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Procedural complications associated with invasive diagnostic procedures after lung cancer screening with low-dose computed tomography

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Abstract

Introduction: Although the National Lung Screening Trial (NLST) has proven low-dose computed tomography (LDCT) is effective for lung cancer screening, little is known about complication rates from invasive diagnostic procedures (IDPs) after LDCT in real-world settings. In this study, we used the real-world data from a large clinical research network to estimate the complication rates associated with IDPs after LDCT.

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Declaration of Competing Interest

Dr. Huo is an employee of and has stockownership in Bristol Myers Squibb, and this work was initiated while he was on faculty at the University of Florida. All the other authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.lungcan.2021.12.020.

Methods: Using 2014–2021 electronic health records and claims data from the OneFlorida clinical research network, we identified case individuals who underwent an IDP (i.e., cytology or needle biopsy, bronchoscopy, thoracic surgery, and other surgery) within 12 months of their first LDCT. We matched each case with one control individual who underwent an LDCT but without any IDPs. We calculated 3-month incremental complication rates as the difference in the complication rate between the case and control groups by IDP and complication severity.

Results: Among 7,041 individuals who underwent an LDCT, 301 (4.3%) subsequently had an IDP within 12 months following the LDCT. The overall 3-month incremental complication rate was 16.6% (95% confidence interval [CI]: 9.9% – 23.1%), higher than that reported in the NLST (9.4%). The overall incremental complication rate was 5.6% (95% CI: 1.9% – 9.6%) for major, 8.6% (95% CI: 3.1% – 14.1%) for intermediate, and 13.2% (95% CI: 8.1% – 18.5%) for minor complications.

Conclusions: It is important to ensure adherence to clinical guidelines for nodule management and downstream work-up to minimize potential harms from screening.

Keywords

Real-world data; Electronic health records; Claims; Clinical research network

1. Introduction

Lung cancer is the leading cause of cancer death in the United States (US) [1]. Screening for lung cancer can help detect the tumor at an early stage, and hence reduce lung cancer mortality. Results from the US National Lung Screening Trial (NLST) showed that using low-dose computed tomography (LDCT) as a screening modality could effectively reduce lung cancer mortality [2]. Currently, numerous professional societies and medical associations have issued guidelines recommending annual lung cancer screening (LCS) using LDCT for individuals at high risk for lung cancer [3–5]. For example, the latest guideline from the US Preventive Services Task Force (USPSTF) recommends annual screening with LDCT for individuals aged 50 to 80 years who have more than a 20 pack-year history of smoking and currently smoke or have quit within the past 15 years [5].

One potential harm of LCS with LDCT is the high rate of false-positive results, which could lead to unnecessary invasive diagnostic procedures (IDPs) and IDP-related complications. The NLST reported a IDP rate of 4.2% and an IDP complication rate ranging from 8.5% to 9.8% [2,6]. As LDCT is being disseminated into clinical practice, one of the major concerns is the high rate of procedural complications. It is generally believed that complication rates of IDPs will be higher in real-world settings than in the NLST due to the highly controlled nature of clinical trials [7]. However, to our knowledge, only one study has examined IDP complication rates after LDCT-based LCS in the real-world setting [8]. In that study, Zhao et al analyzed MarketScan data and found that the overall IDP complication rate following LDCT was 16.6%, which was 77% higher than the NLST reported rate of 9.4%.

One limitation of Zhao et al is that the MarketScan data covered individuals with private health insurance only. In contrast, electronic health records (EHRs) contain clinical data for patients in both public and private health care systems, reflecting the actual clinical environment of medical practice [9]. In the current study, we aimed to estimate the IDP complication rates after LDCT using EHR data from a large clinical research network. We hypothesized that the complication rates in the EHR-based population would be comparable to those reported in Zhao et al. and higher than those reported in the NLST.

2. Materials and Methods

2.1. Data source

We obtained EHR and claims data between 2014 and 2021 from the OneFlorida clinical research network. As part of the National Patient-Centered Clinical Research Network (PCORnet), OneFlorida consists of 12 health care organizations including academic health centers, private health systems, and community clinics in Florida. The OneFlorida data contain linked, longitudinal patient-level EHR and claims data for over 15 million Floridians across all 67 counties of the state. This study was approved by the University of Florida Institutional Review Board.

