



Hypothyroidism increases 90-day postoperative complications in patients undergoing primary single level anterior cervical disectomy and fusion: a matched control analysis

Rushabh M. Vakharia¹, Ajit M. Vakharia², Bijan Ameri³, Timothy Niedzielak³, Chester J. Donnally III⁴, John P. Malloy IV⁵

¹Holy Cross Hospital, Orthopedic Research Institute, Ft. Lauderdale, FL, USA; ²Morehouse School of Medicine, Atlanta, GA, USA; ³Broward General Medical Center, Department of Orthopedic Surgery, Ft. Lauderdale, FL, USA; ⁴University of Miami Hospital, Department of Orthopaedic Surgery, Miami, FL, USA; ⁵East Coast Orthopaedics, Pompano Beach, FL, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Rushabh M. Vakharia. Holy Cross Hospital, Orthopedic Research Institute, 5597 North Dixie Highway, Ft. Lauderdale, FL 33308, USA. Email: Rush.Vakharia@Gmail.com.

Background: Anterior cervical disectomy and fusion (ACDF) is indicated for patients suffering from cervical radiculopathy, myelopathy, and degenerative disc disease, among other diseases. There is paucity in the literature regarding postoperative complications in patients undergoing primary ACDF with a diagnosis of hypothyroidism. The purpose of this study is to compare 90-day postoperative complications in patients with and without hypothyroidism undergoing primary ACDF.

Methods: A retrospective analysis was completed using a national administrative database known as Pearl Diver (Pearl Diver Technologies, Fort Wayne, Indiana) using the International Classification of Disease, ninth revision (ICD-9) codes. The study group consisted of patients having undergone ACDF with an active diagnosis of hypothyroidism 90 days prior to and on the day of surgery. Patients undergoing primary ACDF without hypothyroidism served as the control group. Patients in both groups were randomly matched according to age, gender, and Charlson-Comorbidity Index (CCI). The 90-day postoperative medical complications were assessed along with readmission rates and total cost of care.

Results: There were a total of 107,066 patients equally divided between the 2 cohorts. Patients with hypothyroidism had greater odds of developing complications such as non-healing surgical wound (OR: 2.27; P<0.001), pulmonary embolus (OR: 2.16; P<0.001), myocardial infarction (OR: 2.10; P<0.001), compared to patients in the control group after undergoing primary ACDF. Readmission rates were also higher in patients with hypothyroidism (OR: 1.45; P<0.001). Total cost of care was also greater in patients with hypothyroidism compared to patients without hypothyroidism undergoing primary ACDF.

Conclusions: Hypothyroidism is a risk factor for worse postoperative outcomes in patients undergoing primary ACDF. Appropriate preoperative optimization with thyroid hormone supplementation could potentially minimize the incidence of developing numerous medical complications, in addition to potentially lowering readmission rates and the total cost of care.

Keywords: Anterior cervical disectomy and fusion (ACDF); hypothyroidism; Medicare; degenerative disc disorder; readmission

Submitted Mar 18, 2018. Accepted for publication May 25, 2018.

doi: 10.21037/jss.2018.05.26

View this article at: <http://dx.doi.org/10.21037/jss.2018.05.26>

Introduction

Anterior cervical discectomy and fusion (ACDF) is a proposed treatment for patients suffering from cervical radiculopathy or myelopathy (1). Current data trends have revealed that from 2006–2014 there were 1,059,403 primary ACDF procedures performed in the United States (2,3). In a national trends study performed by Marawar *et al.*, there was almost an 8-fold increase in utilization of ACDF in the population (23/100,000 civilians to 157/100,000 civilians) over a 15-year period, from 1990–2004 (4). These trends were also seen by looking at the annual rates of ACDF performed in the Medicare population (*Figure 1*). The calculated annual growth rate (CAGR) was found to be 4.14% from 2005–2014 for primary ACDF procedures performed in the Medicare population. Despite the positive outcomes following this procedure, as with any surgical procedure, postoperative complications are inevitable.

