Strategic Initiatives for Veterans with Lung Cancer

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Background: Lung cancer is a leading cause of cancer-related mortality among veterans—as well as the US population—despite veterans' access to advanced medical technologies within the Veterans Health Administration (VHA). To improve outcomes, the VHA launched 3 lung cancer treatment initiatives in 2016 and 2017.

Observations: This article summarizes the VHA lung cancer initiatives and discusses future programs aimed to improve care for veterans. The US Department of Veterans Affairs (VA) Partnership to Increase Access to Lung Screening aims to reduce lung cancer mortality among veterans at risk by increasing access to low-dose computed tomography lung screening scans. The VALOR study is a randomized phase 3 clinical trial that evaluates optimal treatment for participants with operable early stage non-small cell lung cancer (NSCLC). This trial plans to enroll veterans with stage I NSCLC who will be randomly assigned to treatment with either surgical lobectomy or stereotactic body radiation therapy. Researchers will follow each participant for at least 5 years to evaluate which treatment, if either, results in a higher overall survival rate. The VA Radiation Oncology Quality Surveillance program compares treatment of veterans with lung cancer in the VHA with quality standards recommended by nationally recognized experts in lung cancer care.

Conclusions: The VHA continues to prioritize resources to improve and assure optimal outcomes for veterans with lung cancer. Future efforts include creating a national network of lung cancer centers of excellence to ensure that treatment decisions for veterans with lung cancer are based on all available molecular information, including data on pharmacogenomic profiles.

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The Veterans Health Administration (VHA) facilitates care for > 7,700 veterans with newly diagnosed lung cancer each year.[1] This includes comprehensive clinical evaluations and management that are facilitated through interdisciplinary networks of pulmonologists, radiologists, thoracic surgeons, radiation oncologists, and medical oncologists. Veterans with lung cancer have access to advanced medical technologies at US Department of Veterans Affairs (VA) medical centers (VAMCs), including the latest US Food and Drug Administration (FDA)-approved targeted radiation delivery systems and novel immunotherapies, as well as precision oncology-driven clinical trials.[2]

Despite access to high-quality care, lung cancer remains the leading cause of cancer-related mortality among VHA enrollees as well as the US population.[3] About 15 veterans die of lung cancer each day; most are diagnosed with advanced stage III or stage IV disease. To address this issue, VHA launched 3 new initiatives between 2016 and 2017 to improve outcomes for veterans impacted by lung cancer. The VA Partnership to increase Access to Lung Screening (VA-PALS) is a clinical implementation project to increase access to early detection lung screening scans at 10 VAMCs. The Veterans Affairs Lung cancer surgery Or stereotactic Radiotherapy (VALOR) is a phase 3 randomized trial that investigates the role of stereotactic body radiation therapy (SBRT) as a potential alternative to surgery for veterans with operable stage I non-small cell lung cancer (NSCLC). The VA Radiation Oncology Quality Surveillance program (VA-ROQS) established national expert-derived benchmarks for the quality assurance of lung cancer therapy.

VA-PALS

The central mission of VA-PALS is to reduce lung cancer mortality among veterans at risk by increasing access to low-dose computed tomography (LDCT) lung screening scans.[4,5] The program was developed as a public-private partnership to introduce structured lung cancer screening programs at 10 VAMCs to safely manage large cohorts of veterans undergoing annual screening scans. The VA-PALS project brings together pulmonologists, radiologists, thoracic surgeons, radiation oncologists, medical oncologists, and computer scientists who have experience developing open-source electronic health record systems for VHA networks. The project was launched in 2017 after an earlier clinical demonstration project identified substantial variability and challenges with efforts to implement new lung cancer screening programs in the VA.[6]

