EDITORIAL

Korean J Intern Med 2025;40:165-167
https://doi.org/10.3904/kjim.2025.029

Treatment strategies for octogenarians with esophageal cancer: changing age-based treatment paradigms

Jaewon Hyung

Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

See Article on Page 230-242

The therapeutic landscape of esophageal cancer has undergone a remarkable evolution over recent decades, with multimodal approaches, including neoadjuvant chemoradiotherapy (CRT) followed by surgery or definitive CRT, becoming standard options for locally advanced disease [1]. Concurrent with these therapeutic advances, we are witnessing a significant demographic shift in the patient population, with an increasing proportion of older adult patients diagnosed with esophageal cancer [2]. This demographic transition poses unique challenges in treatment decision-making, particularly for patients aged 80 years and older, where the delicate balance between treatment efficacy and tolerability becomes increasingly complex and crucial for optimal outcomes. This shift reflects improved life expectancy in the general population and changes in risk factor profiles. Therefore, understanding treatment outcomes in this growing older adult population has become increasingly critical for clinical decision-making and healthcare resource allocation.

Ryu et al. [3] provided valuable insights into the treatment outcomes of octogenarians with esophageal cancer, challenging a few of our preconceptions regarding age-based treatment decisions. The investigators discussed a comprehensive comparison of treatment outcomes between patients aged ≥ 80 years and their younger counterparts while examining the impact of different treatment modalities within the older adult cohort. This multifaceted analysis allowed for a nuanced understanding of age-related differences and the impact of treatment selection on the older adult population.

Several key findings of this study warrant careful consideration. As expected, octogenarians demonstrated higher rates of comorbidities and poorer performance statuses than younger patients. This resulted in a natural selection bias toward nonsurgical approaches, particularly CRT or radiotherapy (RT) alone. However, the most striking observation was that while treatment outcomes showed a trend toward inferior results in the older adult cohort compared to the younger population, the differences were modest, particularly in the CRT/RT group. Furthermore, compared to untreated octogenarians, those who received treatment with curative intent demonstrated significantly superior survival outcomes, albeit with the important caveat that treated patients were generally more fit with fewer comorbidities.

The implications of these findings for surgical management warrant particular attention. While the current study suggests comparable outcomes with surgical intervention in octogenarians (n = 7), this must be interpreted within the broader context of existing literature and real-world clinical experience. Previous meta-analyses and large-scale retrospective studies from the United States have demonstrated increased postoperative complications in older adult patients, with significant implications for both short-term recovery and long-term quality of life [4,5]. Moreover, the comparable survival outcomes between surgery and CRT/RT among the older adult population in this study suggest that many octogenarians prefer nonsurgical approaches, particularly given their potential impact on functional status and independence.

The tolerability of concurrent CRT is another crucial consideration that requires careful examination. While the outcomes were generally comparable to those of younger patients, previous studies have highlighted the increased risk of

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

radiation pneumonitis in older adult patients [6,7]. Certain evidence suggests that paclitaxel-containing regimens may be associated with a higher risk of pneumonitis, warranting careful evaluation of chemotherapy choices and potentially suggesting the need for alternative regimens in older adult patients [8]. In addition, the risk of cytopenia and infection with reduced functional reservoirs in this population necessitates careful consideration of chemotherapy selection and dosing strategies.

The question of RT alone versus concurrent CRT is another decision-making point in older adult patient care. While a few clinicians might be tempted to omit chemotherapy in older adult patients to reduce cytotoxic chemotherapy-related toxicity, data from the Japanese national registry have demonstrated inferior survival with RT alone compared to CRT, even in patients aged ≥ 80 years [9]. This finding suggests that carefully selected older adult patients may benefit from combined-modality therapy, highlighting the importance of appropriate patient selection rather than age-based treatment decisions.

Modern older adult patient assessment approaches have evolved significantly, moving beyond the traditional chronological age and performance status measures. The emerging field of geriatric oncology has introduced sophisticated evaluation tools to better predict treatment tolerance and outcomes. The comprehensive geriatric assessment encompasses multiple domains, including functional status, cognitive function, nutritional status, social support, and detailed comorbidity evaluation [10]. The Clinical Frailty Scale provides a standardized approach for assessing physiological reserves. When used in collaboration with geriatric medicine specialists, these tools may provide a more nuanced and reliable means of determining treatment appropriateness than traditional metrics alone.