The goal of any surgical planning should include identification of preoperative risk factors to reduce peri- and postoperative complications (5). Commonly known risk factors include: increasing age, high body mass index (BMI), tobacco usage, poor nutritional status, chronic obstructive pulmonary disease (COPD), illicit drug use, and poor nutritional status (6). Endocrinopathies such as diabetes and thyroid dysfunction can impact recovery following surgery (7,8). In a recent study by Rodondi *et al.* in 2005, the prevalence of the hypothyroidism was found to be 12.4% (8). This highlights how the prevalence of hypothyroidism has increased nearly 300% from 1988–2005. In this study, the prevalence of hypothyroidism was found to be 23.5% within the Medicare population.

Although the prevalence of patients undergoing primary ACDF and hypothyroid diagnoses are both increasing, the effect of hypothyroidism on postoperative complications in patients undergoing primary single-level ACDF is not well understood. The purpose of this study was to determine whether patients with hypothyroidism are at greater odds of: (I) developing 90-day medical complications; (II) 90-day readmission rates; and (III) incur greater total global 90-day episode of care costs compared to patients without hypothyroidism. We hypothesize that the patients with clinical hypothyroidism are at increased odds of developing postoperative complications than those patients without hypothyroidism, in addition to higher 90-day readmission rates and greater reimbursement rates.

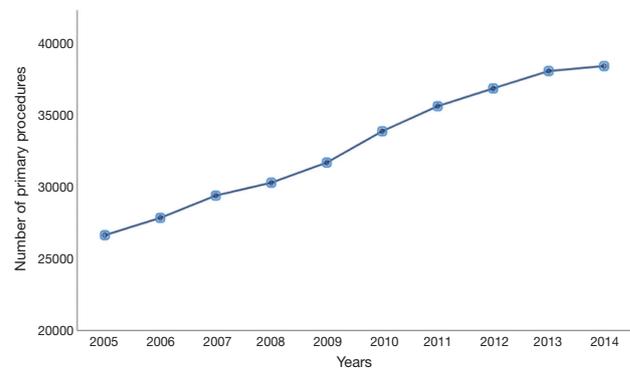


Figure 1 Annual trends of Anterior Cervical Discectomy and Fusion (ACDF) in the Medicare population from 2005–2014.

Methods

A retrospective review from 2005–2014, was performed using the Medicare Standard Analytical Files from the Pearl Diver supercomputer (Pearl Diver Technologies, Fort Wayne, IN). Pearl Diver is compliant with the Health Information Portability and Affordability Act (HIPAA) and contains the records of over 100 million patients. The database allows institutions information such as diagnosis, procedures, length of stay, charges, reimbursements, and complications. Patients were queried using the International Classification of Disease, ninth revision (ICD-9) codes.

The inclusion criteria included all patients who underwent primary ACDF using the ICD-9 procedure code 81.02. All patients in the database with a prior diagnosis of hypothyroidism and diagnosis on the day of their ACDF were queried, and served as the study group. All patients without a diagnosis of hypothyroidism undergoing an ACDF served as the control group. Patients in the study group were randomly matched to patients in the control group with respect to age, gender, and Charlson-Comorbidity Index (CCI). CCI, a measurement of morbidity and mortality risk associated with worse outcomes following orthopedic surgery, was the parameter used to determine the similarity between the study group and control group (7). After the matching process, two mutually exclusive cohorts were formed and were followed for 90 days to determine the incidence of complications between both groups. Complications within the 90-day postoperative period were examined as hospitals are held accountable during this period for all Medicare payments per the Comprehensive Care for Joint Replacement (CJR)

Table 1 Demographic breakdown by age, gender, and Charlson-Comorbidity Index (CCI) in patients with and without hypothyroidism undergoing primary ACDF in the medicare population

Demographics	Distribution	P value
Age (years)		
≤64	20,337 (38.0%)	
65–69	17,498 (32.7%)	
70–74	8,250 (15.4%)	
75–79	4,459 (8.3%)	
80–84	1,902 (3.6%)	
≥85	534 (1.0%)	
Unknown	553 (1.0%)	
Gender		
Female	38,895 (72.6%)	
Male	14,085 (26.3%)	
Unknown	553 (1.0%)	
CCI*	5.45±2.65	1.00

*, compared to the control group. ACDF, anterior cervical discectomy and fusion; CCI, Charlson-Comorbidity Index.

model (9). Excluding readmission rates for physical and occupational therapy, an adjusted relative risk (aRR) was calculated for readmission rates. Cost of care on the day of surgery along with 90-day cost of care was also compared between the cohorts.