Each of the 10 VA-PALS-designated lung cancer screening programs (Atlanta, Georgia; Phoenix, Arizona; Indianapolis, Indiana; Chicago, Illinois; Nashville, Tennessee; Philadelphia, Pennsylvania; St. Louis, Missouri; Denver, Colorado; Milwaukee, Wisconsin; and Cleveland, Ohio) assumes a major responsibility for ordering and evaluating the results of LDCT

scans to ensure appropriate follow-up care of veterans with abnormal radiographic findings. Lung cancer screening programs are supported with a full-time navigator (nurse practitioner or physician assistant) who has received training from the VA-PALS project team with direct supervision by a local site director who is a pulmonologist, thoracic surgeon, or medical oncologist. Lung cancer screening programs establish a centralized approach that aims to reduce the burden on primary care providers for remembering to order annual baseline and repeat LDCT scans. The lung screening programs also manage radiographic findings that usually are benign to facilitate appropriate decisions to minimize the risk of unnecessary tests and procedures. Program implementation across VA-PALS sites includes a strong connection among participants through meetings, newsletters, and attendance at conferences to create a collaborative learning network, which has been shown to improve dissemination of best practices across the VHA.[7,8]

The International Early Lung Cancer Action Program (I-ELCAP), which pioneered the use of LDCT to reduce lung cancer mortality, is a leading partner for VA-PALS.[9] This group has > 25 years of experience overcoming many of the obstacles and challenges that new lung cancer screening programs face.[10] The I-ELCAP has successfully implemented new lung cancer screening programs at > 70 health care institutions worldwide. Their implementation processes provide continuous oversight for each center. As a result, the I-ELCAP team has developed a large and detailed lung cancer screening registry with > 75,000 patients enrolled globally, comprising a vast database of clinical data that has produced > 270 scientific publications focusing on improving the quality and safety of lung cancer screening.[11,12]

These reports have helped guide evidence-based recommendations for lung cancer screening in several countries and include standardized processes for patient counseling and smoking cessation, data acquisition and interpretation of LDCT images, and clinical management of abnormal findings to facilitate timely transition from diagnosis to treatment.[13-15] The I-ELCAP management system detects 10% abnormal findings in the baseline screening study, which declines to 6% in subsequent years.[12] The scientific findings from this approach have provided additional insights into technical CT scanning errors that can affect tumor nodule measurements.[16] The vast amount of clinical data and expertise have helped explore genetic markers.[17] The I-ELCAP has facilitated cost-effectiveness investigations to determine the value of screening, and their research portfolio includes investigations into the longer-term outcomes after primary treatment for patients with screen-detected lung cancers.[18,19]

I-ELCAP gifted its comprehensive clinical software management system that has been in use for the above contributions for use in the VHA through an open source agreement without licensing fees. The I-ELCAP software management system was rewritten in MUMPS, the software programming language that is used by the VA Computerized Patient Record System (CPRS). The newly adapted VA-PALS/I-ELCAP system underwent modifications with VHA clinicians' input, and was successfully installed at the Phoenix VA Health Care System in Arizona, which has assumed a leading role for the VA-PALS project.

The VA-PALS/I-ELCAP clinical management system currently is under review by the VA Office of Information and Technology for broad distribution across the VHA through the VA Enterprise Cloud. Once in use across the VHA, the VA-PALS/I-ELCAP clinical management system will offer a longitudinal central database that can support numerous quality improvement and quality assurance initiatives, as well as innovative research projects. Research opportunities include: (1) large-scale examination of LDCT images with artificial intelligence and machine learning techniques; (2) epidemiologic investigations of environmental and genetic risk factors to better understand the high percentage of veterans diagnosed with lung cancer who were never smokers or had quit many years ago; and (3) multisite clinical trials that explore early detection blood screening tests that are under development.

The VA-PALS project is sponsored by the VHA Office of Rural Health as an enterprise-wide initiative that focuses on reaching rural veterans at risk. The project received additional support through the VA Secretary's Center for Strategic Partnerships with a $5.8 million grant from the Bristol-Myers Squibb Foundation. The VistA (Veterans Health Information Systems

and Technology Architecture) Expertise Network is an additional key partner that helped adapt the VAPALS-ELCAP system for use on VHA networks.