2.2. Study population

Our study population included individuals who underwent an LDCT and had an IDP within 12 months of the LDCT, and a matching cohort of pateints who underwent an LDCT but did not have any IDPs within 12 months of the LDCT. In OneFlorida, we identified individuals who underwent the first LDCT procedure between October 1, 2014 and March 31, 2021 using Current Procedural Terminology (CPT) codes S8032 (effective from October 01, 2014 to September 30, 2016), G0297 (effective from February 5, 2015 to December 31, 2020) and 71,271 (effective from January 1, 2021 onwards). We excluded patients whose first encounter in OneFlorida was less than 12 months before the LDCT date because we used 12 months data before LDCT to calculate Charlson comorbidity index (CCI) scores. We further excluded patients whose last encounter was within 12 months following the LDCT date because we used 12 months data after LDCT to observe the IDPs.

We defined IDPs as specified in previous studies [8,10] and the NLST protocol [2]. The 23 IDPs were categorized into 4 mutually exclusive groups in the order of invasiveness: cytology or needle biopsy, bronchoscopy, thoracic surgery, and other surgery (see eTable 1 for ICD and CPT codes in the Supplement) [2]. Patients who received one IDP were assigned to one of the 4 IDP groups based on the IDP received. Patients who received more than one IDPs were assigned to the group corresponding to the IDP with the highest invasiveness. We matched each case with one control patient randomly selected from patients who underwent an LDCT without any IDPs based on age, sex, CCI, facility location, and year of LDCT. We used data from 12 months before the LDCT to calculate the CCI following the modified algorithm by Klabunde et al. [11]. We defined the index date as the date of the first IDP in the same severity group for cases, and as the date of the LDCT for controls.

We identified complications that occurred within 3 months of the index date and classified the complications into 3 severity groups: minor, intermediate and major. We reported the same 43 categories of complications as listed in the NLST report [2] as well as in previous studies [8,10] (see ICD and CPT codes in eTable 2 in the Supplement). In EHRs, many primary medical conditions and complications are recorded using the same diagnosis codes, so medical conditions were not considered complications if the same diagnosis code appeared within 30 days prior the IDP.

2.3. Data analysis

The complication rate was calculated as the total number of individuals with any complication in an IDP group divided by the total number of individuals in that group. The incremental complication rate was calculated as the difference in the complication rate between the case and control groups. We reported the incremental complication rates by IDP group and by complication severity. Data analyses were performed using python scripts version 3.8.

3. Results

We summarized the characteristics of cases and controls in Table 1. Of the 7,041 patients in OneFlorida who underwent an LDCT, 301 (4.3%) underwent at least one IDP within 12 months following LDCT. Among those who underwent any IDPs, 112 (37.2%) received a cytology test or biopsy, 111 (36.9%) received a bronchoscopy, 51 (16.9%) received thoracic surgery, and 27 (9.0%) received other procedures.

We summarized the incremental complication rates estimated from the present study, Zhao et al, and the NLST, both overall and by IDP type, in Fig. 1. We did not observe any differences in complication rates between cases and controls for the other surgery group, hence this group was removed from further analysis. The overall incremental complication rate for the IDPs was 16.6% (95% confidence interval [CI]: 9.9% – 23.1%), which is the same as that reported in Zhao et al (16.6%) but higher than that reported in the NLST (9.4%). The incremental complication rate by procedure was 16.1% (95% CI: 5.2% – 26.5%) for cytology or needle biopsy, 9.9% (95% CI: 5.1% – 17.0 %) for bronchoscopy, and 41.2% (95% CI: 23.1% – 55.7%) for thoracic surgery.

We reported the incremental complication rates by severity and IDP type in Fig. 2. The overall complication rate was 5.6% (95% CI: 1.9% – 9.6%) for major, 8.6% (95% CI: 3.1% – 14.1%) for intermediate, and 13.2% (95% CI: 8.1% – 18.5%) for minor complications.

