View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Jagiellonian Univeristy Repository

Editorial

Composite metrics in response assessment—new hope in oesophageal cancer?

Janusz Włodarczyk, Jarosław Kużdżał

Department of Thoracic Surgery, Jagiellonian University Collegium Medicum, John Paul II Hospital, Cracow, Poland

Correspondence to: Jarosław Kużdżał, MD, PhD, FETCS. Klinika Chirurgii Klatki Piersiowej, Uniwersytet Jagielloński Collegium Medicum, Szpital im. Jana Pawła II, ul. Prądnicka 80, 31-202 Kraków, Polska. Email: j.kuzdzal@mp.pl.

Provenance: This is an invited Editorial commissioned by Section Editor Dr. Hongcheng Zhu (Department of Radiation Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China).

Comment on: Findlay JM, Bradley KM, Wang LM, *et al*. Predicting Pathologic Response of Esophageal Cancer to Neoadjuvant Chemotherapy: The Implications of Metabolic Nodal Response for Personalized Therapy. J Nucl Med 2017;58:266-75.

Submitted Jul 25, 2017. Accepted for publication Jul 28, 2017.
doi: 10.21037/jtd.2017.08.28
View this article at: http://dx.doi.org/10.21037/jtd.2017.08.28

Oesophageal cancer is still associated with poor prognosis. The progress in systemic treatment, radiation therapy and surgery over the last decades has resulted in only moderate improvement of survival. Neoadjuvant chemoradiotherapy (CRT) has been shown to be associated with tumour response in 60–70% of patients (1), and with complete pathological response (CPR) in 25–30% of patients (2,3). Although it reportedly improves survival, there are several concerns about its routine use. Besides the treatment-related toxicity, the most important issue is lack of reliable predictive factors for pathological tumour and nodal response. In fact, in non-responders the neoadjuvant therapy is harmful, as it delays alternative, potentially effective treatment. Progression during the neoadjuvant therapy is not rare in this subset of patients.

Ideally, if we were able to predict response to particular therapies, we could select them individually for each patient. This goal is unlikely to be achieved in near future, due to the complexity of each individual clinical situation, including genetic and phenotypic variability of particular tumour clones and multiple patient-related factors. More realistic concept was designed and evaluated by the authors from Munich, showing for the first time feasibility of assessment of the metabolic response after first cycle of adjuvant therapy (4-6). Their milestone work paved the way for research programs, which, hopefully, will bring us closer to the individualised treatment of patients with oesophageal cancer.

Among these new approaches one very promising is development of more advanced composite metrics, combining volumetric measurements with basic and relative changes in metabolic activity. Recently, authors from the Oxford University published in the *Journal of Nuclear Medicine* results of the study, aimed at evaluation of several such metrics (7). The authors proposed assessment of:

(I) Metabolic nodal response (mNR);
(II) Metabolic tumour volume (MTV);
(III) Tumour glycolytic volume (TGV).

The rationale for using the metabolic response in lymph nodes rather than in the primary tumour is that most relapses after curative-intent treatment of oesophageal cancer are regional and distant metastases, caused by the highly aggressive clones of malignant cells. The authors provided evidence supporting the assumption that response of these cell lines to the neoadjuvant treatment is more important predictive factor than response in the primary tumour itself. On a molecular level, this can be explained by the expression on GLUT-1 receptors. As shown by Hiyoshi *et al.* and Patching *et al*., overexpression of GLUT-1 in the lymph node metastases correlates with risk of relapse and is negative prognostic factor (8,9).

The Oxford group determined the MTV using a fixed SUV threshold of ≥4. On the other hand, the TGV was calculated as the product of MTV and SUV. Using SUV_{mean}, the TGV_{mean} was calculated, whilst using the SUV_{max} the TGV_{max} was produced. All these metrics can be calculated as baseline values or, ideally, as a composite metric such as ΔMTV, ΔTGV_{max} and ΔTGV_{mean} (7). Combination of spatial data with metabolic response resulted in improved prediction.

