The Cutaneous, Net Clinical, and Health Economic Benefits of Advanced Pneumatic Compression Devices in Patients With Lymphedema

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IMPORTANCE The prevalence and clinical burden of lymphedema is known to be increasing. Nevertheless, evidence-based comparative effectiveness data regarding lymphedema therapeutic interventions have been poor.

OBJECTIVE To examine the impact of an advanced pneumatic compression device (APCD) on cutaneous and other clinical outcomes and health economic costs in a representative privately insured population of lymphedema patients.

DESIGN, SETTING, AND PARTICIPANTS Retrospective analysis of a deidentified private insurance database from 2007 through 2013, and multivariate regression analysis comparing outcomes for the 12 months before and after APCD purchase, adjusting for baseline patient characteristics. Patients with lymphedema who received an APCD who were commercially insured and Medicare managed care enrollees from a large, national US managed care health insurer. The study population was evaluated as cancer-related and non–cancer-related lymphedema cohorts.

INTERVENTION Receipt of an APCD.

MAIN OUTCOMES AND MEASURES Rates of cellulitis, use of lymphedema-related manual therapy, outpatient hospital visits, and inpatient hospitalizations. Lymphedema-related direct costs were measured for home health care, hospital outpatient care, office visits, emergency department use, and inpatient care.

RESULTS The study sample included 718 patients (374 in the cancer cohort and 344 in the noncancer cohort). In both cohorts, use of an APCD was associated with similar reductions in adjusted rates of cellulitis episodes (from 21.1% to 4.5% in the cancer cohort and 28.8% to 7.3% in the noncancer cohort; P < .001 for both), lymphedema-related manual therapy (from 35.6% to 24.9% in the cancer cohort and 32.3% to 21.2% in the noncancer cohort; P < .001 for both), and outpatient visits (from 58.6% to 41.4% in the cancer cohort and 52.6% to 31.4% in the noncancer cohort; P < .001 for both). Among the cancer cohort, total lymphedema-related costs per patient, excluding medical equipment costs, were reduced by 37% (from $2597 to $1642, P = .002). The corresponding decline in costs for the noncancer cohort was 36% (from $2937 to $1883, P = .007).

CONCLUSIONS AND RELEVANCE The study found an association between significant reductions in episodes of cellulitis (cancer vs noncancer cohorts) and outpatient care and costs of APCD acquisition within a 1-year time frame in patients with both cancer-related and non–cancer-related lymphedema.

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Secondary lymphedema affects an estimated 2 to 3 million people in the United States.1,2 Interstitial lymph accumulation contributes to loss of skin integrity, irreversible collagen deposition and induration, and cellulitis.3,4 Lymphedema is characterized by the abnormal accumulation of fluid in tissues that is associated with edema, recurrent cellulitis, loss of physical function, and psychological distress with diminished quality of life.5,7 Lymphedema cannot be cured, but the establishment of the diagnosis and initiation of targeted therapies by dermatologists who frequently care for the patients with cellulitis can ameliorate the effect and progression of the disease.8,9 Antibiotic therapies are useful to modify the risk of a first episode of cellulitis, but patients remain at heightened risk for recurrent cellulitis and/or systemic infection. Lymphedema-related cellulitis is common, functionally important, and dangerous. It thus represents a critically important health endpoint that merits focused study in population-based lymphedema research.

In the absence of a robust comparative effectiveness evidence base, the current standard of lymphedema care is the labor-intensive multimodal approach known as combined decongestive therapy.9 The components of combined decongestive therapy include professionally administered manual lymph drainage, multilayer bandaging, decongestive exercise, skin care, and education in long-term lymphedema self-management. Adjunctive treatment modalities such as use of a pneumatic compression device (PCD) provide additional, and possibly more effective, management options. Pneumatic compression devices have been shown to be effective physiologically, as they improve lymphatic function and lymph flow10 and reduce edema volume,11-16 and clinically, as they improve patient-reported symptoms and quality of life.11,16 Yet, despite the recent expansion of the efficacy evidence base, PCD effectiveness data derived from real-world settings has been sparse.

The measurement of effectiveness, representing a measure of the clinical benefit of a therapy in a general population, is widely considered to represent a key evidentiary gold standard.17 Lymphedema therapeutic effectiveness has been demonstrated in patients with cancer, inasmuch as PCD use has been associated with significant decreases in rates of cellulitis diagnoses, outpatient services, and hospitalization.5 Average baseline health care costs were high but decreased significantly in the year after receipt of a PCD. However, that study did not evaluate the relative benefit of the various types of PCDs currently available, nor did it evaluate the outcomes in individuals with non-cancer-related lymphedema.

