preoperative) clinic visits, for a total reduction of 0–6 follow-up appointments, allowing for up to 3 new patient consults during that time. Bold values are below our predetermined threshold of $50,000 per QALY gained.

of women undergoing breast reconstruction with 2-stage implant-based breast reconstruction.

Cost-utility analysis relies on parameters abstracted from the best available data; therefore, this study has several limitations. The studies upon which probability parameters were based for AeroForm included 4 prospective cohort studies, 1 randomized control trial, and 1 retrospective cohort study for a total of 458 patients. The probability parameters for saline tissue expanders were derived from a meta-analysis which included several types of studies and a total of 14,947 patients. Meta-analyses are prone to inherent limitations associated with pooling data gathered from sources with varied methodology which affects the accuracy of probability estimates. A prospective randomized trial evaluating the efficacy of AeroForm tissue expanders would have provided more accurate complication rates than relying on meta-analyses and other heterogenous studies. Nonetheless, 1- and 2-way sensitivity analyses demonstrated the reproducibility of our findings over a wide range of clinically relevant infection rates with both AeroForm and traditional saline tissue expanders. Another limitation of this study was the use of a nonvalidated survey of 10 academic plastic surgeons with a focus on breast reconstruction randomly selected from the American Society of Plastic Surgeons website. The use of a nonvalidated instrument may have influenced the utility ratings. In addition, cost estimates were based on the perspective of a third-party payer because it is difficult to estimate the productivity costs of surgical site infection to adopt a societal perspective. Neglecting the indirect costs of clinic space utilization in the model may have underestimated the true costs of saline expander use in this model. It is likely that incorporating this would have further emphasized the fiscal benefit of AeroForm tissue expanders, because the clinical time and space dedicated to expander inflation can be instead utilized for revenue-generating activities such as cosmetic injectables or new patient consultations. Finally, this model did not consider the effect of AeroForm tissue expanders on complications other than surgical site infection. The incidence of noninfectious complications has not been demonstrated to vary significantly between AeroForm and traditional saline implants.[9–14]

CONCLUSIONS

It is important to consider novel interventions within an economic context because of the key role that economic considerations play in the assessment and adoption of new medical technology. This cost-utility analysis demonstrates that the use of AeroForm tissue expanders is likely a cost-saving technology for 2-stage implant-based breast reconstruction. This device, when employed in the prepectoral space, may be associated with reduced infection rates and decreased utilization of health care and patient resources.

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