VALOR TRIAL

The VA Cooperative Studies Program (CSP) #2005 VALOR study is a randomized phase 3 clinical trial that evaluates optimal treatment for participants with operable early-stage NSCLC.[20] The trial is sponsored by the CSP, which is responsible for and provides resources for the planning and conduct of large multicenter surgical and clinical trials in VHA.[21] The CSP #2005 VALOR study plans to enroll veterans with stage I NSCLC who will be treated with a surgical lobectomy or SBRT according to random assignment. An alternative surgical approach with a segmentectomy is acceptable, although patients in poor health who are only qualify for a wedge resection will not be enrolled. The CSP will follow each participant for at least 5 years to evaluate which treatment, if either, results in a higher overall survival rate. Secondary outcome measures are quality of life, pulmonary function, health state utilities, patterns of failure, and causes of death.

Although the study design of the VALOR trial is relatively straightforward, recruitment of participants to similar randomized trials of surgery vs SBRT for operable stage I NSCLC outside the VA has historically been very difficult. Three earlier phase 3 trials in the Netherlands and US closed prematurely after collectively enrolling only 4% of planned participants. Although a pooled analysis of 2 of these trials demonstrated a statistically significant difference of 95% vs 79% survival in favor of SBRT at a median follow-up of 40 months, the analysis was underpowered because only 58 of the planned 1,380 participants were enrolled.[22,23]

The CSP #2005 VALOR study team was keenly aware of these past challenges and addressed many of the obstacles to enrollment by optimizing eligibility criteria and follow-up requirements. Enrollment sites were carefully selected after confirming equipoise between the 2 treatments, and study coordinators at each enrollment site were empowered to provide a leading role with recruitment. Multiple communication channels were established for constant contact to disseminate new best practices for recruitment as they were identified. Furthermore, a veteran-centric educational recruitment video, approved by the VA Central Institutional Review Board, was designed to help study participants better understand the purpose of participating in a clinical trial (www.vacsp.research.va.gov/CSP_2005/CSP_2005.asp).

After the first year of recruitment, researchers identified individual clinician and patient preferences as the predominant difficulty with recruitment, which was not easy to address. The CSP #2005 VALOR study team opted to partner directly with the Qualitative Research Integrated within Trials (QuinteT) team in the United Kingdom to adopt its methods to successfully support randomized clinical trials with serious recruitment challenges.[24,25] By working directly with the QuinteT director, the CSP #2005 VALOR team made a major revision to the informed consent forms by shifting focus away from disclosing potential harms of research to an informative document that emphasized the purpose of the study. The work with QuinteT also led to the creation of balanced narratives for study teams to use and for potential participants to read. These provide a more consistent message that describes why the study is important and why clinicians are no longer certain that surgery is the optimal treatment for all patients with operable stage I NSCLC.

The VALOR clinical trial, opened in 2017, remains open at only 9 VAMCs. As of early 2020, it has enrolled more participants than all previous phase 3 trials combined. Once completed, the results from CSP #2005 VALOR study will help clinicians and veterans with operable stage I NSCLC better understand the tradeoffs of surgery vs SBRT as an initial treatment option. Plans are under way to expand the scope of the trial and include investigations of pretreatment radiomic signatures and genetic markers from biopsy tissue and blood samples, to better predict when surgery or SBRT might be the best treatment option for an individual patient.

VA-ROQS

The VA-ROQS was created in 2016 to compare treatment of veterans with lung cancer in the VHA with quality standards recommended by nationally recognized experts in lung cancer care. Partnering with Washington University in St. Louis, Missouri and the American Society for Radiation Oncology, the VHA established

a blue-ribbon panel of experts to review clinical trial data and medical literature to provide evidence-based quality metrics for lung cancer therapy. As a result, 26 metrics applicable to each patient's case were developed, published, and used to assess lung cancer care in each VHA radiation oncology practice.[26]