The most advanced PCD is a device designed for home use that delivers external pneumatic compression through multiple inflatable compartments and uses a calibrated, gradient compressor. These advanced PCDs (APCDs) have more garment chambers than earlier, less advanced devices, and provide a greater level of adjustability and programmability, providing potential individuated treatment advantages.

In this study, we measured the effectiveness of an APCD on cutaneous and systemic clinical outcomes, as well as associated health economic costs within a representative privately insured population of lymphedema patients. This study was designed to evaluate patients with both cancer- and non-cancer-related lymphedema who were prescribed and received an APCD.

Methods

Setting and Data Source

This study was performed using a deidentified Normative Health Information (dNHI) database that included patient claims information from January 1, 2007, through November 30, 2013. The institutional review board of University of Minnesota waived the need for ethical approval and patient informed consent for our retrospective analysis. The dNHI includes over 34 million individuals each year, including both commercially insured and Medicare managed care enrollees from a large, national US managed care health insurer affiliated with Optum Inc (Eden Prairie, Minnesota). The enrollment database includes a geographically diverse US population with similar age and sex distribution to that reported by the US Census Bureau for the commercially insured and the Medicare managed care population.

The dNHI contains enrollment data as well as medical and pharmacy claims data. Medical (facility and professional) claims incorporate diagnosis codes recorded with International Classification of Disease, Ninth Edition, Clinical Modification (ICD-9-CM), procedures recorded with ICD-9-CM procedure codes, Current Procedural Terminology (CPT) codes, or Healthcare Common Procedure Coding System and revenue codes. No identifiable protected health information was accessed during this study, and deidentified data were accessed in accordance with the Health Insurance Portability and Accountability Act.

Study Population

Patients were identified by the presence of a claim for a PCD, identified with HCPCS code E0652 (pneumatic compressor, segmental home model with calibrated gradient pressure) or E0651 (pneumatic compressor, segmental home model without calibrated gradient pressure) from January 1, 2008, through November 30, 2012 (n = 21 104). To identify health care service use and other outcomes, both before and after acquisition of the PCD, patients were required to have continuous enrollment in the health plan with medical and pharmacy benefits for 12 months before and 12 months after the first claim date for the PCD (index date) (n = 6760). To ensure correct identification of a first exposure to PCD use, patients were excluded if they had a claim for a PCD during the preindex period (n = 6702). Finally, to identify patients with a lymphedema diagnosis, the study sample was restricted to individuals with at least 1 claim with a primary or secondary diagnosis code for lymphedema during the 12 months prior to receiving the PCD (n = 3415). Of these patients, 718 acquired the target APCD device and therefore were assigned to the study sample. The total treatment population was then subdivided into cancer and noncancer cohorts.

A cohort of cancer-related lymphedema patients was distinguished a priori in the study sample. Patients were identified as having cancer-related lymphedema if they had...
Advanced PCD Intervention
This study was designed to evaluate the impact of a specific APCD on lymphedema-related cellulitis and systemic clinical and health care cost outcomes in individuals with lymphedema. The APCD used for this analysis was the Flexitouch System (Tactile Medical HCPCS E0652). This device was selected for the relatively robust data from earlier investigations that define both physiologic mechanisms and specific clinical outcomes associated with measurable efficacy, thus offering the possibility to evaluate this potential efficacy in a national insured population. In addition, because the manufacturer is also the provider submitting the insurance claims, it was uniquely feasible to cross-match provider details with device codes to evaluate this single intervention.

Patient Demographic and Clinical Characteristics
The dNHI database included information on patient demographic and socioeconomic characteristics, such as age, sex, race/ethnicity (non-Hispanic Asian, non-Hispanic black, non-Hispanic white, Hispanic, unknown), census region, type of insurance (commercial or Medicare), and average income. In addition, we identified comorbid conditions during the 12 months prior to receipt of the device (baseline). The presence of obesity, diabetes, hypertension, or renal disease was identified through the relevant ICD-9-CM and CPT and/or HCPCS codes in the medical claims. For the cancer cohort, we identified the types of baseline cancer (described above). Finally, we computed the baseline Charlson comorbidity score.

Clinical and Health Care Use Outcomes
A broad, clinically relevant set of health care use outcomes were then evaluated for each patient for the 12 months before and after APCD receipt. Cellulitis infections were identified as the number of medical claims with ICD-9-CM diagnosis codes 457.0, 457.1, or 757.0 during at least 12 months prior to the receipt of the APCD (n = 374). These codes include cancers of the breast; bone, connective tissue, or skin; digestive organs and peritoneum; genitourinary organs; lip, oral cavity, and pharynx; lymphatic and hematopoietic tissue; neuroendocrine tumor; respiratory and intrathoracic organs; and other unspecified sites. Patients whose claim history did not include such cancer codes were designated in the noncancer cohort (n = 344).