4. Discussion

This study was the first to use EHR data from a large clinical research network to estimate the incremental complication rates of IDPs after LDCT. We found that the overall rate of complications from IDPs was 16.6%, which is the same as that reported in claims data and 77% greater than that reported in the NLST. Our estimated complication rates by IDP type were also significantly higher than those reported in the NLST. Our results appear to confirm

the hypothesis that the complication rates associated with IDPs among an LCS population are significantly higher in real-world settings.

Similar to Zhao et al, most complications identified in our study were of minor or intermediate severity. However, the rates of major complications were slightly higher in our study than in Zhao et al. One plausible explanation is that the OneFlorida population is more socioeconomically diverse than the MarketScan population. While the Marketscan data largely cover individuals and their spouse/dependents with employer-sponsored private health insurance, [12] the OneFlorida data cover individuals with either public (e.g. Florida Medicaid) or private health insurance. [13] Research has shown that Medicaid enrollees on average have poorer health than individuals with other types of health insurance. [14]

Further, in one UK study, Balata H et al reported baseline screening performance from 5 UK-based LCS programs. The authors found that, among those with confirmed lung cancer diagnosis, the surgical resection rate was 66%, and 2% had a major complication from invasive investigation or treatment. Of whose without lung caner, the rate of invasive investigations (excluding surgery) was 0.6% and there were no reports of major complications. These complication rates are much lower than those reported in our study and Zhao et al. A plausible explanation is that adherence to guidelines for nodule management and downstream work-up is worse in the real-world settings than in the screening trials. [15] One limitation of our study is that information on smoking pack-years and smoking history was unavailable in the OneFlorida structured EHR data. We were unable to determine whether patients who underwent an LDCT were eligible for LCS based on screening guidelines. Another limitation is that information on LDCT outcomes was only available in clinical notes and unavailable in the structured EHR data that we used for analysis. We were unable to determine whether a patient was positive or negative for lung cancer. Further, our data source, as well as Zhao et al, lacks data on deprivation, an important factor that could potentially explain the differences in complication rates between our study and Zhao et al. Lastly, although we conservatively estimated complication rates as incremental rates by including a control cohort, it is likely that complication rates reported in our study still captured medical issues unrelated to the IDPs.

5. Conclusions

Our study showed that complication rates associated with IDPs among an LCS population were significantly higher in the real-world setting. It is important to ensure adherence to clinical guidelines for nodule management and downstream work-up to minimize potential harms from screening.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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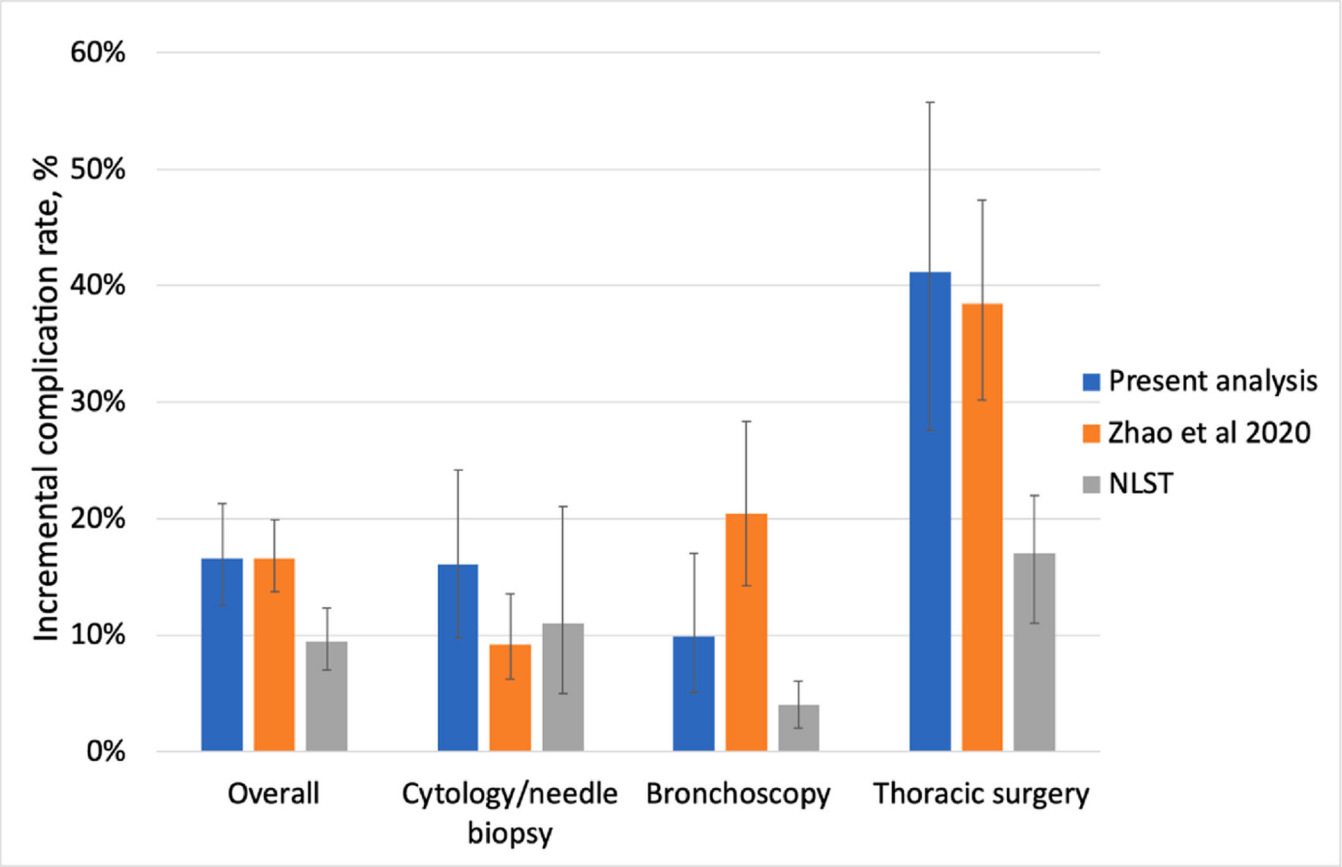