By 2019, the resulting data led to a report on 773 lung cancer cases accumulated from all VHA radiation oncology practices. Performance data for each quality metric were compared for each practice within the VHA, which found that VHA practices met > 80% of all 1,278 metrics scored. Quality metrics included those documented within each patient health record and the specific radiation delivery parameters that reflected each health care provider's treatment. After team investigators visited each center and recorded treatment data, VA-ROQS is now maturing to permit continuous, electronic monitoring of all lung cancer treatment delivered within VHA. As each veteran's case is planned, the quality of the therapy is monitored, assessed, and reported to the treating physician. Each VHA radiation oncologist will receive up-to-date evaluation of each case compared with these evidence-based quality standards. The quality standards are reviewed by the blue-ribbon panel to keep the process current and valid.

FUTURE OF VHA LUNG CANCER CARE

As VHA continues to prioritize resources to improve and assure optimal outcomes for veterans with lung cancer, it is now looking to create a national network of Lung Cancer Centers of Excellence (LCCE) as described in the VA Budget Submission for fiscal year 2021. If Congress approves funding, LCCEs will soon be developed within the VA regional Veteran Integrated Service Network system to ensure that treatment decisions for veterans with lung cancer are based on all available molecular information, including data on pharmacogenomic profiles. Such a network would create more opportunities to leverage public–private partnerships similar to the VA-PALS project. Creation of LCCEs would help the VA leverage an even stronger learning network to support more research so that all veterans who are impacted by lung cancer have access to personalized care that optimizes safety, quality of life, and overall survival. The lessons learned, networks developed, and partnerships established through VA-PALS, VALOR, and VA-ROQS are instrumental toward achieving these goals.

Author disclosures

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Disclaimer

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References

1. Zullig LL, Jackson GL, Dorn RA, et al. Cancer incidence among patients of the U.S. Veterans Affairs Health Care System. *Mil Med.* 2012;177(6):693-701. doi:10.7205/milmed-d-11-00434
2. Dawson GA, Cheuk AV, Lutz S, et al. The availability of advanced radiation oncology technology within the Veterans Health Administration radiation oncology centers. *Fed Pract.* 2016;33(suppl 4):18S-22S.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin.* 2019;69(1):7-34. doi:10.3322/caac.21551
4. National Lung Screening Trial Research Team. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol.* 2019;14(10):1732-1742. doi:10.1016/j.jtho.2019.05.044
5. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT Screening in a randomized trial. *N Engl J Med.* 2020;382(6):503-513. doi:10.1056/NEJMoa1911793
6. Kinsinger LS, Anderson C, Kim J, et al. Implementation of lung cancer screening in the Veterans Health Administration. *JAMA Intern Med.* 2017;177(3):399-406. doi:10.1001/jamainternmed.2016.9022
7. Clancy C. Creating World-class care and service for our nation's finest: how Veterans Health Administration Diffusion of Excellence Initiative Is innovating and transforming Veterans Affairs health care. *Perm J.* 2019;23:18.301. doi:10.7812/TPP/18.301
8. Elnahal SM, Clancy CM, Shulkin DJ. A framework for disseminating clinical best practices in the VA health system. *JAMA.* 2017;317(3):255-256. doi:10.1001/jama.2016.18764
9. Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet.* 1999;354(9173):99-105. doi:10.1016/S0140-6736(99)06093-6
10. Mulshine JL, Henschke CI. Lung cancer screening: achieving more by intervening less. *Lancet Oncol*. 2014;15(12):1284-1285. doi:10.1016/S1470-2045(14)70418-8
11. Henschke CI, Li K, Yip R, Salvatore M, Yankelevitz DF. The importance of the regimen of screening in maximizing the benefit and minimizing the harms. *Ann Transl Med.* 2016;4(8):153. doi:10.21037/atm.2016.04.06
12. Henschke CI, Yip R, Yankelevitz DF, Smith JP; International Early Lung Cancer Action Program Investigators*. Definition of a positive test result in computed tomography screening for lung cancer: a cohort study. *Ann Intern Med.* 2013;158(4):246-252. doi:10.7326/0003-4819-158-4-201302190-00004
13. Zeliadt SB, Heffner JL, Sayre G, et al. Attitudes and perceptions about smoking cessation in the context of lung cancer screening. *JAMA Intern Med*. 2015;175(9):1530-1537. doi:10.1001/jamainternmed.2015.3558
14. Henschke CI, Yankelevitz DF, Yip R, et al. Tumor volume measurement error using computed tomography imaging in a phase II clinical trial in lung cancer. *J Med Imaging (Bellingham).* 2016;3(3):035505. doi:10.1117/1.JMI.3.3.035505