© Journal of Thoracic Disease. All rights reserved.

The study by Findlay *et al.* has of course limitations, some of them discussed by the authors. These include the retrospective character of the study and data collection over a long period of time. Additionally, in 301 patients 11 different chemotherapy (CTH) regimens were used, and T stage was recorded using 7th edition of the TNM system, whilst, N stage—using 6th edition. Certainly, this heterogeneity could have an impact on the results. What even more important, the study considered patients who underwent neoadjuvant CTH only. However, current evidence shows that effectiveness of neoadjuvant CTH is significantly lower that of CRT. The authors cite papers showing minimal or no pathological response in 60% of patients after neoadjuvant CTH (10,11) *vs.* 30–40% of those who underwent neoadjuvant CRT (1). So, the results noted in patients who underwent only CTH may not be directly applied to the CRT cohort and therefore may not be relevant to most patients treated nowadays for oesophageal cancer.

Nevertheless, Findlay *et al.* indicate new philosophy in predictive and prognostic factors in patients treated for oesophageal cancer. The volumetric-metabolic measurements and analysis of mNR may provide new, useful way to individualised therapy. Despite all the limitations, the study of Findlay *et al.* may be the next milestone in research aimed at answering the fundamental question: which therapy is optimal for which patient? This approach warrants further investigation, optimally in prospective, multicentre trials, enabling enrolment of sufficiently large group of patients evaluated and treated in a uniform, protocol-based manner.

Will this turn to be a new hope for patients with oesophageal cancer? Let us hope it will.

Acknowledgements

None.

Footnote

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

References

1. Shapiro J, van Lanschot JJ, Hulshof MC, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol 2015;16:1090-8.
2. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074-84.
3. Donahue JM, Nichols FC, Li Z, et al. Complete pathologic response after neoadjuvant chemoradiotherapy for esophageal cancer is associated with enhanced survival. Ann Thorac Surg 2009;87:392-8; discussion 398-9.
4. Weber WA, Ott K, Becker K, et al. Prediction of response to preoperative chemotherapy in adenocarcinomas of the esophagogastric junction by metabolic imaging. J Clin Oncol 2001;19:3058-65.
5. Ott K, Weber WA, Lordick F, et al. Metabolic imaging predicts response, survival, and recurrence in adenocarcinomas of the esophagogastric junction. J Clin Oncol 2006;24:4692-8.
6. Lordick F, Ott K, Krause BJ, et al. PET to assess early metabolic response and to guide treatment of adenocarcinoma of the oesophagogastric junction: the MUNICON phase II trial. Lancet Oncol 2007;8:797-805.
7. Findlay JM, Bradley KM, Wang LM, et al. Predicting Pathologic Response of Esophageal Cancer to Neoadjuvant Chemotherapy: The Implications of Metabolic Nodal Response for Personalized Therapy. J Nucl Med 2017;58:266-75.
8. Hiyoshi Y, Watanabe M, Imamura Y, et al. The relationship between the glucose transporter type 1 expression and F-fluorodeoxyglucose uptake in esophageal squamous cell carcinoma. Oncology 2009;76:286-92.
9. Patching SG. Roles of facilitative glucose transporter GLUT1 in [18F] FDG positron emission tomography (PET) imaging of human diseases. J Diagn Imaging Ther 2015;2:30-102.
10. Urschel JD, Vasan H, Blewett CJ. A meta-analysis of randomized controlled trials that compared neoadjuvant chemotherapy and surgery to surgery alone for resectable esophageal cancer. Am J Surg 2002;183:274-9.
11. Campbell NP, Villaflor VM. Neoadjuvant treatment of esophageal cancer. World J Gastroenterol 2010;16:3793-803.

Cite this article as: Włodarczyk J, Kuźdżał J. Composite metrics in response assessment—new hope in oesophageal cancer? J Thorac Dis 2017;9(9):2786-2787. doi: 10.21037/jtd.2017.08.28

© Journal of Thoracic Disease. All rights reserved.