Fig. 1.

Comparison of overall and by type of invasive procedure complication rates estimated from the present analysis, Zhao et al's analysis, and the National Lung Cancer Screening Trial (NLST). The whiskers indicate 95% confidence intervals.

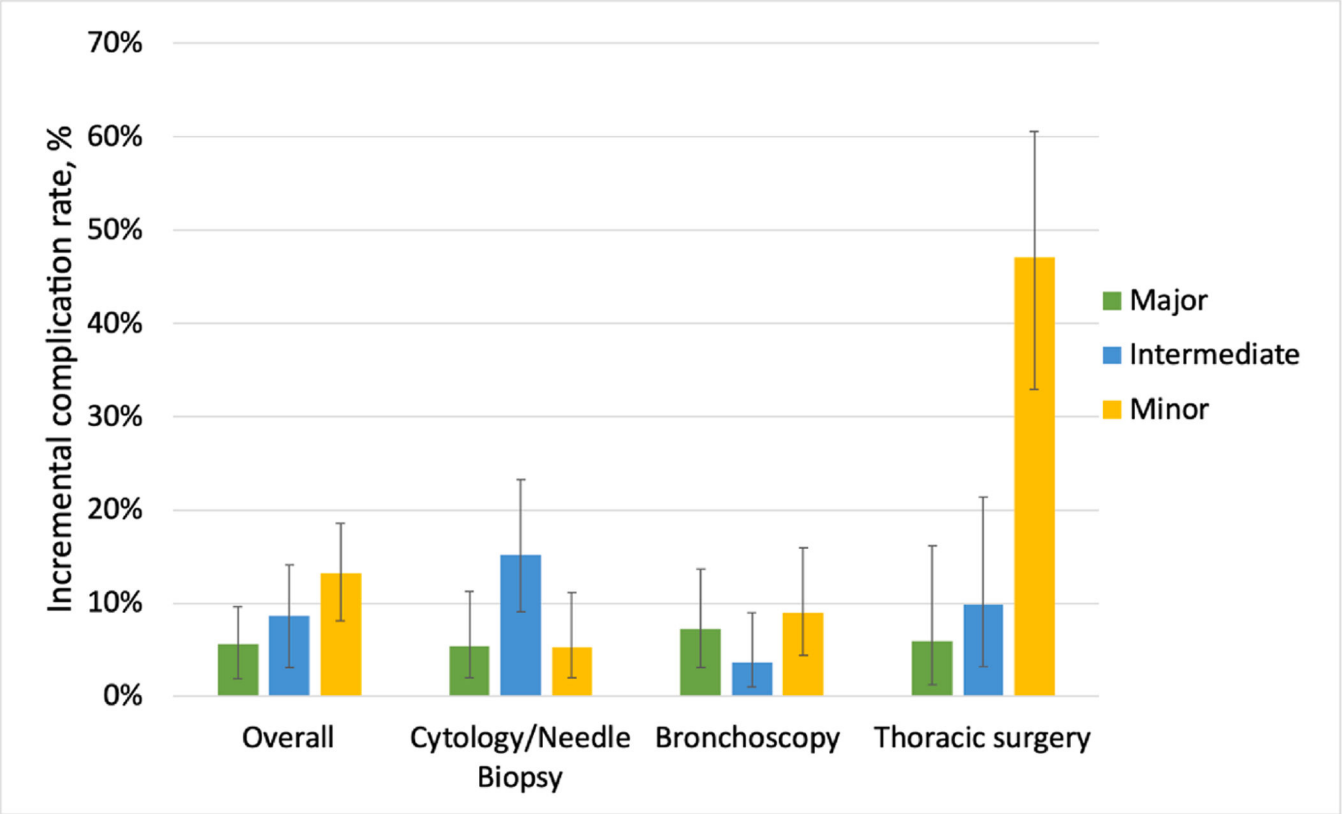

Fig. 2.

Incremental complication rate by severity and type of invasive diagnostic procedure. The whiskers indicate 95% confidence intervals.

Table 1

Characteristics of our case and control cohorts.

	Cases	Controls				
	Total	**Total**	**Cytology or Needle biopsy**	**Bronchoscopy**	**Thoracic surgery**	**Other surgery**
	N = 301 (100%)	**N = 301 (100%)**	**N = 112 (36.9%)**	**N = 111 (37.2%)**	**N = 51 (16.9%)**	**N = 37 (9.0%)**
Age (Mean ± SD)	64.0 ± 6.2	64.0 ± 6.5	64.1 ± 6.7	63.4 ± 6.1	64.9 ± 6.7	64.8 ± 6.8
Gender						
Female	152 (50.5%)	152 (50.5%)	59 (52.7%)	45 (40.5%)	28 (54.9%)	20 (74.1%)