15. Yip R, Henschke CI, Yankelevitz DF, Boffetta P, Smith JP; International Early Lung Cancer Investigators. The impact of the regimen of screening on lung cancer cure: a comparison of I-ELCAP and NLST. *Eur J Cancer Prev.* 2015;24(3):201-208. doi:10.1097/CEJ.0000000000000065
16. Armato SG 3rd, McLennan G, Bidaut L, et al. The Lung Image Database Consortium (LIDC) and Image Database Resource Initiative (IDRI): a completed reference database of lung nodules on CT scans. *Med Phys.* 2011;38(2):915-931. doi:10.1118/1.3528204
17. Gill RK, Vazquez MF, Kramer A, et al. The use of genetic markers to identify lung cancer in fine needle aspiration samples. *Clin Cancer Res.* 2008;14(22):7481-7487. doi:10.1158/1078-0432.CCR-07-5242
18. Pyenson BS, Henschke CI, Yankelevitz DF, Yip R, Dec E. Offering lung cancer screening to high-risk medicare beneficiaries saves lives and is cost-effective: an actuarial analysis. *Am Health Drug Benefits*. 2014;7(5):272-282.
19. Schwartz RM, Yip R, Olkin I, et al. Impact of surgery for stage IA non-small-cell lung cancer on patient quality of life. *J Community Support Oncol.* 2016;14(1):37-44. doi:10.12788/jcso.0205
20. Moghanaki D, Chang JY. Is surgery still the optimal treatment for stage I non-small cell lung cancer? *Transl Lung Cancer Res.* 2016;5(2):183-189. doi:10.21037/tlcr.2016.04.05
21. Bakaeen FG, Reda DJ, Gelijns AC, et al. Department of Veterans Affairs Cooperative Studies Program network of dedicated enrollment sites: implications for surgical trials [published correction appears in *JAMA Surg*. 2014 Sep;149(9):961]. *JAMA Surg.* 2014;149(6):507-513. doi:10.1001/jamasurg.2013.4150
22. Chang JY, Senan S, Paul MA, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials [published correction appears in *Lancet Oncol*. 2015 Sep;16(9):e427]. *Lancet Oncol.* 2015;16(6):630-637. doi:10.1016/S1470-2045(15)70168-3
23. Samson P, Keogan K, Crabtree T, et al. Interpreting survival data from clinical trials of surgery versus stereotactic body radiation therapy in operable Stage I non-small cell lung cancer patients. *Lung Cancer.* 2017;103:6-10. doi:10.1016/j.lungcan.2016.11.005
24. Donovan JL, Rooshenas L, Jepson M, et al. Optimising recruitment and informed consent in randomised controlled trials: the development and implementation of the Quintet Recruitment Intervention (QRI). *Trials.* 2016;17(1):283. Published 2016 Jun 8. doi:10.1186/s13063-016-1391-4
25. Rooshenas L, Scott LJ, Blazeby JM, et al. The QuinteT Recruitment Intervention supported five randomized trials to recruit to target: a mixed-methods evaluation. *J Clin Epidemiol.* 2019;106:108-120. doi:10.1016/j.jclinepi.2018.10.004
26. Hagan M, Kapoor R, Michalski J, et al. VA-Radiation Oncology Quality Surveillance Program. *Int J Radiat Oncol Biol Phys.* 2020;106(3):639-647. doi:10.1016/j.ijrobp.2019.08.064