Statistical Analysis
The final analytic extract included 2 observations for each individual. The first observation corresponded to data obtained during the 12 months prior to the index date, defined as the first claim date at which the APCD was acquired (baseline). The second observation corresponded to the 12-month data obtained after the index date (follow-up). We used a multivariate regression analysis to estimate and compare the clinical and cost outcomes per patient in the baseline period with the corresponding outcomes in the follow-up period, adjusting for the baseline patient demographic, clinical, and socioeconomic characteristics.

For binary outcome variables (cellulitis, inpatient hospitalizations, use of manual therapy, and outpatient visits), we estimated logistic models. For continuous cost outcomes, we estimated ordinary linear regressions. For each outcome, we estimated adjusted outcomes for the pre-APCD period, the follow-up period, and the difference. We allowed the differences in outcomes from baseline to follow-up to vary by patients in the cancer and noncancer cohorts. We conducted 2-tailed t tests to test whether the changes in outcomes from baseline to follow-up differed between cancer and noncancer patients. We reported Huber/White robust standard errors. All analyses were conducted using STATA version 12 (STATA Corp).

Results
We evaluated a cohort of 718 lymphedema patients, 374 in the cancer cohort and 344 in the noncancer cohort. Table 1 presents the demographic and clinical characteristics of this population. The sample included a representative, age-stratified set of lymphedema patients (142 [19.8%] aged 19–44 years; 439 [61.1%] aged 45–64 years; and 132 [18.4%] 65 years or older). Most patients were female (344 [92.0%] in the cancer cohort; 265 [77.0%] noncancer cohort). Hypertension was present in 180 (48.1%) of the cancer cohort and 195 (56.7%) of the noncancer cohort. Obesity and diabetes were also common, but more so in the noncancer cohort (obesity, 43 [11.5%] of the cancer cohort and 131 [38.1%] of the noncancer cohort; diabetes, 57 [15.2%] of the cancer cohort and 95 [27.6%] of the noncancer cohort). In the cancer cohort, the most prevalent health care sites for each patient for the 12-month period preceding and following APCD receipt. The settings included home health care and hospital outpatient, inpatient, and emergency department visits, with separate aggregation of durable medical equipment, laboratory, and pharmacy expenses. Outpatient costs were separated among cellulitis, manual therapy claims (claims that included a PT/OT therapy CPT code), and any other service provided in the hospital outpatient setting. Total costs were calculated as the sum of payment by the health plan and beneficiary, facility payments, and professional service fees. Analogously to clinical outcomes determinations, lymphedema-related costs were identified based on associated primary or secondary ICD-9-CM codes for lymphedema.
malignancy was breast cancer (284 [75.9%]) followed by cancer of the bone, connective tissue, or skin (51 [13.6%]) and genitourinary organ cancers (49 [13.1%]). Not surprisingly, the Charlson comorbidity index was higher in the cancer cohort than the noncancer cohort (4.3 vs 1.3, \( P < .001 \)).

Clinical Outcomes and Lymphedema-Related Health Care Use Table 2 presents lymphedema-related clinical and health care use outcomes adjusted for the differential patient baseline characteristics listed in Table 1 for the cancer and noncancer cohorts. Receipt of the APCD was associated with a significant decline in the rate of cellulitis diagnoses in the cancer group (21.1% to 4.5%; \( P < .001 \)), corresponding to a 79% decline of these limb infections. In the noncancer group, the rates of cellulitis declined from 28.8% to 7.3% (\( P < .001 \)), corresponding to a decline of 75%. For this cohort, there were also significant reductions in the inpatient hospitalization rate (from 7.0% to 3.2% [\( P = .02 \)], representing a 54% decline).

In the cancer cohort, a rate of 35.6% received manual therapy services during the baseline period. During the follow-up period, the rate of manual therapy declined to 24.9% (\( P = .001 \)), representing a decline of 30%. Similarly, the rate of outpatient visits declined from 58.6% to 41.4% (\( P = .001 \)), representing a 29% reduction. Inpatient care was relatively infrequent both in the baseline and the follow-up periods (2.7% and 2.1%, respectively; \( P = .63 \)).
Similar reductions in the adjusted rates of lymphedema-related health care use were observed during the follow-up period for the noncancer cohort. The rates of manual therapy decreased from 32.3% to 21.2% (P = .001), representing a 34% decline, and the rate of outpatient hospital visits decreased from 52.6% to 31.4% (P < .001), a 40% decline. As noted in Table 2, the changes in outcomes between baseline and the follow-up period were similar in magnitude between the cancer and noncancer cohorts.

### Lymphedema-Related Health Care Costs

Table 3 presents lymphedema-related costs, adjusted for the patient baseline characteristics listed in Table 1, for the cancer and noncancer cohorts. Among the cancer cohort, total
costs per patient, excluding medical equipment costs, were reduced by 37% from $2597 to $1642 (P = .002). The greatest contributor to this change was a reduction in outpatient hospital costs from $1517 to $694 (P < .001), a 54% reduction. Among the hospital outpatient costs, PT/OT-related outpatient costs declined about 50% from $287 to $145 (P = .03). Office visit costs also declined by 42% from $468 to $274 (P = .01).