Male	149 (49.5%)	149 (49.5%)	53 (47.3%)	66 (59.5%)	23 (45.1%)	7 (25.9%)
Race/ethnicity [a]						
NHW	181 (60.1%)	207 (68.8%)	71 (63.4%)	81 (72.9%)	37 (72.5%)	18 (66.7%)
NHB	56 (18.6%)	42 (14.0%)	14 (19.6%)	17 (15.3%)	5 (9.8%)	6 (22.2%)
NHO	6 (2.0%)	5 (1.7%)	1 (0.9%)	1 (0.9%)	3 (5.9%)	0 (0)
Hispanic	12 (4.0%)	12 (4.0%)	4 (3.6%)	4 (3.6%)	2 (3.9%)	2 (7.4%)
Unknown	46 (15.1%)	40 (11.5%)	22 (12.5%)	8 (7.2%)	4 (7.8%)	1 (3.7%)
CCI score [b]						
0	95 (31.6%)	95 (31.6%)	39 (34.8%)	25 (22.5%)	20 (39.2%)	11 (40.7%)
1	97 (32.2%)	97 (32.2%)	35 (33.9%)	39 (35.1%)	15 (31.3%)	8 (29.6%)
2+	109 (36.2%)	109 (36.2%)	38 (31.2%)	47 (42.3%)	16 (29.4%)	8 (29.6%)

[a] NHW: Non-Hispanic White; NHB: Non-Hispanic Black; NHO: Non-Hispanic Other.

[b] Charlson comorbidity index scores were grouped as 0 for no comorbidity, 1 for mild, and 2 or higher for moderate to severe.