Therefore, treatment modification strategies should be considered for older adult patients. Dose reduction, altered fractionation schedules, and careful selection of chemotherapy regimens may play a role in optimizing outcomes for this population. The potential role of newer targeted therapies and immunotherapy in older adult patients with appropriate molecular profiles should be considered in the future, as these treatments may offer alternative options with different toxicity profiles. Quality of life considerations are particularly important in older adult patients, where treatment decisions must balance potential survival benefits with functional independence and overall well-being. Future research should incorporate quality of life metrics and patient-reported outcomes as primary endpoints, particularly when comparing different treatment modalities in older adult populations. These findings suggest a paradigm shift from age-based treatment decisions toward more individualized approaches based on functional status, comorbidity burden, and formal frailty assessments. This allows the delivery of meaningful cancer therapy to appropriately select older adult patients while avoiding excessive treatment-related morbidity in more vulnerable individuals.

The development of older adult-specific clinical trials is another crucial requirement in this field. Traditional clinical trials often exclude or underrepresent older patients, leading to a paucity of high-quality evidence. Dedicated trials focusing on older adult patients with appropriate endpoints and toxicity assessments could provide valuable guidance for clinical decision-making. Recently, a phase 1 trial of definitive concurrent chemoradiation with paclitaxel in older adult patients with esophageal squamous cell carcinoma was reported to have an acceptable safety profile [11].

In conclusion, this study provides encouraging evidence that appropriately selected octogenarians can achieve meaningful benefits from curative-intent treatment of esophageal cancer. The challenge of moving forward lies in optimizing patient selection and treatment modifications to maximize benefits while minimizing toxicity in this vulnerable population. Future research should focus on developing better assessment tools and treatment strategies tailored to older patients, ultimately leading to more personalized and effective care for this patient population.

REFERENCES

1. Obermannová R, Alsina M, Cervantes A, et al. Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 2022;33:992-1004.
2. Liu CQ, Ma YL, Qin Q, et al. Epidemiology of esophageal cancer in 2020 and projections to 2030 and 2040. Thorac Cancer 2023;14:3-11.
3. Ryu DG, Choi CW, Kim SJ, Park SB, Jang JO, Son BS. Clinical outcomes of esophageal squamous cell carcinoma in patients aged over 80 years. Korean J Intern Med 2025;40:230-242.
4. Tapias LF, Muniappan A, Wright CD, et al. Short and long-term outcomes after esophagectomy for cancer in elderly patients. Ann Thorac Surg 2013;95:1741-1748.

https://doi.org/10.3904/kjim.2025.029

5. Han Y, Liu S, Guo W, Zhang Y, Li H. Clinical outcomes of oesophagectomy in elderly versus relatively younger patients: a meta-analysis. Interact Cardiovasc Thorac Surg 2019;29:897-905.
6. Anderson SE, Minsky BD, Bains M, Hummer A, Kelsen D, Ilson DH. Combined modality chemoradiation in elderly oesophageal cancer patients. Br J Cancer 2007;96:1823-1827.
7. Xu C, Xi M, Moreno A, Shiraishi Y, et al. Definitive chemoradiation therapy for esophageal cancer in the elderly: clinical outcomes for patients exceeding 80 years old. Int J Radiat Oncol Biol Phys 2017;98:811-819.
8. Chen Y, Ye J, Zhu Z, et al. Comparing paclitaxel plus fluorouracil versus cisplatin plus fluorouracil in chemoradiotherapy for locally advanced esophageal squamous cell cancer: a randomized, multicenter, phase III clinical trial. J Clin Oncol 2019;37:1695-1703.
9. Jingu K, Numasaki H, Toh Y, et al. Chemoradiotherapy and radiotherapy alone in patients with esophageal cancer aged 80 years or older based on the Comprehensive Registry of Esophageal Cancer in Japan. Esophagus 2020;17:223-229.
10. Lee H, Lee E, Jang IY. Frailty and comprehensive geriatric assessment. J Korean Med Sci 2020;35:e16.
11. Hirata K, Yoshida K, Katada C, et al. Definitive chemoradiotherapy with paclitaxel for locally advanced esophageal squamous cell carcinoma in older patients (PARADISE-1): a phase I trial. BMC Cancer 2024;24:873.

Received : January 24, 2025
Accepted : February 7, 2025

Correspondence to
Jaewon Hyung, M.D.
Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: +82-2-3010-1464, Fax: +82-2-3010-6961
E-mail: jhyung@amc.seoul.kr
https://orcid.org/0000-0002-0680-4486

Conflicts of interest
The author discloses no conflicts.

Funding
None