Descriptive and statistical analyses was performed using the programming language R (University of Auckland, New Zealand). Univariate analysis with the use of odds ratios (OR), along with their respective 95% confidence interval (95% CI), and P values were used in our study. Significance was defined as $P < 0.05$.

Results

After the matching process, 107,066 patients met the inclusion criteria and were, split into those with hypothyroidism ($n=53,533$) and those without ($n=53,533$) the diagnosis (Table 1). CCI between the study group and control group was 5.45 ± 2.65 with a P value of 1.00 indicating no difference between the groups. Patients with hypothyroidism undergoing ACDF were found to have greater total odds and incidence of postoperative complications than euthyroid patients 90 days following primary ACDF

(2.75% vs. 1.61%; OR: 1.72; 95% CI: 1.58–1.87; $P < 0.001$) (Table 2). Hypothyroid patients had greater odds of developing a non-healing surgical wound (NHSW) (OR: 2.27; 95% CI: 1.11–4.62; $P=0.0232$), pulmonary embolism (OR: 2.16; 95% CI: 1.51–3.09; $P < 0.001$), and hemorrhage (OR: 2.14; 95% CI: 1.36–3.35; $P < 0.001$) compared to patients without hypothyroidism.

Readmission rates for hypothyroid patients were higher than the control group at each of the time intervals examined (Table 3). Patients with hypothyroidism had greater total odds and incidence (20.61% vs. 14.15%; OR: 1.45; 95% CI: 1.41–1.49; $P < 0.001$) of readmission rates within the first 90 days following primary ACDF, compared to patients in the control group. Cost of care in patients with hypothyroidism was found to be statistically greater day of surgery (\$75,044.06 vs. \$66,948.35, $P < 0.001$), 30-day (\$80,887.25 vs. \$70,374.41, $P < 0.001$), 60-day (\$85,442.97 vs. \$73,095.65, $P < 0.001$), and 90-day (\$90,020.98 vs. \$76,363.64, $P < 0.001$) compared to patients without hypothyroidism undergoing primary ACDF (Table 4).

Discussion

ACDF is commonly indicated for patients suffering from cervical radiculopathy that has not resolved from conservative treatment with nonsteroidal anti-inflammatory drugs, physical therapy, or injection of cervical corticosteroids. Annual trends show the number of ACDF procedures being performed each year are increasing, as is the incidence of hypothyroidism (2,3). This study illustrates hypothyroidism as a modifiable risk factor for decreasing postoperative complications following primary ACDF, and is consistent with the current literature citing the significance of hypothyroidism on postoperative outcomes (10-14).

A database study utilizing the National Hospital Discharge Survey (NHDS) performed by Danescu *et al.* found that patients 60 years and older with hypothyroidism had a greater relative risk (RR) of DVT (RR: 2.23; 95% CI: 2.22–2.25) and PE (RR: 1.94; 95% CI: 1.92–1.96) compared to the control population (15). This finding is consistent with the findings of our study. Müller *et al.* found that 42 patients with hypothyroidism had higher levels of von Willebrand factor compared to patients in his control group (16). Another study performed by Cantürk *et al.* found patients with hypothyroidism presented with elevated levels of fibrinogen, factor VII, plasminogen activating inhibitor-1 (PAI-1), and decreased anti-thrombin III levels, which are associated with the development of thromboembolic

Table 2 Comparison of 90-day medical complications in patients with and without hypothyroidism undergoing primary ACDF within the medicare population