Cost reductions were similar in magnitude for the non-cancer cohort. Total costs, excluding durable medical equipment, reduced by 36% from $2937 during the baseline period to $1883 during the follow-up period (P = .007). Outpatient hospital costs declined by 65% from $1726 to $606 (P < .001). Outpatient hospital costs related to PT/OT halved from $332 to $169 (P = .047). As noted in Table 3, the changes between the baseline and follow-up periods were not significantly different between the cohorts with the exception of other durable medical equipment costs.

Discussion

Our study demonstrates, for the first time to our knowledge, that receipt of an APCD is associated with significant improvements in key clinical endpoints that are central to defining the health of individuals with lymphedema, without regard to specific etiology. The decrease in rates of cellulitis by 79% and 75% in the cancer-related and non–cancer-related cohorts represent a major direct health benefit to all classes of affected patients. As lymphedema is known to serve as the most potent predictor of recurrent cellulitis, raising this risk 9-fold, the benefit observed in the current study verifies that the high risk is lowered by APCD acquisition and use.24

These lower rates of cellulitis are associated with major health service and economic benefits. Individuals with lymphedema, whether cancer-related or not, with higher rates of cellulitis require more intensive outpatient care in rehabilitative settings (eg, by dermatologists, physical therapists, and primary care clinicians), and they may need inpatient hospitalization to treat skin or systemic infection or other complications. Each of these episodes of care, whether designed to prevent adverse events, to improve quality of life (PT/OT), or to treat a systemic adverse event (hospitalization), impairs independence and contributes to high health care expenditures.

As in all administrative data studies, this investigation has limitations. The use of claims data assumes that coding is accurate. The exact clinical circumstances for each health encounter cannot be specifically deduced. We also are not able to account for the degree of device use. Finally, it is not methodologically feasible for a control group of individuals with lymphedema, but no APCD use, to be accurately identified and for unmatched comorbidities to be sufficiently identified to provide an accurate comparison of outcomes. Thus, it cannot be known if use of other support garments or antibiotics differed between groups.

Despite these limitations, our study provides definitive evidence that APCD acquisition is associated with improved clinical outcomes and immediate cost reductions. Our study was not designed to forecast cost reductions beyond the 12-month period after the purchase of the APCD, but cost reductions were achieved primarily through reductions in outpatient and office visits that are likely to persist throughout the duration of the disease.

It is also important to note that the cost reductions that we observed likely represent a lower bound in overall cost reductions associated with such device use. As APCD use compliance cannot be measured from these administrative data sources, and as it is known that compliance directly affects clinical efficacy, these outcome data likely include individual benefits offered device use but for whom high compliance and maximal benefit was not achieved. While our study focused only on health care use and costs based on claims coded with a lymphedema diagnosis, it is likely that other types of health care use are similarly affected. For example, in additional analyses, we found reductions in cellulitis rates, not coded as lymphedema related, in patients with lymphedema; it is likely that these reductions were also due to device-mediated improvements and that a biological relationship existed. In addition, direct health care costs represent a fraction of the overall costs related to the lymphedema burden. To the extent that APCD use improves physical functioning and quality of life, cost reductions owing to improved productivity, lower caretaker costs, and reductions in other nonmonetary costs are likely significant.

The potential public health implications of our findings are substantial. Episodes of cellulitis are often not counted as a key public health hazard, but they represent, for patients with lymphedema, a hallmark event, associated with morbidity and cost, that can be prevented. Lymphedema is a common, chronic cardiovascular disease that contributes to the public health burden. The availability of effective home-based therapeutic interventions can serve individual patients and reduce this burden. While our findings are based on the outcomes from a specific device, it is possible other such devices may also reduce patient burden. This warrants explorations in future studies.

Conclusions

This study demonstrates the clinical and economic effectiveness of a common adjunctive lymphedema treatment modality, APCDs, which is associated with a decrease in episodes of cellulitis. These data also demonstrate other key treatment benefits that improve individual and population health, with an associated cost reduction. Thus, dermatologists, primary care and vascular physicians, and therapists may use PCD therapy to improve skin, limb, and systemic health.

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Conflict of Interest Disclosures: Dr Hirsch serves as Chief Medical Officer of Tactile Medical, a company that manufactures a product used to treat lymphedema. Dr Karaca-Mandic received consultative reimbursement from Tactile Medical for her independent performance of the health economic analyses. These relationships have been reviewed and managed by the University of Minnesota in accordance with its Conflict of Interest policies. No other disclosures are reported.

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