Complications	Hypothyroid (%)	Control (%)	OR	95% CI	P value
NHSW	0.46	0.21	2.27	1.11–4.62	0.0232
PE	0.17	0.08	2.16	1.51–3.09	<0.001
Hemorrhage	0.11	0.52	2.14	1.36–3.35	<0.001
MI	0.15	0.07	2.10	1.43–3.08	<0.001
Hematoma	0.32	0.16	2.03	1.57–2.63	<0.001
Dysphagia	0.35	0.18	1.96	1.53–2.51	<0.001
Wound	0.13	0.07	1.86	1.25–2.78	0.0022
DVT	0.19	0.11	1.81	1.32–2.49	<0.001
Infection	0.44	0.25	1.72	1.39–2.13	<0.001
VCP	0.07	0.05	1.50	0.91–2.46	0.1092
UVCP (partial)	0.07	0.04	1.45	0.86–2.45	0.1544
UVCP (complete)	0.03	0.02	1.33	0.63–2.81	0.4512
Seroma	0.13	0.97	1.32	0.92–1.90	0.1233
OMCI	0.25	0.21	1.22	0.95–1.57	0.1119
ACDF Revision	0.17	0.15	1.14	0.85–1.54	0.3630
CNS complications	0.02	N/A	N/A	N/A	N/A
Pseudarthrosis	0.02	N/A	N/A	N/A	N/A
Total	2.75	1.61	1.72	1.58–1.87	<0.001

ACDF, anterior cervical discectomy and fusion; NHSW, non-healing surgical wound; PE, pulmonary embolism; MI, myocardial infarction; VCP, vocal cord paralysis; UVCP, unilateral vocal cord paralysis; OMCI, other mechanical complications related to the implant; CNS, central nervous system.

Table 3 Adjusted relative risk (aRR) and readmission rates in patients with hypothyroidism undergoing primary anterior cervical discectomy and fusion (ACDF) within the Medicare population

Time interval	Hypothyroid (%)	Control (%)	aRR	95% CI	P value
30 days	4.34	2.77	1.56	1.46–1.66	<0.001
60 days	6.22	3.94	1.57	1.49–1.66	<0.001
90 days	10.04	7.43	1.66	1.59–1.72	<0.001
Total	20.61	14.15	1.45	1.41–1.49	<0.001

and atherosclerotic events (17). In a recent study of 214 patients, Tang *et al.* found that preoperative expression of PAI-1 was a risk factor for the development of DVTs in patients following total hip arthroplasty (OR: 1.18; 95% CI: 1.04–1.29; P=0.011) (18). Müller *et al.* discovered that supplementation of thyroid hormone decreased levels of factor VIII and PAI-1, thus reducing the incidence of

DVTs in patients; suggestive that thyroid hormones within reference range have a protective effect against development of DVTs (16). Hypothyroidism is also associated with elevated levels of C-reactive protein (CRP) and triglyceride levels, both of which have been shown to increase the risk of DVT (16–18).

Furthermore, wound and infection rates were also higher

Table 4 Average charges and reimbursements with standard deviation (SD) at day of surgery, 30-, 60-, and 90-days after primary anterior cervical discectomy and fusion (ACDF)

Time interval	Hypothyroid	Control	P value
Day of surgery			
Charges (SD)	\$75,044.06 (\$85,895.12)	\$66,948.35 (\$74,055.58)	<0.001
Reimbursement (SD)	\$18,551.25 (\$18,244.45)	\$16,676.71 (\$17,682.04)	<0.001
30-day cost			
Charges (SD)	\$80,887.25 (\$94,147.68)	\$70,374.41 (\$80,070.82)	<0.001
Reimbursements (SD)	\$20,307.87 (\$20,827.09)	\$17,728.39 (\$19,506.44)	<0.001
60-day cost			
Charges (SD)	\$85,442.97 (\$103,895.13)	\$73,095.65 (\$87,075.54)	<0.001
Reimbursements (SD)	\$21,351.27 (\$23,188.11)	\$18,371.87 (\$21,190.25)	<0.001
90-day costs			
Charges (SD)	\$90,020.98 (\$111,932.50)	\$76,363.64 (\$94,582.83)	<0.001
Reimbursements (SD)	\$22,303.00 (\$24,847.34)	\$19,099.75 (\$22,790.48)	<0.001

in the study cohort compared to the control group. In a recent animal study, total thyroidectomy performed on rats was done followed by midline abdominal incisions and of suturing the wound (19). Assays of rats with hypothyroidism had decreased type-IV collagen and hydroxyproline during the proliferative phase of wound healing (20). Oral triiodothyronine (T_3) and thyroxine (T_4) have been shown to promote wound healing and improve quality of wounds and increase tensile strength (21,22). Thyroid hormones have been shown to have a protective effect on the epidermal and dermal layers following surgery, by accelerating barrier formation by serving as a catalyst for enzymes in cholesterol sulfate cycle, and hypothyroidism may hinder the epidermal barrier function (22,23). Hypothyroidism also affects synthesis of lamellar granules known as Odland bodies, vital for establishment of normal stratum corneum. In tissue culture studies, triiodothyronine has been shown to directly stimulate proliferation of both epidermal keratinocytes and dermal fibroblasts. Tan *et al.* found hypothyroidism to be a modifiable condition, which predisposed patients undergoing primary total joint arthroplasty to infections (24). In their study, the microorganism profile most commonly affecting their study population was vancomycin-resistant *Enterococcus*, methicillin-resistant *Staphylococcus Aureus*, and coagulase-negative *Staphylococcus Aureus* (24).

Finally, this study demonstrates that hypothyroid patients ensue higher day of care, 30-, 60-, and 90-day

costs (Table 4). Secondary to the results of this study, it can easily be implied that these higher costs are related to increased complication rates in this population. Dasta *et al.* calculated that patients with DVT and PE incurred an additional charge of \$1,594 and \$1,735 per hospitalization day, respectively. Depending on the degree of the severity, patients with DVT or PE required more expensive care compared to patients without these complications (25). Moreover, surgical site infections (SSI) were also higher in our study group and recent studies show that patients with SSI incurred an additional charge of \$52,620 compared to patients without SSI (26). In this study, patients with hypothyroidism had an excess charge of \$13,657.34±\$17,349.67 within 90 days of their procedure, compared to their counterparts (Table 4).

As most large database studies, this review relies heavily on accurate procedural and diagnosis coding, translating to the fact that miscoding and noncoding by providers is a potential source of error. Currently, it is estimated that 1.3% of coding errors are present within the Medicare population (27). Additionally, the study only looked at a single insurer's database, and may not be an accurate representation of patients with hypothyroidism in the United States. Moreover, a selection bias may be present as patients in the study may enter or exit the database as a natural manifestation (28). Lastly, patients undergoing multilevel ACDF are prone to greater complications compared to a single level, however due to the nature of our

study it was not possible for us to numerically differentiate the number of levels operated on, as there is not a different ICD-9 code for multilevel ACDF (1,29).

Conclusions

Various studies have highlighted the increasing prevalence of hypothyroidism, which has been shown to increase in incidence as patients' age. Concurrently, rates of primary ACDF are also increasing within the general population. This study highlights the complications which can arise in patients with hypothyroidism undergoing primary ACDF. The study can serve as another educational tool for physicians to be cognizant of this endocrinopathy and its surgical impact. Furthermore, it can be used to educate hypothyroid patients on the potential complications of ACDF. Optimization of thyroid function preoperatively can minimize the potential complications of ACDF in hypothyroid patients. Future prospective studies should aim at stratifying patients based on thyroid-stimulating hormone (TSH) levels, T₃, and T₄ and comparing postoperative complications following various orthopedic procedures.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: Due to the retrospective nature of the study, i.e., via a HIPAA compliant database without patient identifiers—no Institutional Review Board (IRB) approval was needed.

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Cite this article as: Vakharia RM, Vakharia AM, Ameri B, Niedzielak T, Donnally CJ 3rd, Malloy JP 4th. Hypothyroidism increases 90-day postoperative complications in patients undergoing primary single level anterior cervical disectomy and fusion: a matched control analysis. *J Spine Surg* 2018;4(2):274-280. doi: 10.21037/jss.2018.05.26